Concept richtlijnmodules Cervicaal Radiculair Syndroom

INITIATIEF
Nederlandse Vereniging voor Neurochirurgie

IN SAMENWERKING MET
Nederlandse Vereniging voor Neurologie
Nederlandse Vereniging voor Anesthesiologie
Nederlandse Orthopaedische Vereniging
Koninklijk Nederlands Genootschap voor Fysiotherapie
Nederlandse Vereniging van Rugpatiënten 'de Wervelkolom'

MET ONDERSTEUNING VAN
Kennisinstituut van de Federatie Medisch Specialisten

FINANCIERING
De richtlijnontwikkeling werd gefinancierd uit de Stichting Kwaliteitsgelden Medisch Specialisten (SKMS)

Colofon
CONCEPTRICHTLIJN
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Samenstelling van de werkgroep

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Startpagina

Waar gaat deze richtlijn over?

Deze richtlijn beschrijft de zorg voor volwassen patiënten met een Cervicaal Radiculair Syndroom (CRS) in de tweede- of derdelijnszorg. In de richtlijn komen de volgende onderwerpen aan de orde:

- Welke niet-operatieve behandelingsmogelijkheden er zijn, zoals een halskraag, fysiotherapie en injecties en wat de voor- en nadelen van deze opties zijn,
- Wanneer de beste tijd is om een operatie te overwegen als behandeling voor een CRS,
- Vanaf welke kant geopereerd kan worden en welke voor- en nadelen er zijn bij verschillende benaderingen en welke complicaties kunnen optreden,
- Welke patiënten geschikt zijn voor een nieuwe behandeling met een laser en wat de voor- en nadelen van deze behandeling zijn, en
- Welke nabehandeling er nodig is indien een operatie is verricht en wat de herstelperiode is.

Voor wie zijn deze richtlijnmodules bedoeld?

Deze richtlijn wordt geschreven voor alle zorgverleners die betrokken zijn bij de tweede- of derdelijnszorg voor patiënten met een CRS

Voor patiënten

Een Cervicaal Radiculair Syndroom (CRS) is een verzamelnaam voor klachten die ontstaan door beklemming van een zenuwwortel in de nek. Nekzenuwwortels komen uit het ruggenmerg via de wervelkolom naar buiten, richting de nek en de arm. De beklemming van een zenuwwortel kan onder andere ontstaan als een tussenwervelschijf, een soort kussentje tussen de ruggenwervels, uitstulpt. Dit wordt een cervicale hernia nuclei pulposi (cHNP), ook wel nekhernia, genoemd. Klachten die kunnen ontstaan zijn uitstralende pijn, een doof gevoel, tintelingen en krachtsverlies in nek, schouder en arm.

- Meer informatie over nekpijn is te vinden op Thuisarts: https://www.thuisarts.nl/hernianek
- Meer informatie over een nekhernia is te vinden op de website van de neurochirurgen: https://www.nvvn.org/patienteninfo/wervelkolom-en-ruggenmerg/nekhernia/

Hoe is de richtlijn tot stand gekomen?

Deze modules zijn in 2023 ontwikkeld op initiatief van de Nederlandse Vereniging voor Neurochirurgie (NVvN). De richtlijn is opgesteld door een multidisciplinaire commissie met vertegenwoordigers vanuit de neurochirurgen, neurologen, orthopedisch chirurgen, fysiotherapeuten/manueel therapeuten, anesthesiologen en patiëntenorganisatie De Wervelkolom. Vertegenwoordigers vanuit de Nederlandse Vereniging voor Radiologen (NVvR), Ergotherapie Nederland (EN) en de Vereniging van Oefentherapeuten Cesar en Mensendieck (VvOCM) hebben met de richtlijn meegelezen.

Status van de richtlijn

De richtlijn Cervicaal Radiculair Syndroom is opgenomen in het cluster ‘Wervelkolom gerelateerde aandoeningen’.

Verantwoording

Leeswijzer

Deze verantwoording zal op de Richtlijnendatabase (Richtlijnendatabase.nl) bij elk van de in deze herziende richtlijn opgenomen modules worden geplaatst.

Autorisatie en geldigheid

Autorisatiedatum:	[volgt]
Eerstvolgende beoordeling actualiteit	3 jaar
Geautoriseerd door:	[volgt]. Wordt gevraagd aan: Nederlandse Vereniging voor Neurochirurgie Nederlandse Vereniging voor Neurologie Nederlandse Orthopaedische Vereniging Nederlandse Vereniging voor Anesthesiologie Koninklijk Nederlands Genootschap voor Fysiotherapie Nederlandse Vereniging van Rugpatiënten ‘de Wervelkolom’
Belangrijkste wijzigingen t.o.v. vorige versie:	Er zijn twaalf nieuwe modules ontwikkeld.
Regiehouder(s):	Nederlandse Vereniging voor Neurochirurgie

Algemene gegevens

De ontwikkeling/herziening van deze richtlijnmodule werd ondersteund door het Kennisinstituut van de Federatie Medisch Specialisten (www.demedischspecialist.nl/kennisinstituut) en werd gefinancierd uit de Kwaliteitsgelden Medisch Specialisten (SKMS). De financier heeft geen enkele invloed gehad op de inhoud van de richtlijnmodule.

Samenstelling werkgroep

Voor het ontwikkelen van de richtlijnmodules is in 2022 een multidisciplinaire werkgroep ingesteld, bestaande uit vertegenwoordigers van alle relevante specialismen (zie hiervoor de ‘samenstelling van de werkgroep’) die betrokken zijn bij de zorg voor patiënten met een CRS.

Belangenverklaringen

De Code ter voorkoming van oneigenlijke beïnvloeding door belangenverstrengeling is gevolgd. Alle werkgroepleden hebben schriftelijk verklaard of zij in de laatste drie jaar directe financiële belangen (betrekking bij een commercieel bedrijf, persoonlijke financiële belangen, onderzoeksfinanciering) of indirecte belangen (persoonlijke relaties, reputatiemanagement) hebben gehad. Gedurende de ontwikkeling of herziening van een module worden wijzigingen in belangen aan de voorzitter doorgegeven. De belangenverklaring wordt opnieuw bevestigd tijdens de commentaarfase.
Een overzicht van de belangen van werkgroepleden en het oordeel over het omgaan met eventuele belangen vindt u in onderstaande tabel. De ondertekende belangenverklaringen zijn op te vragen bij het secretariaat van het Kennisinstituut van de Federatie Medisch Specialisten.

Naam lid werkgroep	*Hoofdfunctie*	*Nevenwerkzaamheden*	*Gemelde belangen*	**Ondernomen actie**
Carmen Vleggeert-Lankamp (voorzitter)	Neurochirurg, Leiden Universitair Medisch Centrum, Leiden	* Medisch Manager Neurochirurgie Spaarne Gasthuis, Hoofdorp/ Haarlem, gedetacheerd vanuit LUMC (betaald) * Secretaris Nederlandse Vereniging voor Neurochirurgie (onbetaald) * Secretary Board Cervical Spine Research Society Europe (onbetaald) * Lid commissie Veelbelovende Zorg ZonMw (onbetaald) * Lid Raad van Toezicht Revalidatiecentrum Rijndam (betaald)	*Niet anders dan onderzoeksleider in projecten naar etiologie van en uitkomsten in het CRS. *Co-promotor bij verscheidende trajecten waarbij de winst van een cervicale discusprothese als niet bestaand wordt beschreven. *Spreker op internationale congressen.	*Geen actie*
Akkie Rood	Orthopedisch chirurg, Sint Maartenskliniek, Nijmegen	Lid NOV, DSS, NvA	Geen	*Geen actie*
Erik Thoomes	Fysio-Manueel therapeut / praktijkeigenaar, Fysio-Experts, Hazerswoude	*Promovendus / wetenschappelijk onderzoeker Universiteit van Birmingham, UK,School of Sport, Exercise and Rehabilitation Sciences, College of Life and Environmental Sciences, Centre of Precision Rehabilitation for Spinal Pain (CPR Spine) (onbetaald)	Geen	*Geen actie*
Germine Mochel	Neuroloog DC klinieken (loondienst)	Geen	*Dienstverband bij DC klinieken, alwaar behandeling/diagnostiek patiënten CRS *Meer expertise op gebied van wervelkolom gerelateerde klachten	*Geen actie*
Jan van Zundert	*Anesthesioloog-pijnspecialist. *Hoogleraar pijn geneeskunde MaastrichtUMC+, Maastricht (0.6 fte). Deze functie omvat het regelen van de klinische praktijk, uitwerken en begeleiden van onderzoeksprojecten, begeleiden van PhD. studenten en onderwijs. *Afdelingshoofd multidisciplinair pijncentrum, Lanaken/Genk, België (0.4 fte). Organisatie van de dienst op klinisch vlak en stimuleren van het klinische onderzoek.	Geen	Geen financiering omtrent projecten die betrekking hebben op cervicaal radiculair lijden (17 jaar geleden op CRS onderwerk gepromoveerd, nadien geen PhD CRS-projecten begeleidt).	*Geen actie*
Leen Voogt	*Ervaringsdeskundige CRS. *Voorzitter Nederlandse Vereniging van Rugpatiënten 'de Wervelkolom' (NVVR)	Vrijwilligerswerk voor de patiëntenvereniging (onbetaald).	Geen	*Geen actie*
Maarten Liedorp	Neuroloog in loondienst (0.6 fte), ZBC Kliniek Lange Voorhout, Rijswijk	*lid oudergeleding MR IKC de Piramide (onbetaald) *bestuurslid Waterbuurtvereniging (onbetaald) *lid werkgroep Pijn NVN (onbetaald)	Geen	*Geen actie*

		*lid Dutch Spine Society (onbetaald) *lid Ned Ver Neurologie (onbetaald)		
Martine van Bilsen	Neurochirurg, Radboudumc, Nijmegen	Geen	Geen	*Geen actie*
Ruben Dammers	Neurochirurg, ErasmusMC, Rotterdam	Geen	Geen	*Geen actie*
Naam lid klankbordgroep	***Hoofdfunctie***	***Nevenwerkzaamheden***	***Gemelde belangen***	**Ondernomen actie**
Meimei Yau	Praktijkhouder Yau Oefentherapeut, Oefentherapeut Mensendieck, Den Haag.	Geen	Kennis opdoen, informatie/expertise uitwisselen met andere disciplines, oefentherapeut vertegenwoordigen. KP register	*Geen actie*
Vera Keil	Radioloog, AmsterdamUMC, Amsterdam. Afgevaardigde NVvR Neurosectie	Geen	Als radioloog heb ik natuurlijk een interesse aan een sterke rol van de beeldvorming.	*Geen actie*
Elien Nijland	Ergotherapeut/hand-ergotherapeut (totaal 27 uur) bij Treant zorggroep (Bethesda Hoogeveen) en Refaja ziekenhuis (Stadskanaal)	Voorzitter Adviesraad Hand-ergotherapie (onbetaald)		*Geen actie*

Inbreng patiëntenperspectief

Er werd aandacht besteed aan het patiëntenperspectief door een afgevaardigde van de Nederlandse Vereniging van Rugpatiënten ‘de Wervelkolom’ te betrekken in de werkgroep. De verkregen input is meegenomen bij het opstellen van de uitgangsvragen, de keuze voor de uitkomstmaten en bij het opstellen van de overwegingen (zie kop ‘Waarden en voorkeuren van patiënten’). De conceptrichtlijn is tevens voor commentaar voorgelegd aan de Nederlandse Vereniging van Rugpatiënten ‘de Wervelkolom’ en de eventueel aangeleverde commentaren zijn bekeken en verwerkt.

Kwalitatieve raming van mogelijke financiële gevolgen in het kader van de Wkkgz

Bij de richtlijn is conform de Wet kwaliteit, klachten en geschillen zorg (Wkkgz) een kwalitatieve raming uitgevoerd of de aanbevelingen mogelijk leiden tot substantiële financiële gevolgen. Bij het uitvoeren van deze beoordeling zijn richtlijnmodules op verschillende domeinen getoetst (zie het stroomschema op de Richtlijnendatabase). Uit de kwalitatieve raming blijkt dat er waarschijnlijk geen substantiële financiële gevolgen zijn, zie onderstaande tabel.

Module	Uitkomst raming	Toelichting
Diagnostiek – nieuw ontwikkelde module	Geen financiële gevolgen	Hoewel uit de toetsing volgt dat de aanbeveling(en) breed toepasbaar zijn (5.000-40.000 patiënten), volgt ook uit de toetsing dat het overgrote deel (±90%) van de zorgaanbieders en zorgverleners al aan de norm voldoet en het geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen financiële gevolgen verwacht.
Fysiotherapie (5 deelmodules)	Geen financiële gevolgen	Hoewel uit de toetsing volgt dat de aanbeveling(en) breed toepasbaar zijn (5.000-40.000 patiënten), volgt ook uit de toetsing dat het overgrote deel (±90%) van de zorgaanbieders en zorgverleners al aan de norm voldoet en het geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen financiële gevolgen verwacht.
Corticosteroïd-injecties	Geen financiële gevolgen	Hoewel uit de toetsing volgt dat de aanbeveling(en) breed toepasbaar zijn (5.000-40.000 patiënten), volgt ook uit de toetsing dat het overgrote deel (±90%) van de zorgaanbieders en zorgverleners al aan de norm voldoet en het geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen financiële gevolgen verwacht.
Pulsed Radiofrequency	Geen financiële gevolgen	Hoewel uit de toetsing volgt dat de aanbeveling(en) breed toepasbaar zijn (5.000-40.000 patiënten), volgt ook uit de toetsing dat het overgrote deel (±90%) van de zorgaanbieders en zorgverleners al aan de norm voldoet en het geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen financiële gevolgen verwacht.
Chirurgische decompressie van de zenuwwortel (chirurgisch versus conservatief)	Geen financiële gevolgen	Hoewel uit de toetsing volgt dat de aanbeveling(en) breed toepasbaar zijn (5.000-40.000 patiënten), volgt ook uit de toetsing dat het overgrote deel (±90%) van de zorgaanbieders en zorgverleners al aan de norm voldoet en het geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen financiële gevolgen verwacht.
Timing chirurgische behandeling	Geen financiële gevolgen	Hoewel uit de toetsing volgt dat de aanbeveling(en) breed toepasbaar zijn (5.000-40.000 patiënten), volgt ook uit de toetsing dat het overgrote deel (±90%) van de zorgaanbieders en zorgverleners al aan de norm voldoet en het geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen financiële gevolgen verwacht.
ACDF met plaat (plaat versus geen plaat)	Geen financiële gevolgen	Hoewel uit de toetsing volgt dat de aanbeveling(en) breed toepasbaar zijn (5.000-40.000 patiënten), volgt ook uit de toetsing dat het overgrote deel (±90%) van de zorgaanbieders en zorgverleners al aan de norm voldoet en het geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen financiële gevolgen verwacht.
Anterieure Cervicale Discectomie met Prothese (ACDF versus ACDP)	Geen financiële gevolgen	Hoewel uit de toetsing volgt dat de aanbeveling(en) breed toepasbaar zijn (5.000-40.000 patiënten), volgt ook uit de toetsing dat het overgrote deel (±90%) van de zorgaanbieders en

		zorgverleners al aan de norm voldoet en het geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen financiële gevolgen verwacht.
Anterieure (micro)foraminotomie versus ACDF	Geen financiële gevolgen	Hoewel uit de toetsing volgt dat de aanbeveling(en) breed toepasbaar zijn (5.000-40.000 patiënten), volgt ook uit de toetsing dat het overgrote deel (±90%) van de zorgaanbieders en zorgverleners al aan de norm voldoet en het geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen financiële gevolgen verwacht.
Dorsale benadering bij CRS (anterieur versus dorsaal)	Geen financiële gevolgen	Hoewel uit de toetsing volgt dat de aanbeveling(en) breed toepasbaar zijn (5.000-40.000 patiënten), volgt ook uit de toetsing dat het overgrote deel (±90%) van de zorgaanbieders en zorgverleners al aan de norm voldoet en het geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen financiële gevolgen verwacht.
Predictie conservatief versus chirurgisch	Geen financiële gevolgen	Hoewel uit de toetsing volgt dat de aanbeveling(en) breed toepasbaar zijn (5.000-40.000 patiënten), volgt ook uit de toetsing dat het overgrote deel (±90%) van de zorgaanbieders en zorgverleners al aan de norm voldoet en het geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen financiële gevolgen verwacht.
Postoperatief beleid - Behandeling en werkhervatting bij CRS (2 PICO's)	Geen financiële gevolgen	Hoewel uit de toetsing volgt dat de aanbeveling(en) breed toepasbaar zijn (5.000-40.000 patiënten), volgt ook uit de toetsing dat het overgrote deel (±90%) van de zorgaanbieders en zorgverleners al aan de norm voldoet en het geen nieuwe manier van zorgverlening of andere organisatie van zorgverlening betreft. Er worden daarom geen financiële gevolgen verwacht.

Werkwijze

AGREE

Deze richtlijnmodule is opgesteld conform de eisen vermeld in het rapport Medisch Specialistische Richtlijnen 2.0 van de adviescommissie Richtlijnen van de Raad Kwaliteit. Dit rapport is gebaseerd op het AGREE II instrument (Appraisal of Guidelines for Research & Evaluation II; Brouwers, 2010).

Knelpuntenanalyse en uitgangsvragen

Tijdens de voorbereidende fase inventariseerde de werkgroep de knelpunten in de zorg voor patiënten met CRS. Tevens zijn er knelpunten aangedragen door Ergotherapie Nederland, het Nederlands Huisartsen Genootschap, Nederlandse Vereniging van Ziekenhuizen, Nederlandse Vereniging van Revalidatieartsen, Vereniging van Oefentherapeuten Cesar en Mensendieck, Zorginstituut Nederland, Zelfstandige Klinieken Nederland, via enquête. Op basis van de uitkomsten van de knelpuntenanalyse zijn door de werkgroep concept-uitgangsvragen opgesteld en definitief vastgesteld.

Uitkomstmaten

Na het opstellen van de zoekvraag behorende bij de uitgangsvraag inventariseerde de werkgroep welke uitkomstmaten voor de patiënt relevant zijn, waarbij zowel naar gewenste als ongewenste effecten werd gekeken. Hierbij werd een maximum van acht uitkomstmaten gehanteerd. De werkgroep waardeerde deze uitkomstmaten volgens hun relatieve belang bij de besluitvorming rondom aanbevelingen, als cruciaal (kritiek voor de besluitvorming), belangrijk (maar niet cruciaal) en onbelangrijk. Tevens definieerde de werkgroep tenminste voor de cruciale uitkomstmaten welke verschillen zij klinisch (patiënt) relevant vonden.

Methode literatuursamenvatting

Een uitgebreide beschrijving van de strategie voor zoeken en selecteren van literatuur is te vinden onder 'Zoeken en selecteren' onder Onderbouwing. Indien mogelijk werd de data uit verschillende studies gepoold in een random-effects model. Review Manager 5.4 werd

gebruikt voor de statistische analyses. De beoordeling van de kracht van het wetenschappelijke bewijs wordt hieronder toegelicht.

Beoordelen van de kracht van het wetenschappelijke bewijs

De kracht van het wetenschappelijke bewijs werd bepaald volgens de GRADE-methode. GRADE staat voor 'Grading Recommendations Assessment, Development and Evaluation' (zie http://www.gradeworkinggroup.org/). De basisprincipes van de GRADE-methodiek zijn: het benoemen en prioriteren van de klinisch (patiënt) relevante uitkomstmaten, een systematische review per uitkomstmaat, en een beoordeling van de bewijskracht per uitkomstmaat op basis van de acht GRADE-domeinen (domeinen voor downgraden: risk of bias, inconsistentie, indirectheid, imprecisie, en publicatiebias; domeinen voor upgraden: dosis-effect relatie, groot effect, en residuele plausibele confounding).
GRADE onderscheidt vier gradaties voor de kwaliteit van het wetenschappelijk bewijs: hoog, redelijk, laag en zeer laag. Deze gradaties verwijzen naar de mate van zekerheid die er bestaat over de literatuurconclusie, in het bijzonder de mate van zekerheid dat de literatuurconclusie de aanbeveling adequaat ondersteunt (Schünemann, 2013; Hultcrantz, 2017).

GRADE	Definitie
Hoog	– er is hoge zekerheid dat het ware effect van behandeling dichtbij het geschatte effect van behandeling ligt; – het is zeer onwaarschijnlijk dat de literatuurconclusie klinisch relevant verandert wanneer er resultaten van nieuw grootschalig onderzoek aan de literatuuranalyse worden toegevoegd.
Redelijk	– er is redelijke zekerheid dat het ware effect van behandeling dichtbij het geschatte effect van behandeling ligt; – het is mogelijk dat de conclusie klinisch relevant verandert wanneer er resultaten van nieuw grootschalig onderzoek aan de literatuuranalyse worden toegevoegd.
Laag	– er is lage zekerheid dat het ware effect van behandeling dichtbij het geschatte effect van behandeling ligt; – er is een reële kans dat de conclusie klinisch relevant verandert wanneer er resultaten van nieuw grootschalig onderzoek aan de literatuuranalyse worden toegevoegd.
Zeer laag	– er is zeer lage zekerheid dat het ware effect van behandeling dichtbij het geschatte effect van behandeling ligt; – de literatuurconclusie is zeer onzeker.

Bij het beoordelen (graderen) van de kracht van het wetenschappelijk bewijs in richtlijnen volgens de GRADE-methodiek spelen grenzen voor klinische besluitvorming een belangrijke rol (Hultcrantz, 2017). Dit zijn de grenzen die bij overschrijding aanleiding zouden geven tot een aanpassing van de aanbeveling. Om de grenzen voor klinische besluitvorming te bepalen moeten alle relevante uitkomstmaten en overwegingen worden meegewogen. De grenzen voor klinische besluitvorming zijn daarmee niet één op één vergelijkbaar met het minimaal klinisch relevant verschil (Minimal Clinically Important Difference, MCID). Met name in situaties waarin een interventie geen belangrijke nadelen heeft en de kosten relatief laag zijn, kan de grens voor klinische besluitvorming met betrekking tot de effectiviteit van de interventie bij een lagere waarde (dichter bij het nuleffect) liggen dan de MCID (Hultcrantz, 2017).

Overwegingen (van bewijs naar aanbeveling)

Om te komen tot een aanbeveling zijn naast (de kwaliteit van) het wetenschappelijke bewijs ook andere aspecten belangrijk en worden meegewogen, zoals aanvullende argumenten uit bijvoorbeeld de biomechanica of fysiologie, waarden en voorkeuren van patiënten, kosten (middelenbeslag), aanvaardbaarheid, haalbaarheid en implementatie. Deze aspecten zijn systematisch vermeld en beoordeeld (gewogen) onder het kopje 'Overwegingen' en kunnen (mede) gebaseerd zijn op expert opinion. Hierbij is gebruik gemaakt van een gestructureerd

format gebaseerd op het evidence-to-decision framework van de internationale GRADE Working Group (Alonso-Coello, 2016a; Alonso-Coello 2016b). Dit evidence-to-decision framework is een integraal onderdeel van de GRADE methodiek.

Formuleren van aanbevelingen

De aanbevelingen geven antwoord op de uitgangsvraag en zijn gebaseerd op het beschikbare wetenschappelijke bewijs en de belangrijkste overwegingen, en een weging van de gunstige en ongunstige effecten van de relevante interventies. De kracht van het wetenschappelijk bewijs en het gewicht dat door de werkgroep wordt toegekend aan de overwegingen, bepalen samen de sterkte van de aanbeveling. Conform de GRADE-methodiek sluit een lage bewijskracht van conclusies in de systematische literatuuranalyse een sterke aanbeveling niet a priori uit, en zijn bij een hoge bewijskracht ook zwakke aanbevelingen mogelijk (Agoritsas, 2017; Neumann, 2016). De sterkte van de aanbeveling wordt altijd bepaald door weging van alle relevante argumenten tezamen. De werkgroep heeft bij elke aanbeveling opgenomen hoe zij tot de richting en sterkte van de aanbeveling zijn gekomen.

In de GRADE-methodiek wordt onderscheid gemaakt tussen sterke en zwakke (of conditionele) aanbevelingen. De sterkte van een aanbeveling verwijst naar de mate van zekerheid dat de voordelen van de interventie opwegen tegen de nadelen (of vice versa), gezien over het hele spectrum van patiënten waarvoor de aanbeveling is bedoeld. De sterkte van een aanbeveling heeft duidelijke implicaties voor patiënten, behandelaars en beleidsmakers (zie onderstaande tabel). Een aanbeveling is geen dictaat, zelfs een sterke aanbeveling gebaseerd op bewijs van hoge kwaliteit (GRADE gradering HOOG) zal niet altijd van toepassing zijn, onder alle mogelijke omstandigheden en voor elke individuele patiënt.

Implicaties van sterke en zwakke aanbevelingen voor verschillende richtlijngebruikers		
	Sterke aanbeveling	*Zwakke (conditionele) aanbeveling*
Voor patiënten	De meeste patiënten zouden de aanbevolen interventie of aanpak kiezen en slechts een klein aantal niet.	Een aanzienlijk deel van de patiënten zouden de aanbevolen interventie of aanpak kiezen, maar veel patiënten ook niet.
Voor behandelaars	De meeste patiënten zouden de aanbevolen interventie of aanpak moeten ontvangen.	Er zijn meerdere geschikte interventies of aanpakken. De patiënt moet worden ondersteund bij de keuze voor de interventie of aanpak die het beste aansluit bij zijn of haar waarden en voorkeuren.
Voor beleidsmakers	De aanbevolen interventie of aanpak kan worden gezien als standaardbeleid.	Beleidsbepaling vereist uitvoerige discussie met betrokkenheid van veel stakeholders. Er is een grotere kans op lokale beleidsverschillen.

Organisatie van zorg

In de knelpuntenanalyse en bij de ontwikkeling van de richtlijnmodule is expliciet aandacht geweest voor de organisatie van zorg: alle aspecten die randvoorwaardelijk zijn voor het verlenen van zorg (zoals coördinatie, communicatie, (financiële) middelen, mankracht en infrastructuur). Randvoorwaarden die relevant zijn voor het beantwoorden van deze specifieke uitgangsvraag zijn genoemd bij de overwegingen. Meer algemene, overkoepelende, of bijkomende aspecten van de organisatie van zorg worden behandeld in de module Organisatie van zorg.

Commentaar- en autorisatiefase

De conceptrichtlijnmodule werd aan de betrokken (wetenschappelijke) verenigingen en (patiënt) organisaties voorgelegd ter commentaar. De commentaren werden verzameld en besproken met de werkgroep. Naar aanleiding van de commentaren werd de conceptrichtlijnmodule aangepast en definitief vastgesteld door de werkgroep. De

definitieve richtlijnmodule werd aan de deelnemende (wetenschappelijke) verenigingen en (patiënt) organisaties voorgelegd voor autorisatie en door hen geautoriseerd dan wel geaccordeerd.

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Module 1 Diagnostiek

Uitgangsvraag

Wat is de plaats van fysieke testen bij het stellen van de diagnose cervicaal radiculair syndroom?

Inleiding

In de klinische praktijk is de diagnose van CRS gebaseerd op een combinatie van het klinische beeld van de patiënt, het lichamelijk onderzoek en (zo nodig) diagnostische beeldvorming. Er kunnen verschillende fysieke tests worden uitgevoerd tijdens het lichamelijk onderzoek, maar de diagnostische nauwkeurigheid van deze testen is onbekend. Deze module evalueert de diagnostische accuratesse van fysieke testen voor het aantonen of uitsluiten van een cervicaal radiculair syndroom.

Search and select

A systematic review of the literature was performed to answer the following question: *What is the diagnostic accuracy of diagnostic tests during physical examination for identifying cervical radiculopathy?*

P: Patients who were suspected of having cervical radiculopathy
I: Diagnostic physical tests during physical examination for identifying cervical radiculopathy
C: Not applicable
R: (1) Diagnostic imaging magnetic resonance imaging (MRI) or computed tomography (CT) myelography, or (2) findings during surgery
O: Sensitivity, positive predictive value, specificity, negative predictive value
Timing and setting: Diagnostic trajectory in secondary care

Relevant outcome measures

The guideline development group considered (high) sensitivity and (high) negative predictive value as *critical* outcome measures for decision making; and (high) specificity and (high) positive predictive value as *important* outcome measures for decision making.

The working group defined values for sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) ≥ 0.80 as high; 0.60–0.79 as moderate and <0.60 as low, conform cut-off values presented by Sleijser-Koehorst (2021).

Search and select (Methods)

The databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms until March 23. The detailed search strategy is depicted under the tab Methods. The systematic literature search resulted in 366 hits. Studies were selected based on the following criteria:

- Systematic review (searched in at least two databases, and detailed search strategy, risk of bias assessment and results of individual studies available), randomized controlled trial or observational study comparing diagnostic test during physical examination with a reference test (diagnostic imaging magnetic resonance imaging (MRI) or computed tomography (CT) myelography, or (2) findings during surgery) resulting in diagnostic accuracy measures;
- Patients aged ≥ 18 years;
- Full-text English or Dutch language publication
- Studies including ≥ 20 patients (ten in each study arm); and

- Studies according to PICRO and setting

Initially, seven studies were selected based on title and abstract screening. After reading the full text, three studies were excluded (see the Table with reasons for exclusion under the tab Methods) and four studies were included.

Results

Four studies were included in the analysis of the literature. Important study characteristics and results are summarized in the evidence Tables. The assessment of the risk of bias is summarized in the risk of bias Tables.

Summary of literature

Description of studies

Thoomes (2017) performed a systematic review on the diagnostic accuracy of test for diagnosing cervical radiculopathy performed during a physical examination. Diagnostic accuracy outcomes were compared with a reference standard of imaging or surgical findings. The electronic databases CENTRAL, PubMed (including MEDLINE), Embase, CINAHL, Web of Science and Google Scholar were searched from inception up to March 2016. Criteria for inclusion of studies were: 1) patients who were over 18 years of age, patients suspected of cervical radiculopathy from nerve root compression due to cervical disc herniation/degenerative spondylotic changes, 3) reporting diagnostic accuracy of a physical examination test, carried out in primary or secondary care setting and 4) presenting results from full reports. The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) was used to assess the risk of bias on the following domains: patient selection, index test, reference test and flow and timing. All studies were judged to have a high or unclear risk of bias in for at least one domain. The authors of the systematic review declared no competing interests.

After publication of the systematic review by Thoomes (2017), three other diagnostic accuracy studies were published that matched the predefined PICO (Grondin, 2021; Park, 2017; Sleijser-Koehorst, 2021). These studies are summarized below.

The prospective cohort study by Grondin (2021) tested diagnostic accuracy of single and combined Upper limb neurodynamic tests (ULNTs) and included patients with a diagnostic uncertainty between September 2017 and September 2019. The study was carried out in accordance with the Standards for Reporting Diagnostic accuracy studies (STARD) guidelines. Criteria for inclusion of patients were: 1) between 18 and 65 years of age, 2) reporting arm pain with or without neck pain (for at least 3 months), 3) self-reported pain score between 30 mm and 80 mm on a 100 mm visual analogue scale (VAS) for the previous 24 hours, and 4) a self-reported score of >20% on the Neck Disability Index (NDI). Patients were excluded in case of: 1) inability to understand French, 2) significant neck trauma at time of study, 3) a history of neck or arm surgery, 4) presence of one of the following conditions: cardiovascular/psychiatric/neoplastic/neurological/(extra)pyramidal pathology, cervical myelopathy, diabetes, pregnancy, fibromyalgia or an inflammatory joint condition/arthritis. The reference test was performed by a single neurosurgeon with at least 15 years of experience, consisting of a clinical diagnosis (history and presence of radicular pain/symptoms of cervical radiculopathy), confirmed using imaging verification by MRI. ULNTs were carried out approximately 1 hour after the reference standard by a single physiotherapist with 10 years of experience in neck pain management and with advanced certification for orthopedic assessment. After screening 109 individuals, 85 patients were included in the study, and no missings were reported. The authors declared no competing interests.

The retrospective study by Park (2017) tested the diagnostic accuracy of the Spurling test and the Neck tornado test (Choi's test) and for this purpose reviewed records of 135 patients who were referred to the pain clinic between September 2014 and August 2015. Criteria of inclusion of patients were: 1) presence of neck pain and 2) availability of a cervical spine MRI. Exclusion criteria were: 1) a history of cervical spine surgery, 2) a previous nerve block for cervical radiculopathy, 3) pregnancy and 4) inflammatory disease such as rheumatoid arthritis.
The reference test was performed by a pain clinician with at least 10 years of experience, confirming cervical radiculopathy considering symptoms and MRI. The Spurling test and NNT were performed at an unknown time interval before the reference test. Records of 135 patients were reviewed and no missings were reported. However, the report lacked a detailed patient flow. The authors declared no competing interests.

The prospective cohort study by Sleijser-Koehorst (2021) tested the diagnostic accuracy of the Spurling test, Upper Limb Neurodynamic test and the Shoulder abduction relief test. Criteria of inclusion of patients were: 1) at least 18 years old, 2) ability to understand the Dutch language, 3) Patients were excluded in case they: 1) reported serious cervical pathology (malignancies, (rheumatoid) arthritis, myelopathy or fractures), 2) suffered neurological conditions, diabetes mellitus, complex regional pain syndrome, polyneuropathy or 4) had a history of spinal surgery.
The reference test was performed by a neurosurgeon based on clinical presentation and an MRI scan confirming nerve root compression or irritation at a relevant segmental level. The physical tests were performed by an experienced physiotherapist, prior to the reference standard. Missing data were reported for the Spurling (n= 1), ULNT1 (n= 4) and the Shoulder abduction relief test (n= 3). The authors declared no competing interests.

Characteristics of the included studies are described in Table 1.

***Table 1**. Description of included studies*

Study	Characteristics		Diagnostics			Study design
Setting		**Population**	**Indextest**	**Cut-off value**	**Reference test (cut-off)**	
Thoomes (2017)						
Apelby-Albrecht (2013)	Center for Spinal surgery Country: Sweden Prevalence: 0.69 (95% CI 0.54 to 0.81)	Mean age: NR Female (%): NR Duration of pain: NR	ULNT1 (median), ULNT2a (median), ULNT2b (radial) and ULNT3 (ulnar)	Increase/decrease in symptoms combined with structural differentiation	1: Clinical examination, medical history and; 2: MRI-scan and; 3 history	Diagnostic cohort study
Gumina (2013)	Shoulder Clinical Office and Orthopedic Spine Ambulatory Country: Italy Prevalence: 0.20 (95% CI 0.18 to 0.22)	Mean age: NR Female (%): NR Duration of pain: NR	Arm squeeze test	Higher score (≥ 3 points) on pressure on the middle third of the upper arm compared with the other two areas	1: Clinical examination and; 2: MRI-scan and; 3 history	Cohort study resembling a case control-design
Shabat (2012)	Spine Surgery Unit Country: Israel Prevalence: 0.68 (95% CI 0.71 to 0.75)	Mean age: NR Female (%): NR Duration of pain: NR	Spurling (Ext+Rot+Ax compression)	Increase of symptoms	Complete physical examination and MRI/CT imaging	Cohort study
Shah (2004)	Neurosurgical Unit Country: India Prevalence: 0.86 (95% CI 0.72 to 0.82)	Mean age: NR Female (%): NR Duration of pain: NR	Spurling (Ext+LF+Ax pressure)	Increase of symptoms	T-2 weighted axial MRI	Prospective cohort study
Viikari-Juntura (1989)	Neurosurgery department Country: Finland Prevalence:	Mean age: NR Female (%): NR Duration of pain: NR	Spurling (LF+Rot+Ax compression) Traction	Increase of symptoms	1: conventional neurological examination and; 2: Cervical myelography	Prospective cohort study
Grondin (2021)	Neurosurgery department Country: France Prevalence: 0.317	Mean age (SD): 44 (CR+) and 45 (CR-) Female (%): NR Duration of pain, months (SD): 93 (98) for CR+ and 71 (62) for CR-	ULNT1 (median), ULNT2a (median), ULNT2b (radial) and ULNT3 (ulnar)	Reproduction of a familiar symptomatic complaint combined with structural differentiation	1: diagnosis based on clinical presentation by neurosurgeon and; 2: MRI-scan	Prospective cohort study
Park (2017)	Pain clinic in hospital Country: Korea Prevalence: 0.50 (95% CI 0.41 to 0.58)	Mean age: 53.4 (13.1) Female (%): 57 (42) Duration of pain: NR	Spurling (Ext+Rot+Ax pressure) Neck tornado test (Choi's test)	Reproduction/increase of radicular pain/tingling	1 diagnosis based on clinical presentation by neurosurgeon and; 2: MRI-scan	Retrospective cohort study
Sleijser-Koehorst (2021)	Multidisciplinary clinic Country: the Netherlands Prevalence: 0.37 (0.27 to 0.48)	Mean age (SD): 49.9 (10.7) Female (%): 65 (48.5) Median duration of pain, weeks (IQR): 26 (13- 104)	Index: Spurling (Ext+Rot+LF) Comparators: ULNT1, Shoulder abduction relief test, and cervical distraction test	Index: Reproduction of symptoms Comparators: Reproduction of symptoms and increased/decreased symptoms (ULNT1) or relief of symptoms (Shoulder abduction/cervical distraction	1: diagnosis based on clinical presentation by neurosurgeon and; 2: MRI-scan	Prospective cohort study

Abbreviations: Ax: axial compression/pressure; CR+: subjects with cervical radiculopathy; CR- subjects without cervical radiculopathy; Ext: extension; LF: lateral flexion; NR: not reported; Rot: rotation; SD: standard deviation; ULNT: Upper Limb Neurodynamic Tests

Results

Diagnostic accuracy is assessed below for the following instruments:

1. Upper limb Neural tension tests (ULNT's)
   1.1 Four combined Upper limb Neural tension tests (ULNT's); 1.2 ULNT1 median
2. Arm squeeze test
3. Spurling's test
   3.1 Spurling's test (Ext+ Rot) on "true radicular symptoms"; 3.2 Spurling's test (Ext+ LF); 3.3 Spurling's test (LF+ Rot); 3.4 Spurling's test (Ext+Rot+LF); 3.5 Spurling's test (Ext+Rot+Ax)
4. Traction
5. Shoulder abduction test
6. Neck tornado test (Choi's test)

For each instrument sensitivity, specificity, PPV and NPV were reported and summarized below.

1. Upper limb Neural tension tests (ULNT's)

1.1 Four combined Upper limb Neural tension tests (ULNT's)

Two studies reported on four combined ULNT's as a diagnostic for cervical radiculopathy (Apelby-Albrecht (2013), Grondin (2021), and compared the outcome with clinical examination and MRI as reference. A positive outcome on one of four ULNTs was needed for a diagnosis of CRS. Results are depicted in Table 2 and Table 3.

Table 2 shows the results of Apelby-Albrecht (2013) as summarized in Thoomes (2017). Regarding sensitivity, 5 out of 35 patients (3%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using a combination of 4 ULNT's. Regarding specificity, 5 out of 16 (31%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.87 meaning that 5 out of 39 patients testing positive on a combination of 4 ULNT's, actually did not have cervical radiculopathy. The NPV was 0.92, translating into 1 out of 11 (8%) testing negative with a combination of 4 ULNT's, actually have cervical radiculopathy.

Table 3 shows the results of Grondin (2021). Since no 2x2 Table was presented by the authors for this outcome, the values of TP, FP, FN and TN are derived from sensitivity, specificity, prevalence and included participants reported in the publication.

Regarding sensitivity, 1 out of 27 patients (4%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using a combination of 4 ULNT's. Regarding specificity, 31 of the 58 patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.46 meaning that 31 of the 57 patients testing positive on a combination of 4 ULNT's, actually did not have cervical radiculopathy. The NPV was 0.96, translating into 1 out of 28 (4%) testing negative with a combination of 4 ULNT's, actually have cervical radiculopathy.

Table 2: Diagnostic accuracy of ULNT1, ULNT2a, ULNT2b and ULNT3 combined (Apelby-Albrecht, 2013)

	Reference (clinical examination and MRI) +	-		
combination of 4 ULNT's +	34 (TP)	5 (FP)	39	*PPV: 34/39 = 0.87 (95% CI 0.77 to 0.93)*
combination of 4 ULNT's -	1 (FN)	11 (TN)	12	*NPV: 11/12 = 0.92 (95% CI 0.61 to 0.99)*
	35	16	51	
	Sensitivity: 34/35 = 0.97 (95% CI 0.85 to 1.00)	*Specificity: 11/16 = 0.69 (95% CI 0.41 to 0.89)*		

Table 3: Diagnostic accuracy of ULNT1, ULNT2a, ULNT2b and ULNT3 combined (Grondin (2021)

	Reference (clinical examination and MRI)			
	+	-		
combination of 4 ULNT's +	26 (TP)	31 (FP)	57	*PPV: 26/57 = 0.46 (95% CI 0.39 to 0.52)*
combination of 4 ULNT's -	1 (FN)	27 (TN)	28	*NPV: 27/28 = 0.96 (95% CI 0.79 to 0.99)*
	27	58	85	
	Sensitivity: 1/27 = 0.96 (95% CI 0.81 to 1.00)	*Specificity: 27/58 = 0.47 (95% CI 0.33 to 0.60)*		

1.2 ULNT1 median

Three studies reported on ULNT1 median as a diagnostic for cervical radiculopathy (Apelby-Albrecht, 2013; Grondin, 2021; Sleijser-Koehorst, 2021).

Table 4 shows the results of Apelby-Albrecht (2013) as summarized in Thoomes (2017). Regarding sensitivity, 6 out of 35 patients (17%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using ULNT1 median alone. Regarding specificity, 4 out of 16 (25%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.88 meaning that 4 out of 33 patients testing positive on ULNT1 median alone, actually did not have cervical radiculopathy. The NPV was 0.67, translating into 6 out of 18 (33%) testing negative with ULNT1 median alone, actually have cervical radiculopathy.

Table 5 shows the results of Grondin (2021). Since no 2x2 Table was presented by the authors for this outcome, the values of TP, FP, FN and TN are derived from sensitivity, specificity, prevalence and included participants reported in the publication.

Regarding sensitivity, 11 out of 27 patients (41%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using ULNT1 median alone. Regarding specificity, 14 out of 58 patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.53 meaning that 14 of the 30 patients testing positive on ULNT1 median alone, actually did not have cervical radiculopathy. The NPV was 0.80, translating into 11 out of 55 (20%) testing negative with ULNT1 median alone, actually have cervical radiculopathy.

Table 6 shows the results of Sleijser-Koehorst, 2021). Regarding sensitivity, 21 out of 64 patients (33%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using ULNT1 median alone. Regarding specificity, 22 out of 66 (33%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.66 meaning that 22 out of 65 patients testing positive on ULNT1 median alone, actually did not have cervical radiculopathy. The NPV was 0.68, translating into 21 out of 65 (32%) testing negative with ULNT1 median alone, actually have cervical radiculopathy.

Table 4: Diagnostic accuracy of ULNT1 median alone (Apelby-Albrecht, 2013)

	Reference (clinical examination and MRI) +	-		
ULNT1 median +	29 (TP)	4 (FP)	33	*PPV: 29/33 = 0.88 (95% CI 0.71 to 0.96)*
ULNT1 median -	6 (FN)	12 (TN)	18	*NPV: 12/18 = 0.67 (95% CI 0.41 to 0.86)*
	35	16	51	
	Sensitivity: 29/35 = 0.83 (95% CI 0.66 to 0.93)	*Specificity: 12/16 = 0.75 (95% CI 0.48 to 0.93)*		

Table 5: Diagnostic accuracy of ULNT1 median alone (Grondin (2021)

	Reference (clinical examination and MRI) +	-		
ULNT1 median +	16 (TP)	14 (FP)	30	*PPV: 16/30 = 0.53 (95% CI 0.34 to 0.72)*
ULNT1 median -	11 (FN)	44 (TN)	55	*NPV: 44/55 = 0.80 (95% CI 0.67 to 0.90)*
	27	58	85	
	Sensitivity: 16/27 = 0.59 (95% CI 0.39 to 0.78)	*Specificity: 44/58 = 0.76 (95% CI 0.63 to 0.86)*		

Table 6: Diagnostic accuracy of ULNT1 median alone (Sleijser-Koehorst, 2021))

	Reference (clinical examination and MRI) +	-		
ULNT1 median +	43 (TP)	22 (FP)	65	*PPV: 43/65 = 0.66 (95% CI 0.53 to 0.77)*
ULNT1 median -	21 (FN)	44 (TN)	65	*NPV: 44/6 5= 0.68 (95% CI 0.55 to 0.79)*
	64	66	130	
	Sensitivity: 43/64 = 0.67 (95% CI 0.54 to 0.78)	*Specificity: 44/66 = 0.67 (95% CI 0.54 to 0.78)*		

2. Arm squeeze test

One study reported on the arm squeeze test as a diagnostic for cervical radiculopathy (*Gumina, 2013*), and compared the outcome with clinical examination and MRI as reference. Results are depicted in Table 7.

Regarding sensitivity, 10 out of 305 patients (3%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using the arm squeeze test. Regarding specificity, 43 out of 1262 (3%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.87 meaning that 43 out of 338 patients testing positive on the arm squeeze test, actually did not have cervical radiculopathy. The NPV was 0.99, translating into 10 out of 1229 (1%) testing negative with the arm squeeze test, actually have cervical radiculopathy.

Table 7: Diagnostic accuracy of the arm squeeze test (Gumina, 2013)

	Reference (clinical examination and MRI) +	-		
Arm squeeze test +	295 (TP)	43 (FP)	338	*PPV: 295/338 = 0.87 (95% CI 0.83 to 0.91)*
Arm squeeze test -	10 (FN)	1219 (TN)	1229	*NPV: 1219/1229 = 0.99 (95% CI 0.98 to 0.99)*
	305	1262	1567	
	Sensitivity: 295/305 = 0.97 (95% CI 0.93 to 0.98)	*Specificity: 1219/1262 = 0.97 (95% CI 0.95 to 0.98)*		

3. Spurling's test

Five studies reported on the Spurling's test as a diagnostic for radiculopathy (Park, 2017; Shabat, 2012; Shah, 2004; Sleijser-Koehorst, 2021; Viikari-Juntura, 1989*).* A variety of different movements before Spurling's test was reported, results are depicted in paragraphs 3.1 to 3.5.

Summarized, sensitivity ranged from 0.38 (95% CI 0.22 to 0.56) in Viikari-Juntura (1989) to 0.98 (95% CI 0.92 to 0.99) in Shabat (2012) and specificity ranged from 0.84 (95% CI (95% CI 0.72 to 0.91) in Sleijser-Koehorst (2021) to 1.00 (95% CI 0.56 to 1.00) in Shah (2004).
PPV ranged from 0.78 (95% CI 0.63 to 0.88) in Sleijser-Koehorst (2021) to 1.00 (95% CI 0.85 to 1.00) in Shah (2004), and NPV ranged from 0.32 (95% CI 0.15 to 0.55) in Shah (2004) to NPV: 49/52 = 0.94 (95% CI 0.83 to 0.99) in Shabat (2012).

3.1 Spurling's test (Ext+ Rot) on "true radicular symptoms"

Shabat (2012) reported on Spurling's test using cervical extension combined with ipsilateral rotation. See Table 8 below.

Regarding sensitivity, 3 out of 118 patients (2%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using spurling's test (Ext+ Rot). Regarding specificity, 6 out of 55 (11%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.95, meaning that 6 out of 121 (5%) participants testing positive on Spurling's test (Ext+ Rot), actually did not have cervical radiculopathy. The NPV was 0.94, transliating into 3 out of 52 participants (6%) testing negative with spurling's test (Ext+Rot), actually have cervical radiculopathy.

Table 8: diagnostic accuracy of Spurlings test (Shabat, 2012)

	Reference (MRI/CT) +	-		
Spurling's test (Ext+ Rot) +	115 (TP)	6 (FP)	121	*PPV: 115/121 = 0.95 (95% CI 0.89 to 0.98)*
Spurling's test (Ext+ Rot) -	3 (FN)	49 (TN)	52	*NPV: 49/52 = 0.94 (95% CI 0.83 to 0.99)*
	118	55	173	
	Sensitivity: 115/118 = 0.98 (95% CI 0.92 to 0.99)	*Specificity: 49/55 = 0.89 (95% CI 0.77 to 0.96)*		

3.2 Spurling's test (Ext+ LF)

Shah (2004) reported on Spurling's test using cervical extension combined with ipsilateral lateral flexion. Results are depicted in Table 9 below.

Regarding sensitivity, 15 out of 43 patients (35%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using Spurling's test (Ext+LF). Regarding specificity, 0 out of 7 (0%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 1.00, meaning that all of the 28 participants testing positive on Spurling's test (Ext+LF), actually did have cervical radiculopathy. The NPV was 0.32, translating into 15 out of 22 participants (64%) testing negative with Spurling's test (Ext+LF), actually have cervical radiculopathy.

Table 9: diagnostic accuracy of Spurlings test (Shah, 2004)

	Reference (MRI/operation) +	-		
Spurling's test (Ext+ LF) +	28 (TP)	0 (FP)	28	*PPV: 28/28 = 1.00 (95% CI 0.85 to 1.00)*
Spurling's test (Ext+ LF) -	15 (FN)	7 (TN)	22	*NPV: 7/22 = 0.32 (95% CI 0.15 to 0.55)*
	43	7	50	
	Sensitivity: 28/43 = 0.65 (95% CI 0.49 to 0.79)	*Specificity: 7/7 = 1.00 (95% CI 0.56 to 1.00)*		

3.3 Spurling's test (LF+ Rot)

Viikari-Juntura (1989) reported on Spurling's test using ipsilateral lateral flexion and rotation.

Table 10 shows the results of Viikari-Juntura (1989) as presented by Thoomes (2017). Regarding sensitivity, 20 out of 32 patients (62%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using Spurling's test (Ext+LF). Regarding specificity, 3 out of 54 (6%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.86, meaning that 3 out of 15 (14%) participants testing positive on Spurling's test (Ext+LF), actually did not have cervical radiculopathy. The NPV was 0.80, translating into 20 out of 71 participants (20%) testing negative with Spurlings test (Ext+LF), actually have cervical radiculopathy.

Table 10: diagnostic accuracy of Spurlings test (Viikari-Juntura, 1989)

	Reference (MRI/operation) +	-		
Spurling's test (Ext+ LF) +	12 (TP)	3 (FP)	15	*PPV: 12/15 = 0.86 (95% CI 0.56 to 0.98)*
Spurling's test (Ext+ LF) -	20 (FN)	51 (TN)	71	*NPV: 51/71 = 0.80 (95% CI 0.51 to 0.95)*
	32	54	86	
	Sensitivity: 12/32 = 0.38 (95% CI 0.22 to 0.56)	*Specificity: 51/54 = 0.94 (95% CI 0.83 to 0.99)*		

3.4 Spurling's test (Ext+Rot+LF)

Table 11 shows the results of Sleijser-Koehorst, 2021). Regarding sensitivity, 27 out of 65 patients (41%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using Spurling's test. Regarding specificity, 11 out of 68 (16%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.78, meaning that 11 out of 49 (22%) participants testing positive on Spurling's test, actually did not have cervical radiculopathy. The NPV was 0.68, translating into 27 out of 84 participants (32%) testing negative with Spurling's test, actually have cervical radiculopathy.

Table 11: diagnostic accuracy of Spurlings test (Sleijser-Koehorst, 2021)

	Reference (MRI and clinical presentation) +	-		
Spurling's test (Ext+ LF) +	38 (TP)	11 (FP)	49	*PPV: 38/49 = 0.78 (95% CI 0.63 to 0.88)*
Spurling's test (Ext+ LF) -	27 (FN)	57 (TN)	84	*NPV: 57/84 = 0.68 (95% CI 0.57 to 0.78)*
	65	68	133	
	Sensitivity: 38/65 = 0.59 (95% CI 0.46 to 0.70)	*Specificity: 11/68 = 0.84 (95% CI 0.72 to 0.91)*		

3.5 Spurling's test (Ext+Rot+Ax)

Park (2017) reported on Spurling's test using extension, rotation and downward pressure on the head.

Table 12 shows the results of Park (2017). Regarding sensitivity, 30 out of 67 patients (45%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using Spurling's test. Regarding specificity, 1 out of 68 (1%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.97, meaning that 1 out of 38 (3%) participants testing positive on Spurling's test, actually did not have cervical radiculopathy. The NPV was 0.69, translating into 30 out of 97 participants (31%) testing negative with Spurling's test, actually have cervical radiculopathy.

Table 12: diagnostic accuracy of Spurlings test (Park, 2017)

	Reference (MRI) +	-		
Spurling's test (Ext+ LF) +	37 (TP)	1 (FP)	38	*PPV: 37/38 = 0.97 (95% CI 0.86 to 1.00)*
Spurling's test (Ext+ LF) -	30 (FN)	67 (TN)	97	*NPV: 67/97 = 0.69 (95% CI 0.59 to 0.78)*
	67	68	135	
	Sensitivity: 37/67 = 0.55 (95% CI 0.43 to 0.67)	*Specificity: 67/68 = 0.99 (95% CI 0.92 to 1.00)*		

4. Traction

One study reported on Traction as a diagnostic for cervical radiculopathy (*Viikari-Juntura (1989*)), and compared the outcome with a myelogram as reference. In total, 24 participants received traction as clinical test. Results are depicted in Table 13.

Regarding sensitivity, 10 out of 15 patients (62%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using Traction. Regarding specificity, 1 out of 33 (3%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.83, meaning that 1 out of 6 (17%) participants testing positive on traction, actually did not have cervical radiculopathy. The NPV was 0.76, translating into 10 out of 42 participants (14%) testing negative with traction, actually have cervical radiculopathy.

Table 13: diagnostic accuracy of traction (Viikari-Juntura, 1989)

	Reference (Myelogram) +	-		
Traction +	5 (TP)	1 (FP)	6	*PPV: 5/6 = 0.83 (95% CI 0.37 to 0.99)*
Traction -	10 (FN)	32 (TN)	42	*NPV: 32/42 = 0.76 (95% CI 0.60 to 0.87)*
	15	33	48	
	Sensitivity: 5/15 = 0.33 (95% CI 0.13 to 0.52)	*Specificity: 1/32 = 0.97 (95% CI 0.37 to 0.99)*		

5. Shoulder abduction test

Two studies reported on the shoulder abduction relief test (Viikari-Juntura, 1989; Sleijser-Koehorst, 2021).

Table 14 shows the results of Sleijser-Koehorst (2021). Regarding sensitivity, 32 out of 64 patients (50%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using Shoulder abduction test. Regarding specificity, 17 out of 67 (15%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.65, meaning that 17 out of 49 (35%) participants testing

positive on Shoulder abduction test, actually did not have cervical radiculopathy. The NPV was 0.61, translating into 32 out of 82 participants (39%) testing negative with Shoulder abduction test, actually have cervical radiculopathy.

Table 15 shows the results of Viikari-Juntura (1989) as presented by Thoomes (2017). Regarding sensitivity, 8 out of 15 patients (53%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using Shoulder abduction test. Regarding specificity, 2 out of 13 (15%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.78, meaning that 2 out of 9 (12%) participants testing positive on Shoulder abduction test, actually did not have cervical radiculopathy. The NPV was 0.58, translating into 8 out of 19 participants (42%) testing negative with Shoulder abduction test, actually have cervical radiculopathy.

Table 14: diagnostic accuracy of the shoulder abduction test (Sleijser-Koehorst, 2021)

	Reference (MRI and clinical presentation) +	-		
Shoulder abduction +	32 (TP)	17 (FP)	49	*PPV: 32/49 = 0.65 (95% CI 0.50 to 0.78)*
Shoulder abduction -	32 (FN)	50 (TN)	82	*NPV: 50/82 = 0.61 (95% CI 0.50 to 0.72)*
	64	67	131	
	Sensitivity: 32/64 = 0.50 (95% CI 0.37 to 0.63)	*Specificity: 50/67 = 0.75 (95% CI 0.62 to 0.84)*		

Table 15: diagnostic accuracy of the shoulder abduction test (Viikari-Juntura, 1989)

	Reference (Myelogram) +	-		
Shoulder abduction +	7 (TP)	2 (FP)	9	*PPV: 7/9 = 0.78 (95% CI 0.40 to 0.96)*
Shoulder abduction -	8 (FN)	11 (TN)	19	*NPV: 11/19 = 0.58 (95% CI 0.34 to 0.79)*
	15	13	28	
	Sensitivity: 7/15 = 0.47 (95% CI 0.22 to 0.73)	*Specificity: 11/13 = 0.85 (95% CI 0.54 to 0.97)*		

6. Neck tornado test (Choi's test)

One study reported on the neck tornado test (NNT) as a diagnostic for cervical radiculopathy (Park, 2017).

Table 16 shows the results of Park (2017). Regarding sensitivity, 10 out of 67 patients (15%) with cervical radiculopathy were falsely identified as not having cervical radiculopathy by using the NNT. Regarding specificity, 9 out of 68 (13%) patients without cervical radiculopathy were falsely identified as having cervical radiculopathy. The PPV was 0.86, meaning that 9 out of 66 (14%) participants testing positive on the NNT, actually did not have cervical radiculopathy. The NPV was 0.86, translating into 10 out of 69 participants (14%) testing negative with the NNT, actually have cervical radiculopathy.

Table 16: diagnostic accuracy of the Neck tornado test (Choi's test) (Park, 2017)

	Reference (MRI) +	-		
NNT +	57 (TP)	9 (FP)	66	*PPV: 57/66 = 0.86 (95% CI 0.76 to 0.94)*
NNT -	10 (FN)	59 (TN)	69	*NPV: 59/69 = 0.86 (95% CI 0.75 to 0.93)*
	67	68		
	Sensitivity: 57/67 = 0.85 (95% CI 0.74 to 0.93)	*Specificity: 59/68 = 0.87 (95% CI 0.76 to 0.94)*		

Level of evidence of the literature

1. Upper limb Neural tension tests (ULNT's)

1.1 Four combined Upper limb Neural tension tests (ULNT's)

1.1.1 The level of evidence regarding the outcome measure sensitivity started as "high" and was downgraded by one level to "medium". Since the impact on the risk of bias of the inappropriate time between reference and index test (Apelby-Albrecht, 2013) was estimated not too high, and the high quality of the study by Grondin (2021), there was no downgrading for risk of bias. The number of included patients however was low (Apelby-Albrecht, 2013) (-1, imprecision).

1.1.2 The level of evidence regarding the outcome measures specificity and PPV started as "high" and was downgraded by three levels to "very low". Since the impact on the risk of bias of the inappropriate time between reference and index test (Apelby-Albrecht, 2013) was estimated not too high, and the high quality of the study by Grondin (2021), there was no downgrading for risk of bias. A low number of included patients and confidence intervals crossing the borders of clinical relevance (Apelby-Albrecht, 2013) (-2, imprecision) and strong inconsistency without 95% CI's overlapping (-1, inconsistency).

1.1.3 The level of evidence regarding the outcome measures negative predictive value started as "high" and was downgraded by two levels to "low" because of a low number of included patients and confidence intervals crossing the borders of clinical relevance in both studies (-2, imprecision).

1.2 ULNT1 median alone

1.2.1 The level of evidence regarding the outcome measures sensitivity, PPV and NPV started as high and was downgraded by three levels to very low because of inconsistency (-1, inconsistency) and confidence intervals crossing the borders of clinical relevance (Apelby-Albrecht, 2013; Grondin, 2021; Sleijser-Koehorst, 2021) (-2, imprecision). Since the impact on the risk of bias of the inappropriate time between reference and index test (Apelby-Albrecht, 2013) was estimated not too high, and the high quality of the study by Grondin (2021) and Sleijser-Koehorst (2021), there was no downgrading for risk of bias.

1.2.2 The level of evidence regarding the outcome measure specificity started as high and was downgraded by two levels to low because of a low number of included patients and confidence intervals crossing the borders of clinical relevance (Apelby-Albrecht, 2013, Grondin, 2021 and Sleijser-Koehorst (2021)) (-2, imprecision). Since the impact on the risk of bias of the inappropriate time between reference and index test (Apelby-Albrecht, 2013) was estimated not too high, and the high quality of the study by Grondin (2021) and Sleijser-Koehorst (2021), there was no downgrading for risk of bias.

1.2.3 The level of evidence regarding the outcome measures negative predictive value and positive predictive value started as high and was downgraded by two levels to low because of a low number of included patients and confidence intervals crossing the borders of clinical relevance in both studies (-2, imprecision).

2. Arm squeeze test

The level of evidence regarding the outcome measures sensitivity, specificity, negative predictive value and positive predictive value started at high and was downgraded by two levels to "low" because the sample had a case-control character (-2, risk of bias).

3. Spurling's test

3.1 The level of evidence regarding the outcome measure sensitivity started as high and was downgraded by four levels to very low because of questionable overall risk of bias in Shabat (2012), using different reference tests (Shabat, 2012; Shah, 2004, Viikari-Juntura, 1989) and retrospective inclusion in Park (2017) (-2, risk of bias), strong inconsistency without 95% CI's overlapping between Viikari-Juntura (1989) and Shabat (2012) (-1, inconsistency) and broad confidence intervals (Shah, 2004; Sleijser-Koehorst, 2021) (-1, imprecision).

3.2 The level of evidence regarding the outcome measure specificity started as high and was downgraded by two levels to low because of questionable overall risk of bias in Shabat (2012), using different reference tests (Shabat, 2012; Shah, 2004, Viikari-Juntura (1989)) and retrospective inclusion in Park (2017) (-2, risk of bias), and confidence intervals crossing the borders of clinical relevance (Sleijser-Koehorst, 2021).

3.3 The level of evidence regarding the outcome measure positive predictive value started at high and was downgraded by three levels to very low because of questionable overall risk of bias in Shabat (2012) and using different reference tests (Shabat, 2012; Shah, 2004, Viikari-Juntura (1989)) (-2, risk of bias) and broad confidence intervals crossing borders of clinical relevance (Viikari-Juntura, 1989; Sleijser-Koehorst, 2021) (-1, imprecision)

3.4 The level of evidence regarding the outcome measure negative predictive value started as high and was downgraded by three levels to very low because of questionable overall risk of bias in Shabat (2012) and using different reference tests (Shabat, 2012; Shah, 2004, Viikari-Juntura (1989)) and retrospective inclusion in Park (2017) (-2, risk of bias) and strong inconsistency between all studies without 95% CI's overlapping between Shah (2004) and Shabat (2012) (-1, inconsistency).

4. Traction

4.1 Sensitivity

The level of evidence regarding the outcome measure sensitivity started as high and was downgraded by three levels to very low because of inappropriate exclusion criteria, and not all included patients received the same reference standard or index test, with no study of higher quality to compensate (-2, risk of bias) and a low number of included patients (-1, imprecision).

4.2 Specificity, PPV and NPV

The level of evidence regarding the outcome measures specificity, PPV and NPV started as high and was downgraded by three levels to very low because of inappropriate exclusion criteria, and not all included patients received the same reference standard or index test with no study of higher quality to compensate (-2, risk of bias) and crossing borders of clinical relevance (-1, imprecision).

5. Shoulder abduction test

5.1 Sensitivity, NPV

The level of evidence regarding the outcome measures sensitivity, specificity, negative predictive value and positive predictive value started as high and was downgraded by two levels to low because of inappropriate exclusion criteria, and not all included patients received the same reference standard or index test (Viikari-Juntura, 1989) (-1, risk of bias) and crossing borders of clinical relevance (-1, imprecision).

5.2 Specificity, PPV

The level of evidence regarding the outcome measures sensitivity, specificity, negative predictive value and positive predictive value started as high and was downgraded by three levels to very low because of inappropriate exclusion criteria, and not all included patients received the same reference standard or index test (Viikari-Juntura, 1989) (-1, risk of bias), conflicting results (-1, inconsistency) and crossing borders of clinical relevance (-1, imprecision).

6. Neck tornado test (Choi's test)

The level of evidence regarding the outcome measures sensitivity, specificity, negative predictive value and positive predictive value started as high and was downgraded by three levels to very low because risk of selection bias could not be ruled out due to the retrospective design of Park (2017), with no study of higher quality to compensate (-2, risk of bias) and crossing borders of clinical relevance (-1, imprecision).

Conclusions

1. Four combined Upper limb Neural tension tests (ULNT's)

1.1 Four combined Upper limb Neural tension tests (ULNT's)

1.1.1 Sensitivity

Moderate GRADE	The sensitivity of one positive ULNT out of a cluster of four combined ULNT's is likely high (>0.80) for diagnosing cervical radiculopathy. *Source: Apelby-Albrecht, 2013; Grondin, 2021*

1.1.2 Specificity, PPV

Very low GRADE	The evidence is very uncertain about the specificity and PPV of one positive ULNT out of a cluster of four combined ULNTs for diagnosing cervical radiculopathy. *Source: Apelby-Albrecht, 2013; Grondin, 2021*

1.1.3 NPV

Low GRADE	The evidence suggests that the NPV of one positive ULNT out of a cluster of four combined ULNT's is high (>0.80) for diagnosing cervical radiculopathy. *Source: Apelby-Albrecht, 2013; Grondin, 2021*

1.2 ULNT1 median alone

1.2.1 Sensitivity, PPV, NPV

Very low GRADE	The evidence is very uncertain about the sensitivity, PPV and NPV of ULNT1 alone for diagnosing cervical radiculopathy. *Source: Apelby-Albrecht, 2013; Grondin, 2021; Sleijser-Koehorst, 2021*

1.2.2. Specificity

Low GRADE	The evidence suggests that the specificity of ULNT1 median alone is moderate (>0.60, <0.80) for diagnosing cervical radiculopathy. *Source: Apelby-Albrecht, 2013; Grondin, 2021; Sleijser-Koehorst, 2021*

2. Arm squeeze test

Low GRADE	The evidence suggests that the diagnostic accuracy (sensitivity, specificity, PPV and NPV) is high (>0.80) for the arm squeeze test. *Source: Gumina, 2013*

3. Spurling's test

3.1 Sensitivity, PPV, NPV

Very low GRADE	The evidence is very uncertain about the sensitivity, PPV and NPV of Spurling's test for diagnosing cervical radiculopathy. *Source: Park, 2017; Shabat, 2012; Shah; 2004; Sleijser-Koehorst, 2021, Viikari-Juntura, 1989*

3.2 Specificity

Low GRADE	The evidence suggests that the specificity of Spurlings test for diagnosing cervical radiculopathy is high (>0.80). *Source: Park, 2017; Shabat, 2012; Shah; 2004; Sleijser-Koehorst, 2021, Viikari-Juntura, 1989*

4. Traction

Sensitivity, specificity, negative predictive value, positive predictive value

Very low GRADE	The evidence is very uncertain about the sensitivity, specificity, PPV and NPV of Traction for diagnosing cervical radiculopathy. *Source: Viikari-Juntura (1989*

5. Shoulder abduction test

5. Sensitivity, NVP

Low GRADE	The evidence suggests that the sensitivity of the shoulder abduction test for diagnosing cervical radiculopathy is low (<0.60). *Source: Sleijser-Koehorst, 2021; Viikari-Juntura, 1989*
Low GRADE	The evidence suggests that the sensitivity of the shoulder abduction test for diagnosing cervical radiculopathy is moderate (>0.60, <0.80). *Source: Sleijser-Koehorst, 2021; Viikari-Juntura, 1989*

5.2 Specificity, PPV

Very low GRADE	The evidence is very uncertain about the specificity and PPV of the shoulder abduction test for diagnosing cervical radiculopathy. *Source: Sleijser-Koehorst, 2021; Viikari-Juntura, 1989*

6. Neck tornado test (Choi's test)

Very low GRADE	The evidence is very uncertain about the sensitivity, specificity, PPV and NPV of the Neck tornado test (Choi's test) in diagnosing cervical radiculopathy. *Source: Park, 2017*

Overwegingen – van bewijs naar aanbeveling

Voor- en nadelen van de interventie en de kwaliteit van het bewijs

Om de rol van fysieke testen in het diagnostisch traject van patiënten met een cervicaal radiculair syndroom te bepalen, is in de literatuur gezocht naar de diagnostische accuratesse van fysieke testen. Er werd één systematische review gevonden (Thoomes, 2017). Deze is samengevat, en studies die hierna zijn verschenen zijn aan deze samenvatting toegevoegd (Grondin, 2021; Park, 2017; Sleijser-Koehorst, 2021). De bewijskracht voor de kritieke uitkomstmaat sensitiviteit bij vier gecombineerde ULNT's was *medium*. De bewijskracht voor de kritieke uitkomstmaten sensitiviteit en negatief voorspellende waarde is in alle andere gevallen (upper limb neural tension tests, arm squeeze test, Spurling's test, tractie, Shoulder abduction en de Neck tornado test) laag tot zeer laag. Dit komt door methodologische tekortkomingen (risico op vertekening) en brede betrouwbaarheidsintervallen, vaak in combinatie met kleine studiepopulaties (imprecisie) en (klinische) heterogeniteit. De bewijskracht voor de uitkomstmaat specificiteit en positief voorspellende waarde van de Spurling's test en gecombineerde ULNTs is laag, maar de gepoolde data suggereren wel hoge specificiteit en PPV (> 0,80). Derhalve kunnen er op basis van alleen de literatuur geen sterke aanbevelingen geformuleerd worden.

Mede omdat er nog geen bewijs voor of tegen de diagnostische waarde van klinisch neurologisch onderzoek is en er geen complicaties beschreven zijn bij het uitvoeren van de fysieke testen.

Waarden en voorkeuren van patiënten (en evt. hun verzorgers)

Het belangrijkste doel is de mate van waarschijnlijkheid van de diagnose CRS verhogen zodat een passende behandelstrategie voorgesteld kan worden. Eén van de mogelijke voordelen van het uitvoeren van de fysieke testen om de diagnose CRS te bevestigen is de reproductie van patiënt specifieke klachten. Het feit dat de behandelaar in staat is de (voor de patiënt bekende) klachten op te wekken, kan bij de patiënt vertrouwen wekken in het stellen van de diagnose en daarmee het voorgestelde behandelbeleid. De testen zijn zowel in de eerste lijn als in de tweedelijns gezondheidszorg setting direct uitvoerbaar na het afnemen van de anamnese en vereisen geen vervolgconsult en extra tijdsinvestering van de patiënt. Anders dan een korte verergering (tijdens de fysieke test) van de klachten zijn er voor de patiënt geen nadelen bekend van het uitvoeren van de fysieke testen.

Kosten (middelenbeslag)

Er zijn geen kosteneffectiviteitsstudie voor de uitvoering van deze diagnostiek bij de werkgroep bekend. Voor uitvoering van de fysieke testen zoals door de werkgroep aanbevolen, zijn geen relevante extra kosten noodzakelijk.

Aanvaardbaarheid, haalbaarheid en implementatie

Er is geen onderzoek gedaan naar de aanvaardbaarheid en haalbaarheid van de fysieke testen bij de diagnostiek van CRS. Voor veel medisch specialisten zullen deze fysieke testen wellicht minder of niet bekend zijn; indien gewenst zouden zij zich hierin kunnen laten bijscholen. In principe is iedere fysiotherapeut opgeleid voor het uitvoeren van deze fysieke testen.

Aanbeveling

Rationale van de aanbeveling: weging van argumenten voor en tegen de diagnostische procedure

Gezien de lage tot zeer lage bewijskracht voor de diagnostische waarde van de individuele fysieke testen, is de aanbeveling van de werkgroep voor de diagnose CRS vooral aandacht te

besteden aan anamnese en beeldvorming. Indien de behandelaar meerwaarde ziet van aanvullende testen, is het de aanbeveling om dan een cluster van fysieke testen toe te passen om de mate van waarschijnlijke aanwezigheid van een cervicaal radiculair syndroom vast te stellen. Daarbij kan worden gebruikgemaakt van:

- Spurling's test,
- Gecombineerde Upper Limb Neural Tension testen voor n. medianus, radialis en ulnaris,

De "A" variant van de Spurling is gekozen om de kans op een vals positieve uitslag van reproductie van somatische referred pain te verminderen zoals die opgewekt zou kunnen worden in andere varianten met bijvoorbeeld een positie van lateroflexie in combinatie met extensie en rotatie naar de aangedane zijde.
De diagnostische waarde van het neurologisch onderzoek naar reflexen, spierkracht en sensibiliteit is onbekend. Er is alleen retrospectief onderzoek gedaan bij geopereerde CRS-patiënten. Niettemin acht de werkgroep het neurologisch onderzoek ná een consistente anamnese en positief cluster van voornoemde testen wél van aanvullende waarde. Als de zenuwwortel substantieel gecomprimeerd wordt, zal een motorische en/of sensibele hypofunctie waarneembaar zijn.

Overweeg om als onderdeel van lichamelijk onderzoek een combinatie van de twee onderstaande fysieke testen uit te voeren om de diagnose CRS waarschijnlijker te maken:

- Spurling's test,
- Gecombineerde Upper Limb Neural Tension testen voor nervus medianus, nervus radialis en nervus ulnaris.

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Sleijser-Koehorst MLS, Coppieters MW, Epping R, Rooker S, Verhagen AP, Scholten-Peeters GGM. Diagnostic accuracy of patient interview items and clinical tests for cervical radiculopathy. Physiotherapy. 2021 Jun;111:74-82. doi: 10.1016/j.physio.2020.07.007. Epub 2020 Jul 28. PMID: 33309074.

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Bijlagen bij module ‘diagnostiek’

Implementatieplan

Aanbeveling	Tijdspad voor implementatie: <1 jaar, 1-3 jaar of >3 jaar	Verwacht effect op kosten	Randvoorwaarden voor implementatie (binnen aangegeven tijdspad)	Mogelijke barrières voor implementatie[1]	Te ondernemen acties voor implementatie[2]	Verantwoordelijken voor acties[3]	Overige opmerkingen
Alle aanbevelingen	<1 jaar	Beperkt	*Bekendheid met de richtlijn. *Bekendheid met het bestaan van de diverse fysieke diagnostische testen. *Vaardigheid in het uitvoeren en interpreteren van de diverse fysieke diagnostische testen.	*Onbekend met het bestaan van de diagnostische testen. *Onbekendheid met het uitvoeren en interpreteren van de testen. *Onbekendheid met de kennislacune op het gebied van de diagnostische waarde van “standaard” neurologisch onderzoek (sensibiliteit, reflexen, myotomale kracht).	*Verspreiden en publicatie van de richtlijn. *Optimaliseren kennis en vaardigheden bij zorgverleners. *Opnemen van testuitslagen in (elektronisch) patiënten dossiers en in overdrachten naar andere zorgverleners in 1e en 2e lijn.	*Beroepsverenigingen. *Betrokken zorgverleners. *Degenen die verantwoordelijk zijn voor toevoegingen en veranderingen in verslaglegging; (Afdelingen / IT / ziekenhuisbestuur / maatschappen?)	n.v.t.

[1] Barrières kunnen zich bevinden op het niveau van de professional, op het niveau van de organisatie (het ziekenhuis) of op het niveau van het systeem (buiten het ziekenhuis). Denk bijvoorbeeld aan onenigheid in het land met betrekking tot de aanbeveling, onvoldoende motivatie of kennis bij de specialist, onvoldoende faciliteiten of personeel, nodige concentratie van zorg, kosten, slechte samenwerking tussen disciplines, nodige taakherschikking, etc.

[2] Denk aan acties die noodzakelijk zijn voor implementatie, maar ook acties die mogelijk zijn om de implementatie te bevorderen. Denk bijvoorbeeld aan controleren aanbeveling tijdens kwaliteitsvisitatie, publicatie van de richtlijn, ontwikkelen van implementatietools, informeren van ziekenhuisbestuurders, regelen van goede vergoeding voor een bepaald type behandeling, maken van samenwerkingsafspraken.

[3] Wie de verantwoordelijkheden draagt voor implementatie van de aanbevelingen, zal tevens afhankelijk zijn van het niveau waarop zich barrières bevinden. Barrières op het niveau van de professional zullen vaak opgelost moeten worden door de beroepsvereniging. Barrières op het niveau van de organisatie zullen vaak onder verantwoordelijkheid van de ziekenhuisbestuurders vallen. Bij het oplossen van barrières op het niveau van het systeem zijn ook andere partijen, zoals de NZA en zorgverzekeraars, van belang.

Risk of bias assessment diagnostic accuracy studies (QUADAS II, 2011)

Study reference	Patient selection	Index test	Reference standard	Flow and timing	Comments with respect to applicability
Grondin, 2021	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions? Yes	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? Yes	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test? Yes	Was there an appropriate interval between index test(s) and reference standard? Yes Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the analysis? Yes	Are there concerns that the included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not match the review question? No
	CONCLUSION: Could the selection of patients have introduced bias? **RISK: LOW**	CONCLUSION: Could the conduct or interpretation of the index test have introduced bias? **RISK: LOW**	CONCLUSION: Could the reference standard, its conduct, or its interpretation have introduced bias? **RISK: LOW**	CONCLUSION Could the patient flow have introduced bias? **RISK: LOW**	
Park, 2017	Was a consecutive or random sample of patients enrolled? No Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions? Unclear	Were the index test results interpreted without knowledge of the results of the reference standard? Unclear If a threshold was used, was it pre-specified? Unclear	Is the reference standard likely to correctly classify the target condition? Unclear Were the reference standard results interpreted without knowledge of the results of the index test? Unclear	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the	Are there concerns that the included patients do not match the review question? Yes, since the retrospective design selection bias cannot be ruled out. Are there concerns that the index test, its conduct, or interpretation differ from the review question? Yes/No/Unclear Are there concerns that the target condition as defined by the reference standard does not match

Study reference	Patient selection	Index test	Reference standard	Flow and timing	Comments with respect to applicability
				analysis? Yes	the review question? No
	CONCLUSION: Could the selection of patients have introduced bias? **RISK: HIGH**	CONCLUSION: Could the conduct or interpretation of the index test have introduced bias? **RISK: UNCLEAR**	CONCLUSION: Could the reference standard, its conduct, or its interpretation have introduced bias? **RISK: UNCLEAR**	CONCLUSION Could the patient flow have introduced bias? **RISK: LOW**	
Sleijsler-Koehorst, 2021	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions? Yes	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? Yes (see abstracts)	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test? Yes	Was there an appropriate interval between index test(s) and reference standard? Yes Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the analysis? Yes, apart from minimal amount of missings	Are there concerns that the included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not match the review question? No/Unclear
	CONCLUSION: Could the selection of patients have introduced bias? **RISK: LOW**	CONCLUSION: Could the conduct or interpretation of the index test have introduced bias? **RISK: LOW**	CONCLUSION: Could the reference standard, its conduct, or its interpretation have introduced bias? **RISK: LOW**	CONCLUSION Could the patient flow have introduced bias? **RISK: LOW**	

Judgments on risk of bias are dependent on the research question: some items are more likely to introduce bias than others, and may be given more weight in the final conclusion on the overall risk of bias per domain:

Patient selection:

- Consecutive or random sample has a low risk to introduce bias.
- A case control design is very likely to overestimate accuracy and thus introduce bias.
- Inappropriate exclusion is likely to introduce bias.

Index test:

- This item is similar to “blinding” in intervention studies. The potential for bias is related to the subjectivity of index test interpretation and the order of testing.
- Selecting the test threshold to optimise sensitivity and/or specificity may lead to overoptimistic estimates of test performance and introduce bias.

Reference standard:

- When the reference standard is not 100% sensitive and 100% specific, disagreements between the index test and reference standard may be incorrect, which increases the risk of bias.
- This item is similar to “blinding” in intervention studies. The potential for bias is related to the subjectivity of index test interpretation and the order of testing.

Flow and timing:

- If there is a delay or if treatment is started between index test and reference standard, misclassification may occur due to recovery or deterioration of the condition, which increases the risk of bias.
- If the results of the index test influence the decision on whether to perform the reference standard or which reference standard is used, estimated diagnostic accuracy may be biased.
- All patients who were recruited into the study should be included in the analysis, if not, the risk of bias is increased.

Judgement on applicability:

Patient selection: there may be concerns regarding applicability if patients included in the study differ from those targeted by the review question, in terms of severity of the target condition, demographic features, presence of differential diagnosis or co-morbidity, setting of the study and previous testing protocols.

Index test: if index tests methods differ from those specified in the review question there may be concerns regarding applicability.

Reference standard: the reference standard may be free of bias but the target condition that it defines may differ from the target condition specified in the review question.

Table of excluded studies

Reference	Reason for exclusion
Seliverstova, 2022	Article in Russian (wrong language)
Mizer, 2017	Evaluated subjective history and self-report rather than physical tests (wrong intervention)
Redebrandt, 2022	No sensitivity/specificity/other diagnostic accuracy outcomes were presented (wrong outcome)

Zoekverantwoording

Algemene informatie

Cluster/richtlijn: NVvN Cervicaal Radiculair Syndroom	
Uitgangsvraag/modules: UV1 Wat is de plaats van fysieke testen bij het stellen van de diagnose cervical radiculopathy?	
Database(s): Embase.com, Ovid/Medline	Datum: 23 maart 2023
Periode: vanaf maart 2016 (SR Thoomes 2018, PMID 28838857)	Talen: geen restrictie
Literatuurspecialist: Alies van der Wal	
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting: Voor deze vraag is gezocht op de elementen: - cervical radiculopathy - fysieke testen - diagnostisch filter Het sleutelartikel wordt gevonden met deze search	
Te gebruiken voor richtlijnen tekst: *Nederlands* In de databases Embase.com en Ovid/Medline is op 23 maart 2023 systematisch gezocht naar systematische reviews, RCTs en observationele studies over de diagnostische waarde van fysieke testen bij cervical radiculopathy. De literatuurzoekactie leverde 366 unieke treffers op. *Engels* On the 23rd of March 2023, a systematic search was performed in the databases Embase.com and Ovid/Medline for systematic reviews, RCTs and observational studies about the diagnostical value of physical tests for cervical radiculopathy. The search resulted in 366 unique hits.	

Zoekopbrengst

	EMBASE	OVID/MEDLINE	Ontdubbeld
SR	46	25	59
RCT	72	41	97
Observationele studies	145	108	210
Totaal	263	174	**366***

in Rayyan

Zoekstrategie

Embase.com

No.	Query	Results
#11	#4 AND (#7 OR #8) NOT (#9 OR #10) = observationeel	145
#10	#4 AND #6 NOT #9 = RCT	72
#9	#4 AND #5 = SR	46
#8	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR	13928703

	'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	
#7	'major clinical study'/de OR 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'comparative study'/de OR 'cohort analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti)	6767914
#6	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	3302394
#5	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	733409
#4	#1 AND #2 AND #3 AND [01-03-2016]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	449
#3	'sensitivity and specificity'/de OR sensitivity:ab,ti OR sensitive:ab,ti OR specificity:ab,ti OR 'roc curve':ab,ti OR 'receiver operator':ab,ti OR 'receiver operators':ab,ti OR likelihood:ab,ti OR 'diagnostic error'/exp OR 'diagnostic accuracy'/exp OR 'diagnostic test accuracy study'/exp OR 'inter observer':ab,ti OR 'intra observer':ab,ti OR interobserver:ab,ti OR intraobserver:ab,ti OR validity:ab,ti OR kappa:ab,ti OR reliability:ab,ti OR reproducibility:ab,ti OR ((test NEAR/2 're-test'):ab,ti) OR ((test NEAR/2 'retest'):ab,ti) OR 'reproducibility'/exp OR accuracy:ab,ti OR 'differential diagnosis'/exp OR 'validation study'/de OR 'measurement precision'/exp OR 'diagnostic value'/exp OR 'reliability'/exp OR 'predictive value'/exp OR ppv:ti,ab,kw OR npv:ti,ab,kw OR (((false OR true) NEAR/3 (negative OR positive)):ti,ab)	4684170
#2	'physical examination'/de OR 'physical medicine'/de OR 'physiotherapy'/de OR 'physiotherapist'/de OR 'neurodynamic test'/exp OR 'medical examination'/exp OR 'movement (physiology)'/exp OR physiotherap*:ti,ab,kw OR ((medical* NEAR/3 examin*):ti,ab,kw) OR provocat*:ti,ab,kw OR movement*:ti,ab,kw OR abduction*:ti,ab,kw OR spurling*:ti,ab,kw OR 'arm squeeze test*':ti,ab,kw OR wainner:ti,ab,kw OR (test NEAR/3 cluster):ti,ab,kw OR 'neck tornado test*':ti,ab,kw OR ((tendon* NEAR/3 reflex*):ti,ab,kw) OR manipulat*:ti,ab,kw OR (((manual OR physical* OR neurodynamic OR 'neuro dynamic' OR neurolog*) NEAR/3 (measur* OR assess* OR rating* OR test* OR exam*)):ti,ab,kw) OR (((sensor* OR sensat*) NEAR/3 (impair* OR dysfunction* OR abnormal*)):ti,ab,kw) OR 'valsalva* maneuv*':ti,ab,kw OR (((elvey OR davidson* OR distraction* OR relief* OR tension OR motor OR 'upper limb' OR 'brachial plexus') NEAR/3 test*):ti,ab,kw) OR ultt*:ti,ab,kw OR	1930391

	('shoulder abduction' NEAR/3 (sign OR test*)):ti,ab,kw	
#1	'cervicobrachial neuralgia'/exp OR 'brachial plexus neuropathy'/de OR 'myeloradiculopathy'/de OR 'cervical spondylosis'/de OR 'cervical myelopathy'/exp OR cervicobrachial*:ti,ab,kw OR 'cervico brachial*':ti,ab,kw OR 'cervical brachial*':ti,ab,kw OR (((cervic* OR brachial*) NEAR/3 (neuralg* OR compress* OR radiculop* OR avulsion* OR radiculitis* OR radiculitides* OR syndrome* OR myelopath* OR spondylos* OR osteophytos* OR stenosis* OR degenerat* OR neuritis*)):ti,ab,kw) OR ((radiculalgia:ti,ab,kw OR radiculitis:ti,ab,kw OR radiculitides:ti,ab,kw OR radiculopath*:ti,ab,kw OR polyradiculopath*:ti,ab,kw OR neuralgia:ti,ab,kw OR 'herniated disc*':ti,ab,kw OR hernia:ti,ab,kw OR ((radicular NEAR/3 (pain* OR neuralgia* OR symptom* OR syndrom*)):ti,ab,kw) OR (('nerve root' NEAR/3 (pain* OR inflammation* OR disorder* OR compression* OR avulsion* OR impingement)):ti,ab,kw)) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('radicular pain'/exp/mj OR 'radiculopathy'/exp/mj) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('spinal cord compression'/de OR 'intervertebral disk hernia'/de OR 'intervertebral disk degeneration'/de OR 'stenosis'/de OR 'vertebral canal stenosis'/de OR 'spondylosis'/de OR 'radiculopathy'/de OR 'nerve root compression'/de) AND ('neck'/exp OR 'neck pain'/exp OR 'neck injury'/de OR 'cervical spine'/exp OR 'cervical plexus'/de OR 'cervical spine injury'/de OR 'cervical spinal cord'/exp OR 'cervical spinal cord injury'/exp OR 'cervical vertebral canal'/de))	41947

Ovid/Medline

#	Searches	Results
11	(4 and (7 or 8)) not (9 or 10) = observationeel	108
10	(4 and 6) not 9 = RCT	41
9	4 and 5 = SR	25
8	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or ((exp cohort studies/ or epidemiologic studies/ or multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.))	5384889
7	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies]	4395890
6	exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.	2568292
5	meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or	656938

	systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.	
4	(1 and 2 and 3 and 20160301:20230322.(dt).) not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/)	278
3	exp "Sensitivity and Specificity"/ or (sensitivity or sensitive or specificity).ti,ab. or (ROC-curve or receiver-operator*).ti,ab. or (likelihood or LR*).ti,ab. or exp Diagnostic Errors/ or (inter-observer or intra-observer or interobserver or intraobserver or validity or kappa or reliability).ti,ab. or reproducibility.ti,ab. or (test adj2 (re-test or retest)).ti,ab. or "Reproducibility of Results"/ or accuracy.ti,ab. or Diagnosis, Differential/ or Validation Studies.pt. or exp "Predictive Value of Tests"/ or ppv.ti,ab,kf. or npv.ti,ab,kf. or ((false or true) adj3 (negative or positive)).ti,ab.	3827816
2	Physical Examination/ OR Physical Therapy Specialty/ OR Physical Therapists/ OR exp Neurologic Examination/ OR physiotherap*.ti,ab,kf. OR (medical* adj3 examin*).ti,ab,kf. OR provocat*.ti,ab,kf. OR movement*.ti,ab,kf. OR abduction*.ti,ab,kf. OR spurling*.ti,ab,kf. OR 'arm squeeze test*'.ti,ab,kf. OR wainner.ti,ab,kf. OR (test adj3 cluster).ti,ab,kf. OR 'neck tornado test*'.ti,ab,kf. OR (tendon* adj3 reflex*).ti,ab,kf. OR manipulat*.ti,ab,kf. OR ((manual OR physical* OR neurodynamic OR 'neuro dynamic' OR neurolog*) adj3 (measur* OR assess* OR rating* OR test* OR exam*)).ti,ab,kf. OR (((sensor* OR sensat*) adj3 (impair* OR dysfunction* OR abnormal*)).ti,ab,kf.) OR valsalva* maneuv*.ti,ab,kf. OR (((elvey OR davidson* OR distraction* OR relief* OR tension OR motor OR 'upper limb' OR 'brachial plexus') adj3 test*).ti,ab,kf.) OR ultt*.ti,ab,kf. OR ('shoulder abduction' adj3 (sign OR test*)).ti,ab,kf.	1057190
1	exp Radiculopathy/ or Brachial Plexus Neuropathies/ or Brachial Plexus Neuritis/ or cervicobrachial*.ti,ab,kf. or 'cervico brachial*'.ti,ab,kf. or 'cervical brachial*'.ti,ab,kf. or ((cervic* or brachial*) adj3 (neuralg* or compress* or radiculop* or avulsion* or radiculitis* or radiculitides* or syndrome* or myelopath* or spondylos* or osteophytos* or stenosis* or degenerat* or neuritis*)).ti,ab,kf. or ((radiculalgia or radiculitis or radiculitides or radiculopath* or polyradiculopath* or neuralgia or 'herniated disc*' or hernia or (radicular adj3 (pain* or neuralgia* or symptom* or syndrom*)) or ('nerve root' adj3 (pain* or inflammation* or disorder* or compression* or avulsion* or impingement))).ti,ab,kf. and (exp Cervical Vertebrae/ or exp Neck/ or cervical.ti,ab,kf. or cervico*.ti,ab,kf. or neck.ti,ab,kf.)) or ((Spinal Cord Compression/ or Intervertebral Disc Displacement/ or Spinal Stenosis/ or Intervertebral Disc Degeneration/ or Spondylosis/) and (exp Neck/ or Neck Pain/ or Neck Injuries/ or exp Cervical Vertebrae/ or Cervical Plexus/ or exp Spinal Injuries/ or Cervical Cord/ or exp Spinal Cord Injuries/))	40133

5

Module 2. Conservatieve therapie

De volgende conservatieve behandelingen komen in deze richtlijn aan de orde:

- Fysiotherapie
- Corticosteroïd-injecties
- Pulsed Radiofrequency (PRF)

Module 2.1 Fysiotherapie

Uitgangsvraag

Wat is de rol van fysiotherapie bij de behandeling van patiënten met cervicaal radiculair syndroom (CRS)?

De volgende vijf deelvragen zijn hierbij geformuleerd:

2.1.1. Welke rol heeft een nekkraag in de behandeling van CRS?
2.1.2. Welke rol heeft cervicale tractie in de behandeling van CRS?
2.1.3. Welke rol heeft oefentherapie in de behandeling van CRS?
2.1.4. Welke rol heeft neuromobilisatie in de behandeling van CRS?
2.1.5. Welke rol heeft manuele therapie in de behandeling van CRS?

Inleiding

Wanneer de neurochirurg besluit om een patiënt met een CRS niet te opereren, wordt vaak gekozen voor “watchful waiting”. Er is echter grote variatie in deze afwachtende aanpak: met name wordt er niet standaard doorverwezen naar de fysiotherapeut. Momenteel is onduidelijk welke rol fysiotherapie heeft in de behandeling van patiënten met een CRS. Door fysiotherapie wordt gepoogd het natuurlijke beloop van een CRS, wat meestal gunstig is, te bespoedigen. Doel van de fysiotherapeutische behandeling is het verminderen van klachten en (daarmee) het terugkeren in de activiteiten van het dagelijks leven. In deze module worden verschillende, in recente wetenschappelijke literatuur voorgestelde, fysiotherapeutische interventies geëvalueerd.

Deze module gaat over patiënten met cervicaal radiculair syndroom. Raadpleeg bij nekpijn zonder radiculaire pijn de betreffende richtlijn.

Search and select

A systematic review of the literature was performed to answer the following question:
What is the effect of physiotherapy compared to watchful waiting and/or other forms of physiotherapy in patients with cervical radiculopathy?

P: Patients with cervical radiculopathy
I: Physiotherapy
C: C1. Usual care/ watchful waiting/ placebo or sham (passive control)
C2. Other forms of physiotherapy (active control)
O: Pain, disability, function, quality of life, return to work, psychosocial outcomes, drug consumption, adverse effects

<u>Relevant outcome measures</u>

The guideline development group considered pain, disability, function, and quality of life as a *critical* outcome measure for decision making; and return to work, drug consumption, psychosocial outcomes, and adverse effects as an *important* outcome measure for decision making.

The working group did not define the outcome measures listed above a priori, but used the definitions used in the described study.

The working group defined a 10% difference for continuous outcome measures (weighted mean difference), 10% for dichotomous outcome measures informing on relative risk ($0.91 \leq RR \geq 1.1$), and standardized mean difference (SMD=0,2 (small); SMD=0,5 (medium); SMD=0,8 (large).

Search and select (Methods)

The databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms from January 1st, 2000 until April 25th, 2022. The detailed search strategy is depicted under the Methods tab. The systematic literature search resulted in 339 hits. Studies were selected based on the following criteria:

- Systematic review and/or meta-analysis, with detailed search strategy, risk of bias assessment, and results of individual studies available; or randomized controlled trial (RCT);
- Patients aged ≥ 18 years;
- studies including ≥ 30 (15 in each study arm) patients;
- studies according to the PICO. Any type of physiotherapy performed in the Netherlands as an intervention, and described placebo/ sham, usual care, no treatment, or other forms of physiotherapy performed in the Netherlands as a comparison; and
- full-text English or Dutch language publication.

A total of 57 studies were initially selected based on title and abstract screening. After reading the full text 37 studies were excluded (see the Table with reasons for exclusion under the Methods tab), and 20 studies were included.

Results

Twenty RCTs were included in the analysis of the literature. Important study characteristics and results are summarized in the evidence tables. The assessment of the risk of bias is summarized in the risk of bias tables. The results are analysed for five different intervention types, in line with the formulated sub questions:

- cervical collar
- cervical traction
- exercise
- neurodynamic mobilisation
- manual therapy

Table 1 gives a summary of the different measures or instruments used for the assessment of analysed outcomes.

Table 1. Summary of instruments used for analysed outcome measures.

Outcome	Instrument	Abbreviation	Explanation	Scale
Pain	Visual Analog Scale	VAS	Line on which patients can indicate their pain from 0 (no pain) to 100 (worst pain imaginable)	0 to 100mm or 10cm
	Numerical (Pain) Rating Scale	NR(P)S	An 11-point numerical scale on which patients can indicate their pain from 0 (no pain) to 10 (worst pain imaginable)	0 to 10
Disability	Neck Disability Index	NDI	Ten 5-point questions, after which total score is multiplied by 2 (seldom exceptions). Disability increases with increasing score.	0 to 100 (*or seldom*: 0 to 50)
Function	Range of Motion	ROM	Measuring the mobility angles of the cervical spine with a goniometer.	-180° to 180°
	Patient-Specific Functional Scale	PSFS	Self-administered questionnaire in which patients are asked to identify three to five activities that are difficult to perform and rate them from 0 (unable to perform activity) to 10 (able to perform activity). Summed score or the average score of three is used.	0 to 10, 0 to 30 or 0 to 50
	Disabilities of Arm, Shoulder and Hand	QuickDASH	Self-administered questionnaire with 11 items (3 for symptoms, 8 for function), which can be scored from 1 (no difficulty) to 5 (extreme difficulty/unable to do). Score is calculated as {(sum of scored items/number of items)-1} x25	0 to 100
Quality of Life	Short Form 36	SF-36	A multidimensional instrument consisting of 36 questions; higher scores indicating a better health status. It can generate 2 summary scores: Physical (PCS) and Mental Component Score (MCS).	0 to 100
	EuroQoL-5D	EQ-5D	This questionnaire generates an index score based on 5 questions on quality of life, and has a VAS for current health state. Higher scores represent better (perceived) health.	Index: 0 to 1 VAS: 0 to 100
Psycho-social outcomes	Fear-avoidance beliefs questionnaire	FABQ	A questionnaire with 16 items scored on a 7-point scale, assessing the patients' fear-avoidance beliefs about how physical activity and work affect their pain. The points from all questions are summed to a total score, with higher scores indicating more fear-avoidance behaviours.	0 to 96

Submodule 2.1.1. Nekkraag

1. Cervical collar

Description of studies for treatment with a cervical collar

Two RCTs reported on outcomes after the treatment with a cervical collar. Detailed information on both studies can be found in the Evidence Table.

Aksoy (2018) investigated the effect of soft and semi-rigid cervical collars in patients with acute cervical radiculopathy. Adult patients diagnosed with cervical radiculopathy and neck pain ≥4 on a visual analog scale (VAS) were randomized into three groups: a group with a soft cervical collar plus home exercises (Group 1, n = 30), a semi-rigid cervical collar plus home exercises (Group 2, n = 26), or a home exercise-only group (Group 3, n = 29). The collars were worn 8 hours per day, every day in the first 2 weeks, after which collar time was reduced every other day by one hour; until collar wearing was discontinued after 4 weeks. The exercises consisted of cervical isometric strength, cervical mobilisation, and shoulder pro- and retraction exercises, 2 times 10 repetitions, twice a day, every day, for 6 weeks. After 6 weeks, pain intensity (through VAS), disability (through the Neck Disability Index, NDI), and quality of life (through the Short-Form 36, SF-36) were measured.

To evaluate the effectiveness of treatment with a semi-hard collar or physiotherapy, Kuijper (2009) randomized patients with recent onset (<1 month) cervical radiculopathy into either a treatment group with a semi-hard collar and advice to rest for 3 to 6 weeks (n = 69), or a treatment group with biweekly physiotherapy sessions and home exercises for 6 weeks (n = 70), or a wait-and-see group who could continue daily activities without specific treatment (n = 66). After six weeks, the outcomes assessed were neck and arm pain (VAS), disability (NDI), return to work, and drug consumption.

Results

Outcomes are assessed below for the following comparisons:

Passive comparison (C1):

- Semi-rigid collar to wait-and-see (Kuijper 2009)

Active comparison (C2):

- Semi-rigid collar to exercise (Kuijper 2009)
- Semi-rigid collar as add-on to exercise (Aksoy 2018)
- Soft collar as add-on to exercise (Aksoy 2018)
- Soft collar to semi-rigid collar (Aksoy 2018)

1a. Neck pain

Neck pain was measured by both authors with a VAS (higher scores representing more pain), at six weeks after randomization to treatment. Outcomes reported on a 100 mm scale have been converted to scores on a 10 cm scale. The different comparisons performed in the studies are shown in Figure 1a. For the studies that used more than one study arm for comparison (i.e. >2 study arms), the population in the study arm was divided by the number of comparisons in which it was used (e.g. the semi-rigid collar arm of Kuijper, 2009 is used in comparison 1.1.1. and 1.1.2., therefore the number of participants in that study arm is divided over both comparisons to prevent accounting for the same population more than once.

Due to the heterogeneity in control groups, no pooled estimate for the found results in pain was calculated.

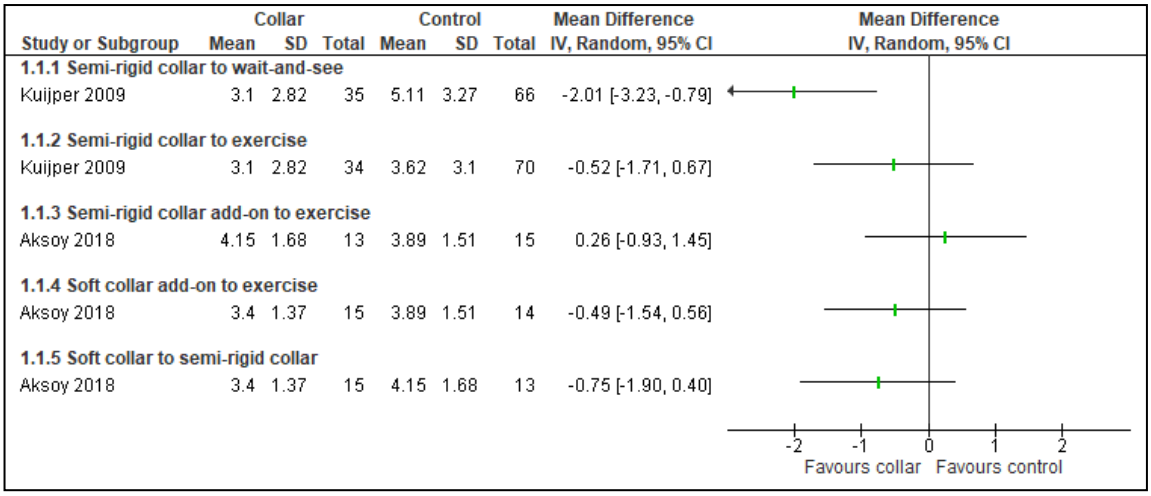

Figure 1a. *Studies comparing treatment with collar to wait-and-see (C1) or exercise/other type of collars (C2), for the outcome neck-pain (using the Visual Analog Scale, VAS).*

1b. Disability

Disability was measured by both authors using the Neck Disability Index (NDI). Disability increases with increasing score (maximum score of 100). Results are depicted in Figure 1b. For those study arms used more than once for comparison, the population is divided by the number of comparisons in which it was used. Due to the heterogeneity in comparisons and control groups, no pooled estimate was calculated.

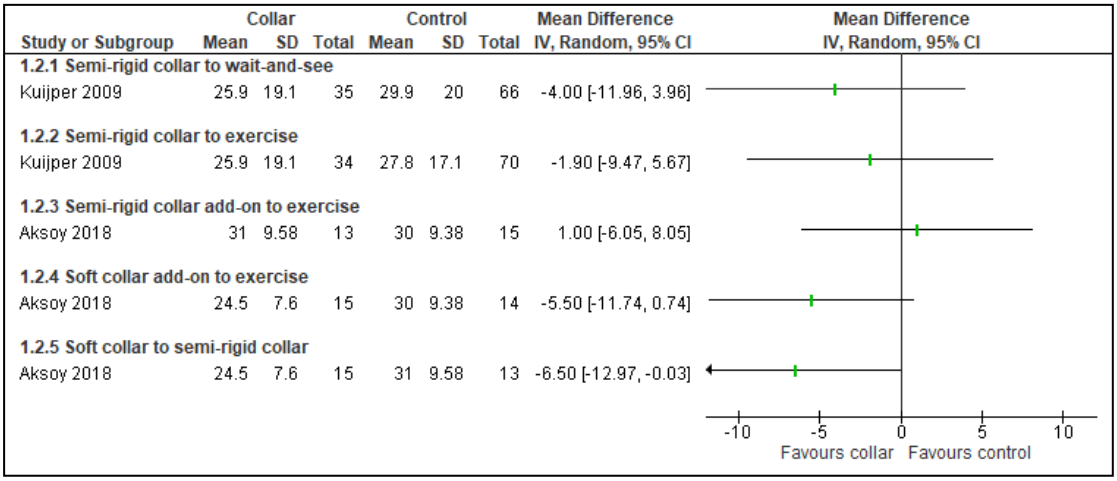

Figure 1b. *Studies comparing treatment with collar to wait-and-see (C1) or exercise/other type of collars (C2), for the outcome disability (using the Neck Disability Index, NDI).*

1c. Function

The outcome function was not reported in the studies.

1d. Quality of life

Aksoy (2018) reported on quality of life outcomes using the SF-36, which can generate two summary scores: the Physical Component Score (PCS) and Mental Component Score (MCS), on a 100-point scale.

Regarding PCS, a mean difference for the group with a semi-rigid collar as add-on to exercise – at six weeks of follow-up – was observed of -1.60 [95%CI -4.62 to 1.42] compared to the exercise-only group. For the soft collar group compared to exercise-only group, this difference was -3.80 [95%CI -6.54 to -1.06].

Regarding the MCS, a mean difference for a semi-rigid collar as add-on to exercise versus exercise only, of -2.50 [95%CI -5.40 to 0.40] at six weeks was observed. The soft collar as add-on to exercise showed only a difference of -0.60 [95%CI -3.03 to 1.83].

The mean differences between collar type (soft versus semi-rigid) were 1.90 [95%CI -0.55 to 4.35] for PCS and -2.20 [95%CI -5.14 to 0.74] for MCS. All differences in quality of life (PCS and MCS) were not clinically relevant.

1e. Return to work

Kuijper (2009) reported on partial or complete sick leave after six weeks. A no-significant difference in partial or complete sick leave of 20 (out of 68, 29%), 30 (out of 67, 45%), and 24 (out of 63, 38%) patients was observed in the collar, physiotherapy, and control group, respectively.

1f. Drug consumption

Kuijper (2009) reported on the use of opiates after six weeks. In the collar group, 13 patients (out of 68, 19%) used opiates at that time point. In the physiotherapy group, 13 patients (out of 66, 20%), and 16 patients in the control group (out of 63, 25%) used opiates, respectively. The opiate use between these groups did not differ with statistical significance.

1g. Psychosocial outcomes, 1h. Adverse effects

The outcomes psychosocial outcomes, function, and adverse effects were not reported in the studies.

Level of evidence of the literature

1a. Cervical collar: Pain (critical)

The level of evidence regarding the outcome measure **pain** was downgraded by 3 levels to *very low* because of selective outcome reporting and possible selection bias (-1, risk of bias); conflicting results and methodological heterogeneity between studies (-1, inconsistency); and the low number of included patients with the confidence intervals crossing the border of clinical relevance (-1, imprecision).

1b. Cervical collar: Disability (critical)

The level of evidence regarding the outcome measure **disability** was downgraded by 3 levels to *very low* because of selective outcome reporting and possible selection bias (-1, risk of bias); conflicting results and methodological heterogeneity between studies (-1, inconsistency); and the low number of included patients with the confidence intervals crossing the border of clinical relevance (-1, imprecision).

1c. Cervical collar: Function (critical)

The outcome function was not reported and could not be graded.

1d. Cervical collar: Quality of life (critical)

The level of evidence regarding the outcome measure **quality of life** was downgraded by 3 levels to *very low* because of inadequate allocation concealment, per protocol analysis, possible selective outcome reporting and possible selection bias (-2, risk of bias); and the inclusion of a single study with a low number of patients (-1, imprecision).

1e. Cervical collar: Return to work (important)

The level of evidence regarding the outcome measure **return to work** was downgraded by 3 levels to *very low* because of deviation from protocol in outcome reporting and possible selection bias (-1, risk of bias); and the inclusion of a single study with a low number of patients (-2, imprecision).

1f. Cervical collar: Drug consumption (important)

The level of evidence regarding the outcome measure **drug consumption** was downgraded by 3 levels to *very low* because of deviation from protocol in outcome reporting and possible selection bias (-1, risk of bias); and the inclusion of a single study with a low number of patients (-2, imprecision).

1g. Cervical collar: Psychosocial outcomes (important), 1h. Cervical collar: Adverse effects (important)

The psychosocial outcomes and adverse effects were not reported and could not be graded.

Conclusions

1a. Cervical collar: Pain (critical)

Very low GRADE	The evidence is uncertain about a difference in effect of soft or semi-rigid collars on pain, compared to a wait-and-see approach, exercise, or in addition to exercise, in patients with cervical radiculopathy. No type of collar (soft or semi-rigid) seems to be preferential over the other with regard to pain. *Source: Aksoy (2018), Kuijper (2009)*

1b. Cervical collar: Disability (critical)

Very low GRADE	The evidence is uncertain about a difference in effect of soft or semi-rigid collars on disability, compared to a wait-and-see approach, exercise, or in addition to exercise, in patients with cervical radiculopathy. A soft collar is suggested to be less debilitating than a semi-rigid collar. *Source: Aksoy (2018), Kuijper (2009)*

1c. Cervical collar: Function (critical)

- GRADE	The outcomes function was not reported and could not be graded.

1d. Cervical collar: Quality of life (critical)

Very low GRADE	The evidence is very uncertain about the effect of a soft or semi-rigid cervical collar in addition to exercise therapy on quality of life, in patients with cervical radiculopathy. *Source: Aksoy (2018)*

1e. Cervical collar: Return to work (critical)

Very low GRADE	The evidence is very uncertain about a difference in effect of a semi-rigid cervical collar compared to exercise therapy or a wait-and-see approach on sick leave, in patients with cervical radiculopathy. *Source: Kuijper (2009)*

1f. Cervical collar: Drug consumption (important)

Very low GRADE	The evidence is very uncertain about a difference in effect of a semi-rigid cervical collar compared to exercise therapy or a wait-and-see approach on opiate use, in patients with cervical radiculopathy. *Source: Kuijper (2009)*

1g. Cervical collar: Psychosocial outcomes (important), 1h. Cervical collar: Adverse effects (important)

- GRADE	The psychosocial outcomes and adverse effects were not reported and could not be graded. *Source: -*

Submodule 2.1.2. Cervicale tractie

2. Cervical traction

Description of studies for treatment with cervical traction

Five RCTs reported on outcomes after treatment with cervical traction for patients with cervical radiculopathy.

Bukhari (2016) aimed to determine the effects of mechanical and manual traction, when performed in addition to manual therapy and home exercises. Patients were randomized into a group receiving a single session of mechanical traction (n =15), applied for 10 minutes with a 10 second pull and 5 seconds rest, with 10% of body weight, or into a group receiving a single session of manual traction (n = 21), applied 10 times with a 10 second pull and 5 seconds rest. Both groups received manual therapy through segmental mobilization after the cervical traction. Patients in both groups were advised to do a home exercise program with active range of motion, stretching, and isometric strengthening exercises, 3 days a week for 6 weeks. Pain on a NRS and disability (NDI, from 0 to 50) were assessed after 6 weeks.

In Fritz (2014)'s RCT, the effectiveness of cervical traction in addition to exercises was examined. Patients were randomized into a group receiving either mechanical traction (n = 31), over-the-door traction (n = 27) or a control group receiving physiotherapy sessions (n = 28). Patients in all three groups received 10 individual physiotherapy sessions over 4 weeks, plus an active exercise program to be performed daily on the days between therapy session. Mechanical traction was performed intermittently with 60 seconds pull and 20 seconds relaxation, for 15 minutes during the individual therapy sessions, whereas continuous over-the-door traction was administered with a device for 15 minutes at home, daily on days of no physical therapy sessions. Outcome measures assessed were disability (NDI) and pain, after 4 weeks, 6 months, and 12 months.

Moustafa (2014) investigated the immediate and long-term effects of a multimodal program with the addition of two different traction approaches. All included patients received a multimodal program with pain relief methods (consisting of infrared radiation for 15 minutes, interferential therapy for 20 minutes at 100 Hz and massage); muscle strengthening exercises twice daily, which increase in duration or resistance during the treatment; and thoracic spine manipulation through thrust techniques. The control group (n = 72) received this multimodal treatment only. The ventroflexion traction group (n = 72) received in addition to the multimodal treatment intermittent traction with increasing force, and an on/off cycle of 50/10 for 20 minutes. The H-reflex based traction group (n = 72) received a similar traction protocol as the ventroflexion traction group, only with a different head posture. All interventions were performed 3 times a week for 4 weeks. Disability (NDI, scoring from 0 to 50) and pain (NRS) were assessed after 4 weeks and 12 months.

The study of Ojoawo (2018) compared the effects of cervical traction and transverse oscillatory pressure to a control group in patients with cervical radiculopathy. The control group (n = 25) received active exercises, ice packs to the cervical region for 7 minutes, and massage. A second group (n = 25) received in addition to control treatment over-the-door cervical traction with a water bath loaded to 10% of the patient's body weight, for 15 minutes. To the last group (n = 25), transverse oscillatory pressure (TOP) was administered by the therapist manually, on the side of the pain, for 3 times 20 seconds, with 2 minutes of rest in between. They also received the treatment of the control group. All interventions

were given twice a week for 6 weeks, after which pain (VAS) and disability (NDI) were assessed.

The study of Young (2009) examined the effects of manual therapy and exercise, with or without the addition of cervical traction. Consecutive patients with unilateral upper-extremity pain were randomized into a mechanical traction group (n = 45), which received intermittent traction for 15 minutes (increasing traction force per visit) with an on/off cycle of 50/10, and the cervical spine at 15 degrees flexion angle, or a sham traction group (n = 36) with equal traction protocol, yet with a maximum of 2.3 kg applied force. Both groups received sessions including: postural education; manual therapy of the upper and mid-thoracic spine through thrust- or non-thrust manipulation, after which they received non-thrust manipulation of the cervical spine (30 seconds or 15-20 repetitions); isometric and strengthening exercises of neck and shoulders. These sessions were on average 2 times per week for 4.2 weeks. In addition, patients in both groups received a home exercise program. The outcome assessment was at 4 weeks. Pain (NRS), disability (NDI, scoring from 0 to 50), function (Patient-Specific Functional Scale, PSFS) and psychosocial outcomes were measured.

Results

Outcomes are assessed below for the following comparisons:

Passive comparison (C1):

- Mechanical traction to control (Ojoawo 2018)
- Mechanical traction to control as add-on to manual therapy and exercise (Young 2009)

Active comparison (C2):

- Mechanical traction to manual therapy (Ojoawo 2018)
- Mechanical traction as add-on to manual therapy (Moustafa 2014)
- Mechanical traction as add-on to exercise(Fritz 2014)
- Mechanical traction to manual traction (Bukhari 2016)

As the focus of the research question lies on cervical traction, patients receiving different types of mechanical traction in the studies of Fritz (2014) and Moustafa (2014) have been analyzed as one intervention group.

2a. Pain

All authors reporting on cervical traction, reported on the outcome of pain, after 4 weeks (Bukhari 2016, Ojoawo 2018) or 6 weeks (Fritz 2014, Moustafa 2014, Young 2009). All scores on VAS were converted to values on a 0 to 10 scale, to enable comparison between studies. The results from the studies are presented in Figure 2a. For the traction-group of Ojoawo (2018), the population is divided by the number of comparisons in which it was used (divided over comparison 2.1.1. and 2.1.3.).

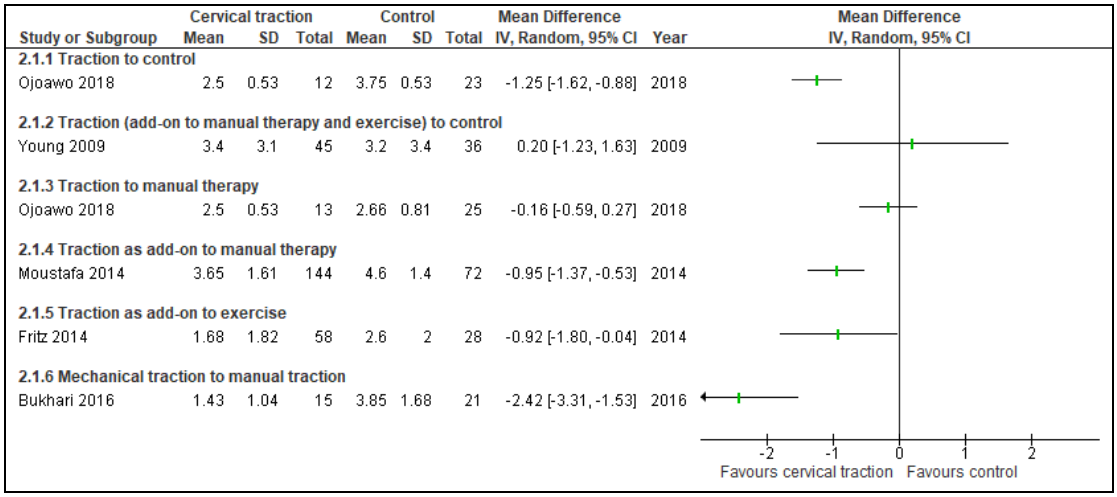

Figure 2a. *Studies comparing treatment with cervical traction to standard treatment or sham traction (C1); or manual therapy, exercise, or manual traction (C2), for the outcome pain.*

For the passive control groups (C1; comparisons 2.1.1 and 2.1.2 from figure 2a), a pooled result in mean difference of -0.70 [95% CI -2.08 to 0.68] is found. For the active control groups (C2, comparisons 2.1.3, 2.1.4 and 2.1.5), a pooled mean difference in pain score of -0.64 [95%CI -1.23 to -0.05] is calculated. Despite the latter being significant, both numbers are not clinically relevant and need to be interpreted with caution, due to the large methodological and statistical heterogeneity (I^2 = 73% and I^2 = 76%, respectively).

2b. Disability

All studies reported on disability through the NDI. Scores that have been reported on a 0 to 50 scale have been multiplied by 2 (Buhari 2016; Moustafa 2014; Young 2009), to ensure comparison with scores from 0 to 100. The results from the studies are presented in Figure 2b.

A pooled result in mean difference of NDI for passive comparison C1 of 0.46 [95% CI –-7.25 to 8.18] is found (Figure 2b; 2.2.1 and 2.2.2), and for active comparison C2 (Figure 2b; 2.2.3, 2.2.4, 2.2.5) a value of -6.18 [95% CI -20.53 to 8.17]. For this last comparison, large methodological and statistical heterogeneity are present (I^2 = 98%), with the study from Moustafa (2014) only including patients with proven discogenic complaints (possibly explaining the deviating result found in this study).

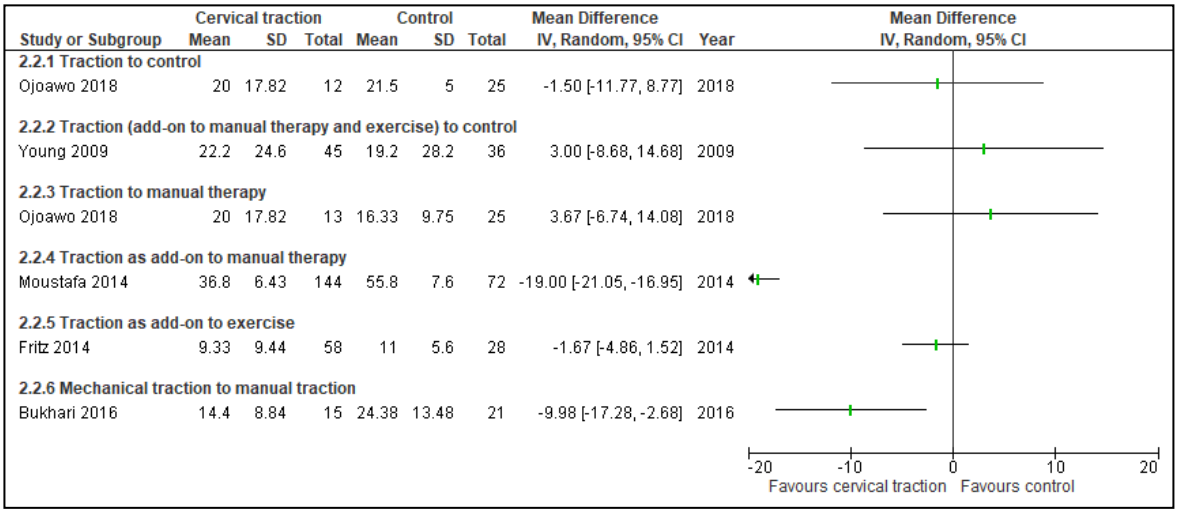

Figure 2b. *Studies comparing treatment with cervical traction to standard treatment or sham traction (C1); or manual therapy, exercise, or manual traction (C2), for the outcome disability.*

2c. Function

Results on the outcome function are presented by Young (2009), on the PSFS, using a scale from 0 to 10 (higher scores representing higher function). After 4 weeks of treatment, the traction group had a mean score of 7.0 (SD 3.8), whereas the sham-traction group scored 6.7 (SD 4.3); resulting in a mean difference of 0.29 [95%CI -1.8 to 1.2]. This difference is not statistically significant, nor clinically relevant.

2d. Quality of life, 2e. Return to work, 2f. Drug consumption

The outcomes quality of life, return to work, and drug consumption were not reported in the studies.

2g. Psychosocial outcomes

Young (2009) reported on psychosocial outcomes in both treatment groups by using the FABQ, on the physical activity and work subscale. A mean difference of -1.8 [95%CI -6.6 to 3.0] was found on the physical activity subscale in favour of traction compared to sham-traction, as higher scores denote higher levels of fear-avoidance. A mean difference of 2.9 [95% -8.1 to 13.9] was found on the work subscale (indicating that sham traction renders better results). Results of both comparisons were not statistically different, nor clinically relevant.

2h. Adverse effects

For 76 patients (88.4%), Fritz (2014) had adverse-reaction data available. A total of 43 patients (56.6%) reported at least 1 reaction perceived as treatment related; most commonly neck pain (42.1%), arm pain (25.0%) and stiffness (19.7%). Of all these reported adverse reactions, 5.6% was rated as severe. The authors report no differences among treatment groups in number, type, duration or severity of adverse reactions.

Level of evidence of the literature

2. Cervical traction

2a. Cervical traction: Pain (critical)

The level of evidence regarding the outcome measure **pain** was downgraded by 3 levels to *very low* because of possible selective outcome reporting and selection bias (-1, risk of bias); conflicting results (-1, inconsistency); and a low number of included patients with the interval of the pooled estimate crossing the border of clinical relevance (-1, imprecision).

2b. Cervical traction: Disability (critical)

The level of evidence regarding the outcome measure **disability** was downgraded by 3 levels to *very low* because of possible selective outcome reporting and selection bias (-1, risk of bias); conflicting results (-1, inconsistency); a low number of included patients with the pooled estimate crossing the border of clinical relevance and clinical difference (-1, imprecision).

2c. Cervical traction: Function (critical)

The level of evidence regarding the outcome measure **function** was downgraded by 3 levels to *very low* because of possible selection bias and possible selective outcome reporting (-1, risk of bias); and the inclusion of a single study with a low number of included patients (-2, imprecision).

2d. Cervical traction: Quality of life (critical); 2e. Cervical traction: Return to work (important); 2f. Cervical traction: Drug consumption (important)
The outcomes quality of life, return to work, and drug consumption were not reported and could not be graded.

2g. Cervical traction: Psychosocial outcomes (important)
The level of evidence regarding the outcome measure **psychosocial outcomes** was downgraded by 3 levels to *very low* because of possible selection bias and possible selective outcome reporting (-1, risk of bias); and a low number of included patients with the interval of the estimate crossing a border of clinical relevance (-2, imprecision).

2h. Cervical traction: Adverse effects (important)
The level of evidence regarding the outcome measure **adverse effects** was downgraded by 3 levels to *very low* because of large loss of follow-up and possible selective outcome reporting (-1, risk of bias); and the inclusion of a single study with a low number of included patients (-2, imprecision).

Conclusions

2a. Cervical traction: Pain (critical)

Very low GRADE	The evidence is uncertain about cervical traction decreasing pain in patients with cervical radiculopathy, and this effect tends to diminish when additional treatment approaches (such as manual therapy or exercise) are adopted. The evidence is very uncertain whether mechanical traction is preferential over manual traction. *Source: Bukhari (2016), Ojoawo (2019), Fritz (2014), Moustafa (2014), Young (2009)*

2b. Cervical traction: Disability (critical)

Very low GRADE	The evidence is uncertain that cervical traction has any clinically relevant effect on disability, compared with other treatments or as add-on to other treatments. The evidence is very uncertain about the preference of mechanical traction over manual traction. *Source: Bukhari (2016), Ojoawo (2019), Fritz (2014), Moustafa (2014), Young (2009)*

2c. Cervical traction: Function (critical)

Very low GRADE	The evidence is very uncertain about the effect of a multimodal program with intermittent cervical traction compared to a similar program with sham traction on self-reported functioning, in patients with cervical radiculopathy. *Source: Young (2009)*

2d. Cervical traction: Quality of life (critical); 2e. Cervical traction: Return to work (important); 2f. Cervical traction: Drug consumption (important)

- GRADE	The outcomes quality of life, return to work, and drug consumption were not reported and could not be graded.

2g. Cervical traction: Psychosocial outcomes (important)

Very low GRADE	The evidence is very uncertain about the effect of a multimodal program with intermittent cervical traction compared to a similar program with sham traction on fear-avoidance beliefs, in patients with cervical radiculopathy. *Source: Young (2009)*

2h. Cervical traction: Adverse events (important)

Very low GRADE	The evidence is very uncertain about the occurrence of adverse events, which seem frequent but mild, in patients with cervical radiculopathy receiving cervical traction as add-on to an exercise program, compared to an exercise program only. *Source: Young (2009)*

5

Submodule 2.1.3. Oefentherapie

3. Exercise

Description of studies on exercise

Three studies reported on outcomes after exercise treatment.

On the study of Kuijper (2009) has been elaborated above in the collar section, as one treatment arm received a cervical collar. One other group served as a control group without specific treatment, and one treatment arm received physiotherapy with a focus on mobilising and stabilising the cervical spine. This group received guided physiotherapy sessions consisting of hands-off graded activity exercises to strengthen the neck muscles, twice a week for 6 weeks. In addition, physiotherapists educated the patients on home exercises, which had to be practiced every day. Pain, disability, return to work and drug consumption were measured after 6 weeks; the comparison between the exercise group and control group is described in this section.

Diab (2012) investigated the effect of forward head posture correction in patients with cervical spondylotic radiculopathy. Patients with unilateral radiculopathy (in C5-C6 or C6-C7) and a craniovertebral angle ≤ 50 degrees were randomly assigned to an exercise group (n = 48) or a control group (n = 48). Both groups received 10 weeks of infrared radiation on the neck for 10 minutes, followed by continuous ultrasound application on the upper trapezius for 10 minutes, 3 times a week. The exercise group received an additional posture-corrective exercise program during those 10 weeks for 4 times a week, with 3 sets of 12 repetitions of two different strengthening exercises, and three stretching exercises to be held for 30 seconds each. Pain was measured using VAS after 10 weeks.

Dedering (2018) compared the effects of a neck-specific training program to prescribed physical activity. Patients with cervical radiculopathy were randomized into eighter a neck-specific training program (n = 72) or prescribed physical activity (n = 72). The neck-specific training program consisted of 3 sessions per week during 3 months. The program started with gentle isometric neck movement, gradually progressing to low-load endurance training, individually tailored based on the patient's response. The patients were also provided with a manual on the neck-specific training program including instructions for progression. The other randomization group received prescribed physical activity, which comprised of an individual counselling session, after which written recommendations were given on aerobic and/or muscular physical activity (not neck-specific), for 3 times per week 30 minutes, during 3 months. In addition, both groups received information folders with the elements of the intervention: pain physiology, consequences of stress and exercise, relaxation techniques, coping strategies, and ergonomic advice. The follow-up was 24 months. Neck pain (VAS), disability (NDI, expressed as a percentage from 0 to 100), quality of life (using the EuroQol-5D (EQ-5D)), and psychosocial outcomes (Fear-avoidance beliefs questionnaire (FABQ)) were all measured at baseline and after 3, 6, 12, and 24 months.

Results

Outcomes are assessed below for the following comparisons:

Passive comparison (C1):

- Exercise to wait-and-see/control (Kuijper 2009, Diab 2012)

Active comparison (C2):

- Exercise to other forms of exercise (Dedering 2018)

Note that the comparison of collar to exercise from the study of Kuijper (2009) has been addressed in the collar-section. From the article of Dedering (2018), results after 3 months are analyzed, to increase comparability in follow-up time with the articles of Kuijper (2009) and Diab (2012).

3a. Pain

All authors assess pain through VAS. Kuijper (2009) and Diab (2012) compared an exercise intervention to a passive control group (C1) at 6 and 10 weeks respectively, whereas Dedering (2018) compared a specific training programme to another physical exercise intervention (C2) after 3 months. The different comparisons performed in the studies are shown in Figure 3a, with a pooled estimate for the comparison of exercise to a passive control group. It shows a statistically significant but not clinically relevant difference in VAS score for exercise compared to passive control (C1), and no difference between different forms of exercise (C2).

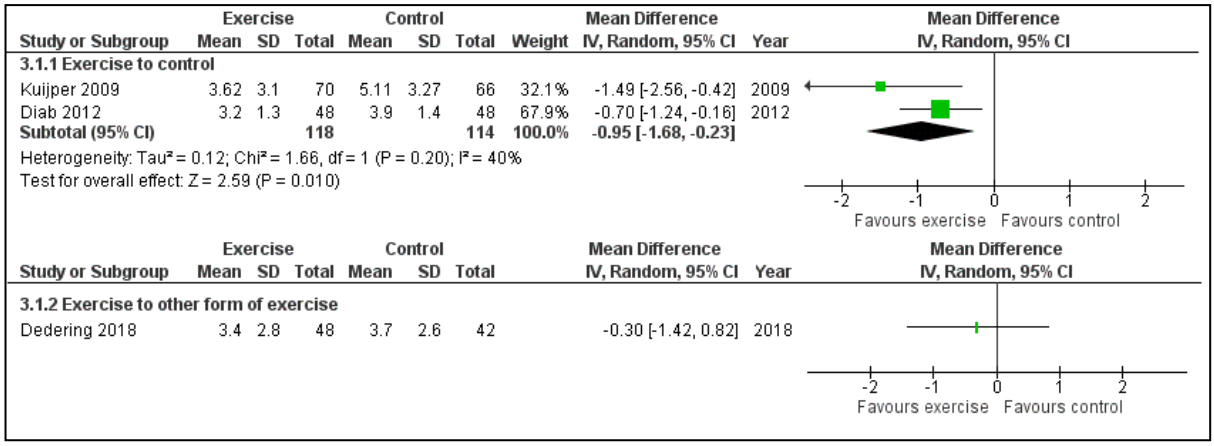

Figure 3a. *Studies comparing exercise to passive control (C1) or exercise (C2), for the outcome pain (using the Visual Analog Scale, VAS).*

3b. Disability

Both Kuijper (2009) and Dedering (2018) assessed disability using the NDI, at six weeks and three months, respectively. No statistically significant or clinical relevant difference was found between exercise and control groups, or neck-specific training and prescribed physical activity groups. No pooled estimate was calculated as only two studies with different comparisons reported outcomes on disability.

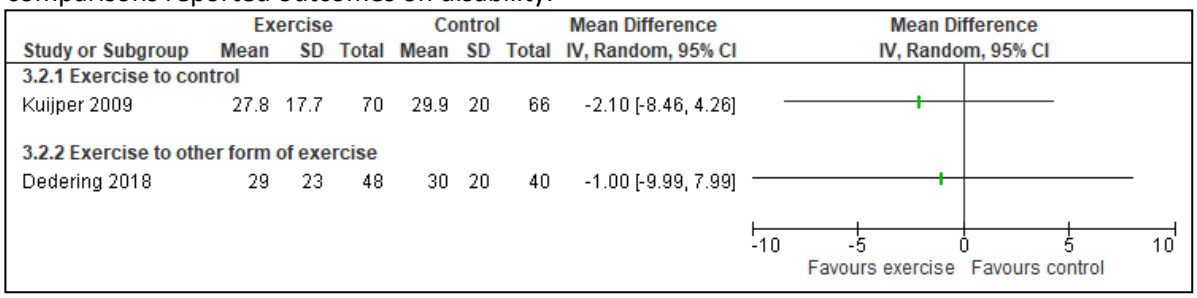

Figure 3b. *Studies comparing exercise to passive control (C1) or exercise (C2), for the outcome disability (using the Neck Disability Index, NDI).*

3c. Function

The outcome function was not reported in the studies.

3d. Quality of Life

Measured using the EQ-5D, Dedering (2018) reported on the outcome quality of life over time. This questionnaire generates an index score (from 0 to 1, representing full health), and

a VAS for current health state from worst imaginable (0) to best imaginable (100). For the neck-specific training group, the mean index score increases from 0.49 (SD ±0.34) at baseline to 0.64 (SD ±0.31) at 3 months. For the prescribed physical activity group, the index score increases from 0.56 (SD ±0.30) to 0.65 (SD ±0.31). The difference at 3 months (calculated with a mixed-model ITT analysis) is -0.03 [95%CI -0.15 to 0.09]. The VAS for current health shows a similar trend, with a mean difference at 3 months of -4 [95%CI -13 to 5]. Similar results (not statistically significant, nor clinically relevant) were found after 24 months of follow-up.

3e. Return to work

Kuijper (2009) reported on partial or complete sick leave after six weeks; results are presented under heading 1d.

3f. Drug consumption

Kuijper (2009) reported on the use of opiates after six weeks; results are presented under heading 1e.

3g. Psychosocial outcomes

Dedering (2018) measured psychosocial outcomes with the FABQ, with higher scores indicating higher levels of fear-avoidance beliefs. The score decreased for the neck-specific training group from 33 (SD ±16) to 29 (SD ±17) after 3 months, and from 29 (SD ±14) to 26 (SD ±14) in the prescribed physical activity group, resulting in a mean difference through a mixed-model ITT analysis of 6 [95%CI 0 to 12]. This difference became slightly smaller after 24 months, when a mean difference of 3 [95%CI -3 to 10] was found. These findings are not statistically significant nor clinically relevant.

3h. Adverse events

The outcome adverse events was not reported.

<u>Level of evidence of the literature</u>

3a. Exercise: Pain (critical)

The level of evidence regarding the outcome measure **pain** was downgraded by 3 levels to *very low* because of selective outcome reporting and high drop-out rates (-1, risk of bias); heterogeneity (-1, inconsistency); and a low number of included patients with the confidence intervals crossing the border of clinical relevance (-1, imprecision).

3b. Exercise: Disability (critical)

The level of evidence regarding the outcome measure **disability** was downgraded by 2 levels to *low* because of deviation from protocol in outcome reporting and high drop-out rates (-1, risk of bias); and a low number of included patients (-1, imprecision).

3c. Exercise: Function (critical)

The outcome function was not reported and could not be graded.

3d. Exercise: Quality of life (critical)

The level of evidence regarding the outcome measure **quality of life** was downgraded by 3 levels to *very low* because of a high drop-out rate and selective outcome reporting (-1, risk of bias); the control group receiving exercise treatment as well (yet in another form) (-1, bias due to indirectness); and the inclusion of a single study with a low number of patients with the confidence intervals crossing the border of clinical relevance (-1, imprecision).

3e. Exercise: Return to work (important)
The level of evidence regarding the outcome measure **return to work** was scored similar to outcome 1d. The level of evidence was *very low*.

3f. Exercise: Drug consumption (important)
The level of evidence regarding the outcome measure **drug consumption** was scored similar to outcome 1e. The level of evidence was *very low*.

3g. Exercise: Psychosocial outcomes (important)
The level of evidence regarding the outcome measure **psychosocial outcomes** was downgraded by 3 levels to *very low* because of a high drop-out rate and selective outcome reporting (-1, risk of bias); the control group receiving exercise treatment as well (yet in another form) (-1, bias due to indirectness); and the inclusion of a single study with a low number of patients with the confidence intervals crossing the border of clinical relevance (-2, imprecision).

3h. Exercise: Adverse effects (important)
The outcome adverse effects was not reported and could not be graded.

Conclusions

3a. Exercise: Pain (critical)

Low GRADE	The evidence suggests that exercise might have a beneficial effect on pain, compared to regular treatment or a wait-and-see approach in patients with cervical radiculopathy. A neck-specific training program does not seem preferential over individualized prescribed physical activity. *Source: Dedering (2018), Diab (2012), Kuijper (2009)*

3b. Exercise: Disability (critical)

Low GRADE	The evidence suggests that (specific forms of) exercise has no additional positive effect on disability, compared to a wait-and-see approach or other forms of exercise in patients with cervical radiculopathy. *Source: Dedering (2018), Kuijper (2009)*

3c. Exercise: Function (critical)

- GRADE	The outcome function was not reported and could not be graded.

3d. Exercise: Quality of life (critical)

Very low GRADE	The evidence is very uncertain about the effect of a neck-specific training program compared to individualized prescribed physical activity on quality of life, in patients with cervical radiculopathy. *Source: Dedering (2018)*

3e. Exercise: Return to work (critical)

Very low GRADE	The evidence is very uncertain about a difference in effect of exercise therapy compared to a cervical collar or a wait-and-see approach on sick leave, in patients with cervical radiculopathy. *Source: Kuijper (2009)*

3f. Exercise: Drug consumption (important)

Very low GRADE	The evidence is very uncertain about a difference in effect of exercise therapy compared to a cervical collar or a wait-and-see approach on opiate use, in patients with cervical radiculopathy. *Source: Kuijper (2009)*

3g. Exercise: Psychosocial outcomes (important)

Very low GRADE	The evidence is very uncertain about the effect of a neck-specific training program compared to individualized prescribed physical activity on fear-avoidance beliefs, in patients with cervical radiculopathy. *Source: Dedering (2018)*

3h. Exercise: Adverse effects (important)

- GRADE	The outcome adverse effects was not reported and could not be graded. *Source: -*

Submodule 2.1.4. Neurodynamische mobilisatie

4. Neurodynamic mobilisation

Description of studies on neurodynamic mobilisation

In the study of Ayub (2019), the role of active versus passive upper extremity neurodynamic mobilisation was determined. To this end, female patients between 30 and 50 years of age and with neck pain for 6 months or more were randomized into passive neurodynamic mobilisation treatment or active neurodynamic mobilisation treatment. The passive neurodynamic mobilisation treatment (n = 22) consisted of moist heat packs for 10 minutes, followed by mechanical traction of the cervical spine for 15 minutes. Also 3 sets of slow gentle segmental mobilisation (unilateral posterior anterior glide) with 15-20 repetitions were performed. In the active neurodynamic mobilisation, only 6 to 8 repetitions of active upper extremity neurodynamic mobilisation were performed. After 4 weeks of 3 treatment sessions per week, pain (NRS), disability (NDI, scale not reported), and cervical ROM were measured.

Basson (2020) aimed to establish the effect of neurodynamic mobilisation in patients with nerve related neck and arm pain. Adult patients with a recent onset of pain (≤ 12 weeks) and with a positive upper limb neurodynamic test were randomized with a 1:2 ratio into the usual care group (n = 26) or the neurodynamic mobilisation plus usual care group (n = 60). Usual care consisted of (unilateral) posterior-anterior mobilisation of the cervical an thoracic spine, exercises and the advice to stay active. The neurodynamic mobilisation group received in addition neurodynamic mobilisation along the tract of the nerve, directly and indirectly, concentrating on areas where the nerve is mechano-sensitive to palpation. From hand or elbow up along the arm, first rib, scalene and into the neck, first in a non-tensioned position, progressing into a more tensioned position as pain and irritability improved. The number of treatments was determined by the treating physiotherapist, resulting in a mean number of treatments for both groups of 4. After 6 weeks, pain (NRS), function (PSFS), and quality of life (EQ-5D) were assessed.

The RCT of Ibrahim (2021) aimed to determine the efficacy of tensioning neurodynamic mobilisation techniques on neck and arm pain. To this end, patients aged 20 to 40 years with a history of cervical radiculopathy of > 3 months, were randomized into a control treatment arm (n = 20) or the tensioning neurodynamic mobilisation technique arm (n = 20). The control treatment group received traditional physiotherapy, which in this case comprised infrared radiation for 20 minutes on the neck, and manual cervical traction, with a 15 second pull and 30 second rest, for 3 sets of 10 repetitions. The intervention group received in addition tensioning neurodynamic mobilisation of the brachial plexus: with the arm in neurodynamic testing position, 10 cycles of elbow extension and flexion (each 3 seconds) were administered. Both treatments were performed for 3 sessions per week, over the course of 3 weeks, after which pain (VAS) was assessed.

Kayiran (2021) investigated the efficacy of neurodynamic mobilisation combined with conservative physiotherapy on cervical posture and pain in patients with cervical disc herniation, for whom surgery was not recommended by the neurosurgeon. Randomization took place, into either the intervention treatment or control treatment. The control treatment study arm (n = 35) received 3 weeks conservative physiotherapy with 5 sessions per week, with hotpacks for 20 minutes, transcutaneous nerve stimulation (TENS) for 20 minutes at 100 Hz, continuous mode ultrasound for deep heating for 5 minutes at 1 MHz, and 10 times 5-second exercises for stretching and strengthening. The intervention treatment arm (n = 36) received in addition to the 5-weekly conservative therapy sessions

for 3 weeks, also neurodynamic mobilisation on radial, median and ulnar nerves, 10 times 10 seconds for each nerve, for a total of 10 sessions over 3 weeks. After the treatment period, pain (VAS), disability (NDI, scale not reported), and cervical ROM were assessed on the patients that had not dropped out (n = 60).

Kim (2017) examined the effects of neurodynamic mobilisation as add-on to manual cervical traction compared with manual cervical traction alone on pain, disability, and ROM. A total of 30 patients were randomized to receive either conservative physiotherapy (consisting of hot packs for 20 minutes and TENS at 60 Hz for 15 minutes) plus manual cervical traction (6 repetitions of 1 minute pull with 30 seconds rest), (n =15), or the intervention treatment (n = 15) in which, in addition to conservative physiotherapy and manual traction, neurodynamic mobilisation was applied. Neurodynamic mobilisation was administered during the manual cervical traction, using a slider technique for the median nerve in a smooth and rhythmic manner (with elbow extension/flexion and wrist flexion/extension), for 6 times 1 minute with 30 seconds rest in between. Both groups received 8 week treatment, with 3 sessions per week. After 4 and 8 weeks, the authors assessed pain (NRS), disability (NDI, on a 0 to 50 scale), and cervical ROM.

The study of Rodriguez-sans (2017) assessed the effect of a cervical lateral glide neural mobilisation, compared to no treatment. Consecutive patients seeking treatment for unilateral cervicobrachial pain (confirmed by MRI), existing for > 3 months, were randomized into a waiting list group (n = 29) or a cervical lateral glide neural mobilisation group (n = 29). In the latter, patients received neurodynamic mobilisation administered by a physiotherapist to the contralateral side of the pain, in a slow oscillating manner, continuously for 2 minutes. A total of 5 consecutive applications was performed, with one minute rest in between. Patients received neurodynamic mobilisation for 5 days a week, over the course of 6 weeks. After 6 weeks, the outcomes assessed were pain (NRS) and function (on quick-Disability of Arm, Shoulder and Hand questionnaire, QuickDASH, and through measurement of ipsilateral cervical rotation).

Savva (2016) investigated the effect of neurodynamic mobilisation with simultaneously applied intermittent cervical traction on various outcomes. Consecutive patients with unilateral cervical radiculopathy confirmed by MRI or CT, who were referred to the physiotherapy department, were randomized into the intervention or control group. The intervention group (n = 21) received 3 weekly sessions for 4 weeks of intermittent, pain-free cervical traction with a 1-minute pull and 1 minute rest, for 6 sets. During the cervical traction, slider neurodynamic mobilisation using a median nerve bias was applied. This in contrast to the control group (n = 21), in which patients did not receive any type of treatment. Both groups were asked to avoid prescription or over-the counter analgesia or anti-inflammatory medications. After 4 weeks, pain (NRS), disability (NDI), and function (PSFS and cervical ROM) were assessed.

Savva (2021) evaluated the effects of cervical traction, with or without the addition of neurodynamic mobilisation, on pain, function and disability. Three groups were created consisting of consecutive patients with unilateral cervical radiculopathy, aged 20 to 75 years. The first group (n = 22) received cervical traction for 10 sets of a 1-minute pull and 30 seconds rest, with simultaneous neurodynamic mobilisation of the median nerve through passive elbow, wrist, and finger flexion and extension. The second group (n = 22) received similar cervical traction, yet sham neurodynamic mobilisation was administered through sustained elbow and wrist position, with only flexion and extension of the fingers. Both groups received 3 treatment sessions per week, for 4 weeks. The third group (n = 22) was

randomized to the waiting list without any type of treatment for 4 weeks. After that, pain (NRS), disability (NDI, scale 0 to 50), and function (PSFS and cervical ROM) were analyzed.

Results

Outcomes are assessed below for the following comparisons:

Passive comparison (C1):

- Neural mobilisation to waiting list (Rodriguez-sans 2017)
- Neural mobilisation plus cervical traction to waiting list (Savva, 2016; Savva 2021)
- Neural mobilisation to control (sham), as add-on to cervical traction (Savva, 2021)

Active comparison (C2):

- Neural mobilisation as add-on to cervical traction (Ibrahim 2021, Kim 2017)
- Neural mobilisation as add-on to exercise (Kayiran 2021)
- Neural mobilisation as add-on to manual therapy (and exercises) (Basson 2020)
- Active neural mobilisation to passive neural mobilisation (Ayub 2019)

4a. Pain

All authors researching neurodynamic mobilisation, reported on pain outcomes through the NRS or VAS. Either after 3 weeks (Ibrahim 2021, Kayiran 2021), after 4 weeks (Ayub 2019, Kim 2017, Savva 2016, Savva 2021), or after 6 weeks (Basson 2020, Rodriguez-sans 2017). All scores on VAS were converted to values on a 0 to 10 scale, to enable comparison between studies.

The results of the study of Ayub (2019) are reported in median with interquartile range, for which the mean and SD are calculated according to Wan (2014). Ibrahim (2021) reports median and range, for which the mean is calculated from Hozo (2005), and SD from Walter & Yao (2007).

The different comparisons from the studies are shown in Figure 4a. For those arms used more than once for comparison (Savva, 2021), the population is divided by the number of comparisons in which it was used.

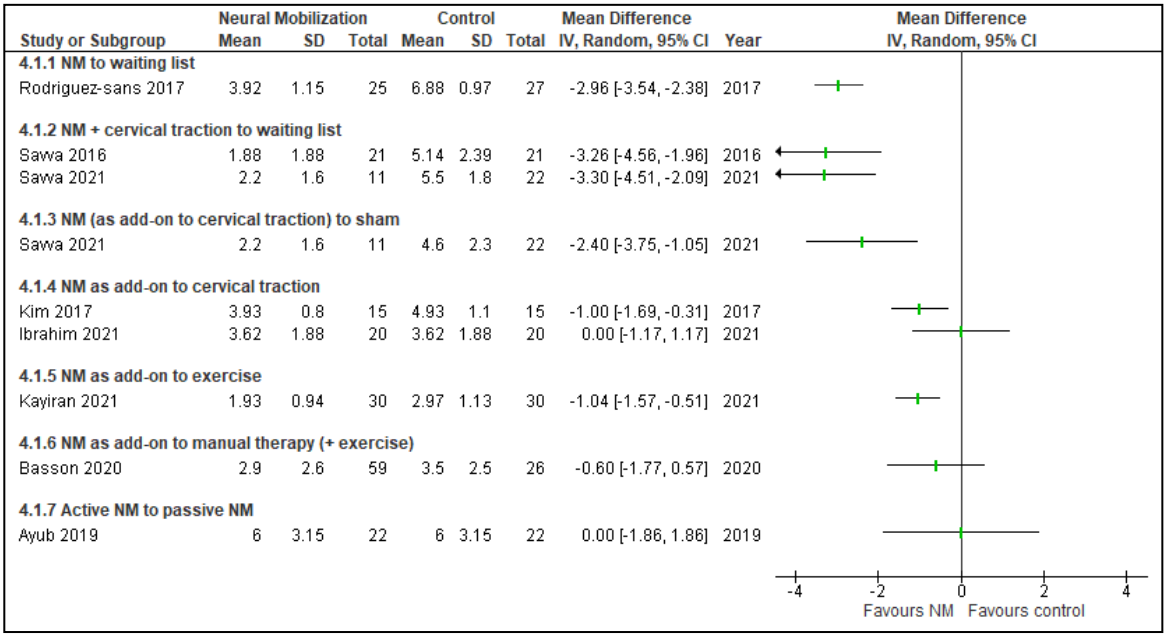

Figure 4a. *Studies comparing neurodynamic mobilisation to control treatment or sham (C1) or to other forms of treatment (C2), for the outcome pain.*

The passive comparison C1 (Figure 4a; 4.1.1, 4.2.1, 4.1.3) resulted in a mean difference of -2.98 [95%CI -3.44 to -2.52]. This difference is statistically significant and clinically relevant. The active comparison C2 (Figure 4a; 4.1.4, 4.1.5, 4.1.6) resulted in a mean difference -0.88 [95%CI -1.25 to -0.5]. This difference is statistically significant, but not clinically relevant.

4b. Disability

Five studies reported disability results using the NDI, yet two studies did not define which scale NDI was used and are therefore excluded from this analysis (Ayub 2019, Kayiran 2021). The other three studies reported on a scale from 0 to 50 (Kim 2017, Savva 2021) or from 0 to 100 (Savva 2016); the former two converted to a 0 to 100 scale. All scores are measured after 4 weeks, which are presented in Figure 4b.

The studies comparing neurodynamic mobilisation to control treatment (C1; Savva 2016, Savva 2021) resulted in a mean difference of -22.75 [95%CI -39.5 to -6.0], both statistically significant and clinically relevant.

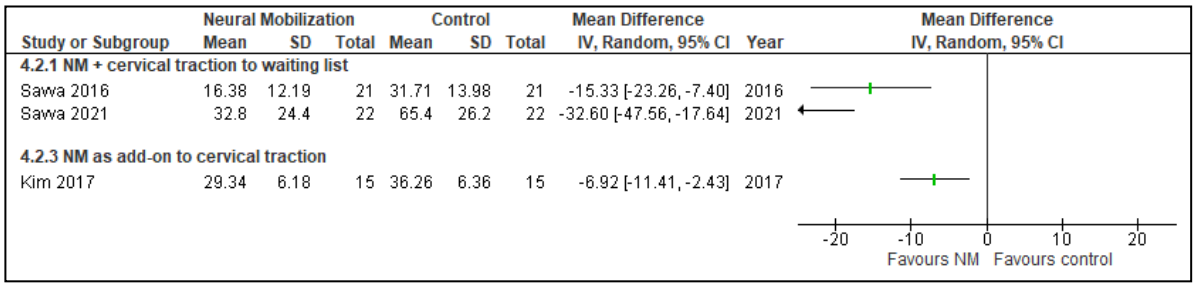

Figure 4b. *Studies comparing neurodynamic mobilisation to control treatment (C1) or to other forms of treatment (C2), for the outcome disability.*

4c. Function

Cervical Range of Motion (ROM)

Six studies reported on ROM (measured with a goniometer) for cervical movements (Ayub 2019, Kayiran 2021, Kim 2017, Rodriguez-sans 2017, Savva 2016, Savva 2021). However, as Ayub (2019) reported medians with interquartile range not seeming to correspond with the

values found by other authors, the results of the study are not taken into account when calculating the pooled values. Found ROM values are shown in Table 4.

All authors comparing neurodynamic mobilisation to active treatment (C2) (Ayub 2019, Kayiran 2021, Kim 2017), show increasing values in ROM for both the intervention and control group, whereas studies comparing neurodynamic mobilisation with passive treatment (C1, waiting list) (Rodriguez-sans 2017, Savva 2016, Savva 2021), patients in the control group seem to have a decreased cervical ROM after follow-up.

Patient-specific Functional Scale (PSFS)

Three studies reported functional outcomes on the PSFS, either on a scale from 0 to 10 (Savva 2016, Savva 2021), or on a scale from 0 to 30 (Basson 2020), with higher scores representing higher function. A standardized mean difference is reported in Figure 4f.

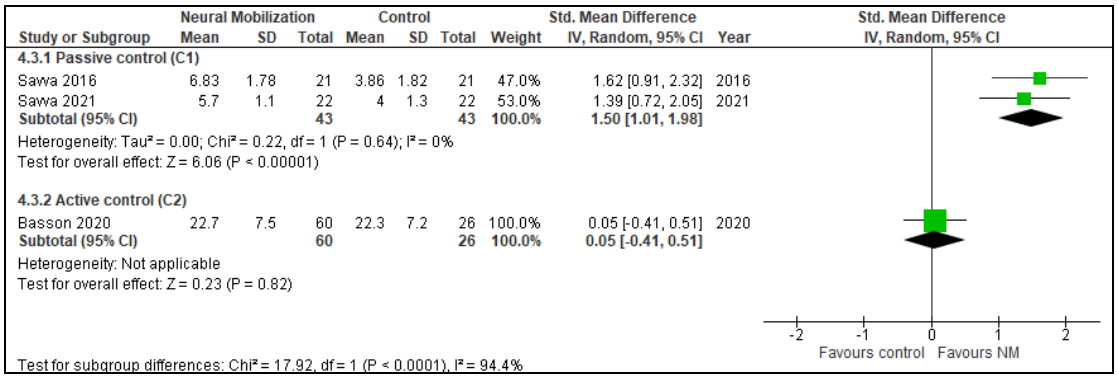

Figure 4c. *Studies comparing neurodynamic mobilisation to control treatment (C1) or to other forms of treatment (C2), for the outcome function on the PSFS.*

Quick Disability of Arm, Shoulder and Hand (QuickDASH)

Rodriguez-sans (2017) reported on function and symptoms of the upper limb through the QuickDASH. After 6 weeks of treatment, the score in the waiting list control group barely decreased (from 58.7 ± 9.5 to 58.6 ± 9.4), whereas a >30% decrease was observed in the cervical lateral glide group (from 56.6 ± 8.9 to 37.1 ± 11.4). This resulted in a statically significant and clinically relevant mean difference of -21.5 [95%CI -27.4 to -15.73].

4d. Quality of Life

Basson (2020) measured quality of life through the EQ-5D after 6 weeks of treatment. Score in quality of life increased similarly in the usual care and neurodynamic mobilisation group, from 72.4 ± 15.8 to 83.0 ± 11.8 and from 72.4 ± 19.6 to 84.1 ± 11.1, respectively. This resulted in a non-significant mean difference of 1.1 in favour of the neurodynamic mobilisation group [95%CI -4.3 to 6.3]. After 12 months, this difference increased slightly, yet remained non-significant.

4e. Return to work, 4f. Drug consumption, 4g. Psychosocial outcomes, 4h. Adverse effects

The outcomes return to work, drug consumption, psychosocial outcomes, and adverse effects were not reported in the studies.

Table 4. Studies comparing neural mobilisation to control treatment or sham (C1) or to other forms of treatment (C2), for the outcome Range of Motion (ROM) in degrees.

Study	Comparison	ROM mean difference [95%CI]					
				Side bending		Rotation	
		Flexion	Extension	Ipsilateral (or right*)	Contralateral (or left*)	Ipsilateral (or right*)	Contralateral (or left*)
C1							
Rodriguez-sans, 2017	neurodynamic mobilisation to waiting list	N.R.	N.R.	N.R.	N.R.	8.0 [4.9 to 11.1]	N.R.
Savva, 2016	neurodynamic mobilisation plus cervical traction to waiting list	5.7 [0.5 to 11.0]	8.8[-0.5 to 18.1]	6.4 [1.6 to 11.1]	6.0 [1.5 to10.4]	7.9 [1.5 to 14.3]	10.6 [3.6 to 17.6]
Savva, 2021		5.9 [0.8 to 11.0]	5.8 [-3.1 to 14.7]	6.2 [1.4 to 11.1]	6.3 [2.2 to 10.4]	8.7 [1.7 to 15.7]	13.5 [6.7 to 20.3]
Pooled result		*5.8 [2.2 to 9.5]*	*7.2 [0.8 to 13.6]*	*6.3 [2.9 to 9.7]*	*6.2 [3.2 to 9.2]*	*8.1 [5.5 to 10.7]*	*12.1 [7.2 to 17.0]*
C2							
Kayiran, 2021	neurodynamic mobilisation as add-on to exercise	3.9 [1.1 to 6.7]	6.2 [3.0 to 9.5]	4.4 [1.5 to 7.3]*	5.6 [2.6 to 8.6]*	-0.7 [-5.3 to 3.8]*	-0.3 [-5.4 to 4.8]*
Kim, 2017	neurodynamic mobilisation as add-on to cervical traction	3.3 [0.3 to 6.4]	5.1 [2.2 to 8.0]	2.6 [0.7 to 4.5]*	2.4 [0.9 to 3.9]*	2.4 [0.3 to 4.5]*	3.6 [1.8 to 5.4]*
Pooled result		*3.6 [1.6 to 5.7]*	*5.6 [3.4 to 7.8]*	*3.2 [1.6 to 4.7]*	*3.0 [1.7 to 4.3]*	*1.5 [-1.3 to 4.3]*	*2.4 [-1.1 to 5.9]*
Ayub, 2019	Active neuromobilisation to passive neuromobilisation^	-10.0 [-20.8 to 0.8]	0 [-10.2 to 10.2]	-7.5 [-19.7 to 4.7]*	-7.5 [-19.9 to 4.9]*	5.0 [-3.2 to 13.2]*	-5.0 [-10.6 to 0.6]*

** right or left instead of ipsilateral or contralateral.*

^calculated mean difference based on medians with interquartile range (not taken into account in pooled results).

Level of evidence of the literature

4a. Neurodynamic mobilisation: Pain (critical)

The level of evidence regarding the outcome measure **pain** was downgraded by 3 levels to *very low* because of possible selection bias and selective or biased outcome reporting in some studies (-1, risk of bias); heterogeneity in methodology and results (-1, inconsistency); and intervals of estimates crossing the border of clinical relevance and clinical difference (-1, imprecision).

4b. Neurodynamic mobilisation: Disability (critical)

The level of evidence regarding the outcome measure **disability** was downgraded by 3 levels to *very low* because of possible selective outcome reporting (-1, risk of bias); and a low number of included studies and patients (-2, imprecision).

4c. Neurodynamic mobilisation: Function (critical)

The level of evidence regarding the outcome measure **function** was downgraded by 3 levels to *very low* because of possible selection bias and selective or biased outcome reporting in some studies (-1, risk of bias); methodological heterogeneity (-1, inconsistency); and the intervals of pooled estimates crossing the border of clinical relevance (-1, imprecision).

4d. Neurodynamic mobilisation: Quality of life (critical)

The level of evidence regarding the outcome measure **quality of life** was downgraded by 3 levels to *very low* because of an early stop in recruitment of patients (-1, risk of bias); and the inclusion of a single study with a low number of included patients (-2, imprecision).

4e. Neurodynamic mobilisation: Return to work (important); 4f. Neural mobilisation: Drug consumption (important); 4g. Neurodynamic mobilisation: Psychosocial outcomes (important); 4h. Neurodynamic mobilisation: Adverse effects (important)

The outcomes return to work, drug consumption, psychosocial outcomes and adverse effects were not reported and could not be graded.

Conclusions

4a. Neurodynamic mobilisation: Pain (critical)

Very low GRADE	The evidence is uncertain about the effect of neurodynamic mobilisation on pain, yet a stronger positive effect of neurodynamic mobilisation on pain is found when compared to passive controls (C1), and a neutral effect on pain when compared to active controls (C2), in patients with cervical radiculopathy. The evidence is very uncertain whether active neurodynamic mobilisation is preferential over passive neural mobilisation. *Source: Ayub (2019), Basson (2020), Ibrahim (2021), Kayiran (2021), Kim (2017), Rodriguez-sans (2017), Savva (2016), Savva (2021)*

4b. Neurodynamic mobilisation: Disability (critical)

Very low GRADE	The evidence is uncertain about the effect of neurodynamic mobilisation on disability, yet a stronger positive effect of neurodynamic mobilisation on disability is found when compared to passive controls (C1), than when compared to active controls (C2), in patients with cervical radiculopathy. *Source: Kim (2017), Savva (2016), Savva (2021)*

4c. Neurodynamic mobilisation: Function (critical)

Very low GRADE	The evidence is uncertain about the effect of neurodynamic mobilisation on range of motion and patient-specific functional scale, yet a stronger positive effect of neurodynamic mobilisation on disability is found when compared to passive controls (C1), than when compared to active controls (C2), in patients with cervical radiculopathy. The evidence is very uncertain about the larger positive effect found of neurodynamic mobilisation on the Disability of Arm, Shoulder and Hand, compared to waiting-list controls, in patients with cervical radiculopathy. *Source: Ayub (2019), Basson (2020), Kayiran (2021), Kim (2017), Rodriguez-sans (2017), Savva (2016), Savva (2021)*

4d. Neurodynamic mobilisation: Quality of life (critical)

Very low GRADE	The evidence is very uncertain about the effect of neurodynamic mobilisation as add-on to manual therapy and exercise on quality of life, in patients with cervical radiculopathy. *Source: Basson (2020)*

4e. Neurodynamic mobilisation: Return to work (important); 4f. Neurodynamic mobilisation: Drug consumption (important); 4g. Neurodynamic mobilisation: Psychosocial outcomes (important); 4h. Neurodynamic mobilisation: Adverse effects (important)

- GRADE	The outcomes return to work, drug consumption, psychosocial outcomes and adverse effects were not reported and could not be graded. *Source: -*

Submodule 2.1.5. Manuele Therapie

5. Manual therapy

Description of studies on manual therapy

Four studies reported on outcomes after manual therapy treatment.

Hassan (2020) compared the effects of different manual therapy techniques in the management of cervical radiculopathy. Patients (through purposive sampling) were randomized into a group receiving oscillatory mobilisation (n = 23) through unilateral postero-anterior glide on the involved segment for three sets of 15 repetitions; or into a group receiving sustained stretch mobilisation (n = 23) through three sets of cervical traction and cervical segment flexion, coupled with side bending and rotation. Both groups received 7 treatments over the course of 2 weeks, plus a home exercise plan consisting of stretching and strengthening exercises, after which heat therapy and transcutaneous electric nerve stimulation was administered for 10 minutes. The outcomes of interest were pain (NRS), disability (NDI) and function (Range of motion, ROM) after 2 weeks.

On the study of Ojoawo (2019) has been elaborated above in the cervical traction section, as one treatment arm received cervical traction in addition to the control treatment (n = 25). Another treatment arm received transverse oscillatory pressure (TOP) in addition to the control treatment (n = 25), and the control group received advice on exercises, ice packs, and massage (n = 25). The outcomes pain (VAS) and disability (NDI) were assessed after 6 weeks.

Shafique (2019) had the objective to determine the effect of Mulligan Spinal Mobilisation with arm movement, compared to multimodal treatment with neurodynamics and manual traction. Cervical radiculopathy patients with unilateral complaints and limited cervical ROM were randomized into one of two groups. The control group (n = 16) received treatment consisting of a hot pack applied for 10 minutes, active range of motion exercises with 3 sets of 10 repetitions and isometric exercises repeated 20 times with a 6-10 second hold, a neurodynamic sliding technique for 10 repetitions, and manual traction for 10 minutes with a 10-second pull and 5 seconds rest. The intervention group (n = 15) received the control treatment, plus spinal mobilisation with arm movement through maintaining transverse glide with 10 repetitions in the first sessions, increasing to 30. Both groups received 2 treatment sessions per week, for the duration of 3 weeks. After treatment, pain (NRS), disability (NDI) and cervical ROM were assessed.

In the RCT of Young (2019), the immediate and short-term effects of thoracic manipulation were compared to sham manipulation. Consecutive patients with unilateral upper extremity pain, paresthesia or numbness, and an NDI score of > 10 (out of 50) were included. The patients were randomized to receive either thoracic spine manipulation (n = 22) or sham manipulation (n =21). Thoracic spine manipulation was performed with a high-velocity, low-amplitude thrust technique, directed bilaterally to the upper and mid-thoracic spine. Audible cavitations had to be present to for each manipulation for it to be considered a success. In the sham manipulation group, the physiotherapist had his hand opened with the fingers extended over the inferior vertebrae, and no thrust manipulation was delivered. Forty-eight to 72 hours after treatment, pain (NRS), disability (NDI, from 0 to 50), cervical range of motion, neck endurance, and adverse events were recorded.

Results

Outcomes are assessed below for the following comparisons:

Passive comparison (C1):

- Manual therapy to control (Ojoawo 2018)
- Manual therapy to sham (Young 2019)

Active comparison (C2):

- Manual therapy as add-on to multimodal treatment (with neurodynamic mobilisation and exercise) (Shafique 2019)
- Manual therapy to other forms of manual therapy (Hassan 2020)

5a. Pain

All authors of the RCTs on manual therapy, reported on the outcome pain, either on VAS or NRS. Pain scores are reported after 6 weeks (Ojoawo, 2019), 3 weeks (Shafique, 2019), or 2 weeks (Hassan, 2020). All scores on VAS were converted to values on a 0 to 10 scale, to enable comparison between studies.

Young (2019) showed a mean difference in NRS score between the manual therapy and sham manual therapy group after 48 to 72 hours of -3.10 [95% CI -4.45 to -1.75]. Because of limited comparability concerning the timing of pain measurement, the results have not been included in figure 5a and the pooled calculations.

The results of the study of Hassan (2020) are reported in median with interquartile range. The mean and SD are calculated according to Wan (2014). The different comparisons from the studies are shown in Figure 5a.

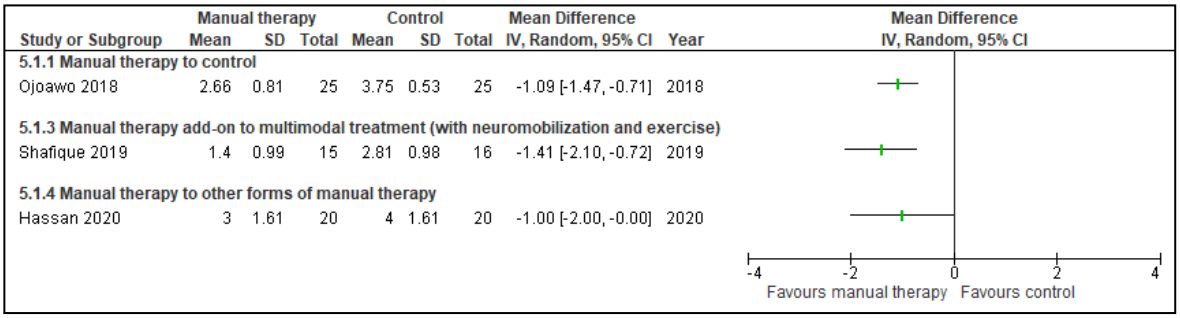

Figure 5a. *Studies comparing manual therapy to control treatment (C1) or to other forms of treatment (C2), for the outcome pain.*

The pooled value for mean difference in pain after manual treatment compared to control treatment (C1), as add-on to multimodal treatment (C2) or to other forms of manual therapy, is -1.15 [95%CI -1.46 to -0.83]. This difference is clinically relevant, despite being statistically significant.

5b. Disability

The outcome disability using NDI was assessed by four authors, yet two failed to report on the scale used for assessing NDI (Hassan 2020, Shafique 2019).

Ojoawo (2018) reported a mean difference in NDI of -5.17 [95% -9.47 to -0.87] between the manual therapy group and the control treatment group, after 6 weeks (on a scale from 0 to 100). Despite this effect being statistically significant, as it is not a difference of ≥10%, it is not clinically relevant.

When manual therapy is compared to sham, as in the study of Young (2019), a between-group difference in NDI score 72 hours after intervention was found of -8.0 [95%CI -11.6 to -4.5] (on a scale from 0 to 50).

5c. Function

Three studies reported on cervical ROM, after 2 weeks (Hassan, 202), after 3 weeks (Shafique, 2019); and after 72 hours of treatment (Young, 2019). However, no direct comparisons could be made, as Hassan (2020) reported medians with interquartile range not seeming to correspond with the values found by other authors, and Young (2019) reported on differences compared to baseline after 72 hours instead of absolute ROM in degrees.

Hassan (2020) found significant differences in flexion (median 47 compared to 24), extension (median 59 to 45), and right (median 80 to 50) and left side rotation (median 80 to 53.5) between oscillatory mobilisation and sustained stretch mobilisation.

Shafique (2019) found the largest difference in side bending to the right, with a mean 29.9 degrees in the control group, and mean 51.6 degrees in the spinal mobilisation with arm movement group (no SDs reported).

Young (2019) found significant differences in change from baseline between the manual therapy group and sham manual therapy group for all movements, except side bending to the asymptomatic side. ROM for all movements improved in the intervention group, whereas the control group showed little to no improvement in ROM.

5d. Quality of life, 5e. Return to work, 5f. Drug consumption, 5g. Psychosocial outcomes

The outcomes quality of life, return to work, drug consumption, psychosocial outcomes were not reported in the studies.

5h. Adverse events

Young (2019) recorded adverse events directly after treatment and after 48 to 72 hours. No increase in neck, arm, or hand symptoms were reported, and no participants reported soreness lasting more than 3 hours after treatment.

<u>Level of evidence of the literature</u>

5a. Manual therapy: Pain (critical)

The level of evidence regarding the outcome measure **pain** was downgraded by 3 levels to *very low* because of high risk of selection bias, unclear allocation concealment, and a per protocol analysis (-2, risk of bias); and a low number of included patients with the confidence intervals crossing the border of clinical relevance (-1, imprecision).

5b. Manual therapy: Disability (critical)

The level of evidence regarding the outcome measure **disability** was downgraded by 3 levels to *very low* because of risk of selection bias, possible selective outcome reporting and early stop of one trial (-1, risk of bias); applicability as one of the studies reported outcomes after 72 hours (-1, bias due to indirectness); and a low number of included studies and patients (-1, imprecision).

5c. Manual therapy: Function (critical)

The level of evidence regarding the outcome measure **function** was downgraded by 3 levels to *very low* because of risk of selection bias, unclear allocation concealment, and inadequate

analysis (-2, risk of bias); applicability as one of the studies reported outcomes after 72 hours (-1, bias due to indirectness).

5d. Manual therapy: Quality of life (critical); 5e. Manual therapy: Return to work (important); 5f. Manual therapy: Drug consumption (important); 5g. Manual therapy: Psychosocial outcomes (important)

The outcomes quality of life, return to work, drug consumption, and psychosocial outcomes were not reported and could not be graded.

5h. Manual therapy: Adverse effects (important)

The level of evidence regarding the outcome measure **adverse events** was downgraded by 3 levels to *very low* because of the limited applicability of the results (48-72 hours) for the assessment of adverse events (-2, bias due to indirectness); and the inclusion of a single study with a low number of patients (-1, imprecision).

Conclusions

5. Manual therapy

5a. Manual therapy: Pain (critical)

Very low GRADE	The evidence is uncertain about the beneficial effect manual therapy might have on pain, compared to multimodal treatment, or in addition to multimodal treatment, in patients with cervical radiculopathy. *Source: Hassan (2020), Ojoawo (2019), Shafique (2019)*

5b. Manual therapy: Disability (critical)

Very low GRADE	The evidence is uncertain about the beneficial effect of manual therapy on disability, compared to control treatment or sham, in patients with cervical radiculopathy. *Source: Ojoawo (2019), Young (2019)*

5c. Manual therapy: Function (critical)

Very low GRADE	The evidence is extremely uncertain about the effect of manual therapy on range of motion in patients with cervical radiculopathy. *Source: Hassan (2020), Shafique (2019), Young (2019)*

5d. Manual therapy: Quality of life (critical); 5e. Manual therapy: Return to work (important); 5f. Manual therapy: Drug consumption (important); 5g. Manual therapy: Psychosocial outcomes (important)

- GRADE	The outcomes quality of life, return to work, drug consumption, and psychosocial outcomes were not reported and could not be graded.

5h. Manual therapy: Adverse events (important)

Very low GRADE	The evidence is very uncertain about the occurrence of adverse events, in patients with cervical radiculopathy receiving thoracic manipulation compared to sham treatment. *Source: Young (2019)*

Overwegingen – van bewijs naar aanbeveling

Voor- en nadelen van de interventie en de kwaliteit van het bewijs

In deze module worden verschillende fysiotherapeutische interventies geëvalueerd als behandeling van patiënten met cervicaal radiculair syndroom (CRS). In totaal zijn er twintig RCTs gevonden die de half harde halskraag, cervicale tractie, oefentherapie, neurodynamische mobilisatie of manuele therapie onderzochten. De bewijskracht voor de cruciale uitkomstmaten 'disability', 'functioneren', en 'kwaliteit van leven' was voor alle interventies *zeer laag*, behalve voor de interventie oefentherapie. Voor oefentherapie resulteerde de bewijskracht in *laag* m.b.t. de cruciale uitkomstmaten.

De zeer lage bewijskracht betekent dat andere studies kunnen leiden tot nieuwe inzichten. De studiepopulaties en interventies waren niet altijd goed met elkaar te vergelijken en daarnaast bevatten de studies enkele methodologische beperkingen. Daarom kunnen er op basis van de literatuur geen harde conclusies geformuleerd worden.

Bij patiënten met een CRS is er sprake van bewegend disfunctioneren mede op basis van de aanwezige radiculaire (en soms neuropathische) pijn en andere sensorische en motorische disfuncties vanwege de radiculopathie. Na het verdwijnen van de oorzaak van een CRS, verdwijnen niet altijd alle disfuncties zonder een specifiek daarop gerichte interventie (Hides, 1996). Fysiotherapie kan een aanvulling zijn op het natuurlijk herstelproces bij patiënten met een CRS en, ná het herstel, essentieel zijn in het herstellen van ontstane disfuncties zoals spierkrachtverlies. Een fysiotherapeutisch behandelprogramma is altijd multimodaal (Thoomes, 2022).

Waarden en voorkeuren van patiënten (en evt. hun verzorgers)

Het is de mening van de werkgroep dat de beslissing om fysiotherapeutische begeleiding te zoeken vooral aan de patiënt over moet worden gelaten. Als de patiënt besluit zich te laten begeleiden door een fysiotherapeut, is het wel wenselijk dat de behandelend fysiotherapeut ruime ervaring heeft met het behandelen en begeleiden van patiënten met een CRS, om onnodige exacerbaties of bijwerkingen te voorkomen.

De belangrijkste doelen van de fysiotherapeutische interventies zijn afhankelijk van het stadium waar de aandoening zich in bevindt. In de initiële, reactieve fase waarin de reactiviteit van de zenuwwortel nog voorop staat, zal de focus vooral liggen op uitleg en advies hoe de verergering van klachten het best te voorkomen is. Daarbij zijn correct gebruik van effectieve pijnmedicatie (in overleg met de (huis)arts) en wellicht het overwegen van het gebruik van een half harde halskraag van belang. Self-empowerment van de patiënt is nu ook al van belang. In de subacute fase zal de focus van de interventies verschuiven naar een meer actieve aanpak, rekening houdend met de belastbaarheid van de individuele patiënt. Hierin kunnen de interventies die de werkgroep voorstelt allemaal een rol spelen. In de eindfase van herstel verschuift de focus van de fysiotherapeutische interventies nog meer naar zelfredzaamheid van de patiënt en het geven van de tools waarmee hij/zij zijn eigen belastbaarheid en individuele disfuncties zelf actief verder gestructureerd kan verbeteren.

Kosten (middelenbeslag)

Er is weinig bekend over de kosteneffectiviteit van fysiotherapie bij patiënten met CRS (Alvin, 2014). In 2019 vergeleek één studie chirurgie (ACDF) met conservatief beleid van cervicale epidurale injecties in combinatie met fysiotherapie (Rihn, 2019). Deze analyses suggereerde dat ACDF kosten-effectiever is ($6.768) in vergelijking met cervicale epidurale injecties in combinatie met fysiotherapie (Rihn, 2019). Daarnaast is onderzocht dat het merendeel van de kosten gerelateerd aan CRS, veroorzaakt wordt door het diagnostisch traject (Barton, 2019).

Davidson (2020) rapporteerde de kosten van niet-operatieve therapie voorafgaand aan ACDF-chirurgie in Amerika. De totale directe kosten van alle niet-operatieve therapieën voorafgaand aan ACDF-chirurgie waren $17.255.828 met $1.278 aan fysiotherapie per patiënt als hoogste gemiddelde gefactureerde dollars.

Op basis van kostenanalyses (Barton, 2019; Rihn, 2019; Davidson, 2020) is het dus aannemelijk dat vanuit het oogpunt van kosteneffectiviteit, fysiotherapie aanbevolen kan worden. Daarbij moet opgemerkt worden dat voor sommige subgroepen een andere overweging kan gelden en de beste managementstrategie bij elke patiënt individueel beoordeeld moet worden. Zo kunnen de volgende variabelen geassocieerd zijn met een beter resultaat van de operatie: korte duur van pijn, vrouwelijk geslacht, lage gezondheidskwaliteit, hoge niveaus van angst vanwege nek-/armpijn, lage zelfredzaamheid en een hoge mate van angst vóór de behandeling (Enquist, 2015). In de module 'Timing chirurgische behandeling' spreekt de werkgroep zich hier ook nog verder over uit.

Aanvaardbaarheid, haalbaarheid en implementatie

Op het gebied van aanvaardbaarheid, haalbaarheid en implementatie voorziet de werkgroep geen grote uitdagingen. Patiënten met een CRS ervaren klachten van het bewegend functioneren. Fysiotherapeuten zijn de experts in het bewegend (dis)functioneren. Zeker gezien de direct toegankelijke positie in de eerstelijnszorg, zijn zij daarmee bij uitstek geschikt om een belangrijke rol in te spelen in een conservatieve behandelstrategie.
De beschreven interventies in deze module vallen in principe allemaal binnen het beroepscompetentieprofiel van de fysiotherapie (KNGF, 2021). Echter worden niet alle interventies in het basis curriculum van de algemeen fysiotherapeut gedoceerd. Onder andere de manipulaties en de neurodynamische mobilisaties maken deel uit van de specialisatie opleiding tot manueel therapeut. Zo worden manueel therapeuten opgeleid tot het behandelen van complexe problemen van het bewegen (dis)functioneren (KNGF, 2021; NVMT, 2023). De werkgroep adviseert daarom om bij het inzetten van een conservatief beleid, patiënten ter overweging mee te geven een manueel therapeut te consulteren.
Hoewel fysiotherapeuten direct toegankelijk zijn, wordt de bekostiging voor een groot deel vanuit de Aanvullende Verzekering (AV) vergoed. Slechts een beperkt deel van de zogenaamde "chronische aandoeningen" (de zgn. lijst Borst of Bijlage 1. van het Besluit zorgverzekering) wordt vanuit de Basisverzekering vergoed. Niet iedereen in Nederland heeft een AV zodat, dus vanuit financieel oogpunt bekeken hebben niet alle patiënten vergelijkbare toegang heeft tot fysiotherapie. Dit kan een mogelijke barrière zijn voor patiënten.

Aanbevelingen

Aanbeveling 1 – Halskraag

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventies

De bewijskracht voor de uitkomsten 'pijn', 'beperkingen', 'kwaliteit van leven', 'terugkeer in het arbeidsproces' en 'gebruik van opiaten' op basis van beschikbare literatuur is zeer laag. Ofwel, het is onduidelijk is of een half-harde halskraag een gunstig effect heeft bij patiënten met CRS. De werkgroep acht op basis van expert opinion in combinatie van het bewijs uit één studie (Kuijper, 2009) van goede methodologische kwaliteit dat het dragen van een half harde halskraag een te overwegen interventie is.

> Overweeg het dragen van een half harde halskraag in de eerste zes weken na het ontstaan bij patiënten met een cervicaal radiculair syndroom om nekpijn te verminderen.

Aanbeveling 2 – Cervicale tractie

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventie

De bewijskracht voor de uitkomsten pijn, beperkingen, functie en psycho-sociale uitkomsten op basis van beschikbare literatuur is zeer laag. Ofwel, het is onduidelijk is of cervicale tractie een gunstig effect heeft bij patiënten met CRS. Gezien de biomechanische implausibiliteit van de interventie, het vóórkomen van bijwerkingen na de interventie, in combinatie met de uitkomst van een systematische review (Colombo, 2020) is het de mening van de werkgroep dat cervicale tractie niet aanbevolen dient te worden bij patiënten met CRS.

Zie af van het verrichten van cervicale tractie bij patiënten met een cervicaal radiculair syndroom gezien de onduidelijke positieve effecten en de mogelijke bijwerkingen na de interventie.

Aanbeveling 3 – Oefentherapie

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventie

De bewijskracht voor de uitkomstmaten 'pijn' en 'disfunctioneren' was laag. Voor de overige uitkomstmaten was er zeer lage bewijskracht op basis van twee studies. Het is de mening van de werkgroep, in combinatie met resultaten van een recente Delphi studie (Thoomes, 2022) en een systematische review (Mallard, 2022), dat gerichte oefentherapie een te overwegen interventie is bij patiënten met CRS.

Overweeg gerichte oefentherapie bij een fysiotherapeut met ruime ervaring met de behandeling van CRS, bij patiënten met een cervicaal radiculair syndroom om functie van de cervicale wervelkolom te verbeteren.

Aanbeveling 4 – Neurodynamische mobilisatie

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventie

De bewijskracht voor de uitkomsten 'pijn', 'beperkingen', 'functie' en kwaliteit van leven' op basis van beschikbare literatuur is zeer laag. Ofwel, het is onduidelijk of neurodynamische mobilisaties een gunstig effect hebben op pijn, beperkingen, functie en kwaliteit van leven bij patiënten met CRS. Er wordt een sterker effect gevonden wanneer neurodynamische mobilisaties vergeleken worden met een "passive control'. Mede hierom én in combinatie met resultaten van een recente Delphi studie (Thoomes 2022) is het de mening van de werkgroep in dat neurodynamische mobilisaties een te overwegen interventie is bij patiënten met CRS.

Overweeg neurodynamische mobilisaties bij een fysiotherapeut, bij patiënten met CRS om pijn te verminderen.

Aanbeveling 5 – Manuele therapie

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventie

De bewijskracht voor de uitkomsten 'pijn', 'beperkingen' en 'functie' op basis van beschikbare literatuur is zeer laag. Ofwel, het is onduidelijk of manuele therapie een gunstig effect heeft op pijn, beperkingen en functie bij patiënten met CRS. Het is de mening van de werkgroep in combinatie met resultaten van een recente Delphi studie (Thoomes, 2022) dat manuele therapie een te overwegen interventie is bij patiënten met CRS.

Overweeg manuele therapie bij een fysiotherapeut, bij patiënten met cervicaal radiculair syndroom om pijn te verminderen en functie van de cervicale wervelkolom te verbeteren.

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Bijlagen bij module 2.1 Fysiotherapie

Implementatieplan

Aanbeveling	Tijdspad voor implementatie: < 1 jaar, 1 tot 3 jaar of > 3 jaar	Verwacht effect op kosten	Randvoorwaarden voor implementatie (binnen aangegeven tijdspad)	Mogelijke barrières voor implementatie[1]	Te ondernemen acties voor implementatie[2]	Verantwoordelijken voor acties[3]	Overige opmerkingen
Alle aanbevelingen	< 1 jaar	Beperkt	• Zorgverleners moeten adequate expertise hebben om fysiotherapie toe te passen. • Bekendheid met richtlijn.	• Vergoeding voor fysiotherapie. • Meer kennis over de verschillende behandelingen.	• Voldoende kennis bij / scholing voor zorgverleners. • Afspraken met zorgverzekeraars. • Verspreiden van richtlijn.	• Beroepsverenigingen. • Zorgverlener.	Niet van toepassing.

[1] Barrières kunnen zich bevinden op het niveau van de professional, op het niveau van de organisatie (het ziekenhuis) of op het niveau van het systeem (buiten het ziekenhuis). Denk bijvoorbeeld aan onenigheid in het land met betrekking tot de aanbeveling, onvoldoende motivatie of kennis bij de specialist, onvoldoende faciliteiten of personeel, nodige concentratie van zorg, kosten, slechte samenwerking tussen disciplines, nodige taakherschikking, etc.

[2] Denk aan acties die noodzakelijk zijn voor implementatie, maar ook acties die mogelijk zijn om de implementatie te bevorderen. Denk bijvoorbeeld aan controleren aanbeveling tijdens kwaliteitsvisitatie, publicatie van de richtlijn, ontwikkelen van implementatietools, informeren van ziekenhuisbestuurders, regelen van goede vergoeding voor een bepaald type behandeling, maken van samenwerkingsafspraken.

[3] Wie de verantwoordelijkheden draagt voor implementatie van de aanbevelingen, zal tevens afhankelijk zijn van het niveau waarop zich barrières bevinden. Barrières op het niveau van de professional zullen vaak opgelost moeten worden door de beroepsvereniging. Barrières op het niveau van de organisatie zullen vaak onder verantwoordelijkheid van de ziekenhuisbestuurders vallen. Bij het oplossen van barrières op het niveau van het systeem zijn ook andere partijen, zoals de NZA en zorgverzekeraars, van belang.

Evidence Tables

1. Studies reporting on the use of a collar							
Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison/ control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comment**
Aksoy, 2018	Type of study: RCT Setting and country: Single centre, Turkey Funding and conflicts of interest: none	Inclusion criteria: Patients with cervical radiculopathy confirmed through MRI, aged 18-65, neck pain on VAS ≥4 Exclusion criteria: (1) previous surgical operation on the c-spine, (2) other systemic, neurological or psychiatric problems; (3) rheumatic and infectious disease; (4) current malignancy; (5) motor deficit in upper extremity; (6) previous treatment with cervical collar; (7) complaints >12 weeks N total at baseline: 101 Intervention: 67 (34 group 1 and 33 group 2) Control: 33 Important prognostic factors: *age:* I: 41 (G1), 40 (G2) C: 46 *Sex:* I: 23% M (G1), 46% M (G2) C: 38% M *VAS score neck pain:* I: 8.26 (G1), 8.30 (G2) C: 7.72 *NDI score:* I: 66 (G1), 64 (G2) C: 55 Groups comparable at baseline?	Intervention treatment: Group 1 (G1): soft cervical collars (soft sponge) plus control treatment Group 2 (G2): semi-rigid cervical collars (plastazote foam material) plus control treatment - For week 1 and 2, wear collar 8 hours every day - For week 3 and 4, reduce collar time every other day by one hour, quit collar at end of week 4.	Control treatment: Home exercises comprising cervical isometric, cervical mobilisation, and shoulder protraction and retraction exercises for 6 weeks, twice a day, with 2x 10 repetitions at each session. Advice to avoid holding the neck in prolonged flexion or extension during daily activities and to use a suitable pillow during sleep. The use of NSAID was allowed when necessary.	Length of follow-up: 6 weeks Loss-to-follow-up: Intervention: 4 (G1) and 7 (G2) (10.9%) *Reasons:* failed to complete, due to discomfort of collar (n = 7), no excuse given (n = 4) Control: 5 (5%) *Reasons* (describe): discontinuation with unknown reason Incomplete outcome data: 14 (13.9%) *Same as above*	Outcome measures and effect size (95%CI): Pain on VAS (mean difference, 95%CI) Soft collar as add-on to exercise -0.49 [-1.23 to 0.25] Semi-rigid collar as add-on to exercise 0.26 [-0.59 to 1.11] NDI (mean difference, 95%CI) Soft collar as add-on to exercise -5.5 [-9.9 to -1.1] Semi-rigid collar as add-on to exercise 1.0 [-4.0 to 6.0] Quality of Life (SF-36) (mean difference, 95%CI) Soft collar as add-on to exercise PCS: -3.80 [-6.54 to -1.06] MCS: -0.60 [-3.03 to 1.83] Semi-rigid collar as add-on to exercise PCS: -1.60 [-4.62 to 1.42] MCS: -2.50 [-5.40 to 0.40]	

		Yes					
Kuijper, 2009	Type of study: RCT Setting and country: 3 hospitals, the Netherlands Funding and conflicts of interest: non-commercial organisation for salary of research nurse, no conflicts of interest	Inclusion criteria: Patients referred by GPs with <1 month symptoms and signs of cervical radiculopathy, aged 18-75 years, with arm pain VAS ≥40mm and radiation of pain distal to elbow. In addition, either provocation of arm pain by neck movements, or sensory changes in ≥1 dermatome, or diminished deep tendon reflexes in the arm, or muscle weakness had to be present. Exclusion criteria: (1) clinical signs of spinal cord compression, (2) previous treatment with physiotherapy or cervical collar N total at baseline:205 Intervention: 139 (69 group 1 and 70 group 2) Control: 66 Important prognostic factors[2]: *age ± SD:* I: 47.0 ± 9.1 (G1), 46.7 ± 10.9 (G2) C: 47.7 ± 10.6 *Sex:* I: 55% M (G1), 49% M (G2) C: 48% M *VAS score neck pain* I: 57.4 ± 27.5 (G1), 61.7 ± 27.6 (G2) C: 55.6 ± 31.0 *NDI* I: 41.0 ± 17.6 (G1), 45.1 ± 17.4 (G2) C: 39.8 ± 18.4 Groups comparable at baseline? Yes	Intervention treatment: Group 1 (G1): semi-hard collar (one of six sizes with best fit) - for week 1-3 wear collar during the day, and the advice to take as much rest as possible. - For week 4-6, reduce collar time, quit collar at end of week 6 Group 2 (G2): Guided physiotherapy sessions consisting of hands off graded activity exercises to strengthen the superficial and deep neck muscles, twice a week for 6 weeks. In addition, physiotherapists educated the patients on home exercises, and practice those every day. Written and oral reassurance about the usually benign course of the symptoms was given to patients in both G1 and G2.	Control procedure: Continuation of daily activities without specific treatment other than written and oral reassurance about the usually benign course of the symptoms. The use of painkillers was allowed when necessary.	Length of follow-up: 6 months Loss-to-follow-up: 5 for primary outcome (6 weeks), 13 for entire follow-up (6 months) Intervention: 6 (G1, 8.7%) and 2 (G2, 2.9%)) *Reasons:* not provided Control: 5 (7.6%) Reasons: not provided Incomplete outcome data: 13 (6.3%) *Same as above*	Outcome measures and effect size (95%CI): Pain on VAS after 6 weeks (mean difference, 95%CI) Collar compared to no intervention -20.1 [-30.4 to -9.8] Collar compared to exercise -5.20 [-15.0 to 4.6] Exercise compared to no intervention -1.49 [-2.56 to -0.42] NDI after 6 weeks (mean difference, 95%CI) Collar compared to no intervention -4.0 [-10.6 to 2.6] Collar compared to exercise -1.9 [-7.9 to 4.1] Exercise compared to no intervention -2.10 [-8.46 to 4.26] Use of opiates after 6 weeks (relative risk, 95%CI) Collar compared to no intervention 0.75 [0.39 to 1.44] Collar compared to exercise 0.97 [0.49 to 1.94] Exercise compared to no intervention 0.78 [0.41 to 1.48] Working status after 6 weeks (relative risk, 95%CI) Collar compared to no intervention 0.77 [0.48 to 1.25] Collar compared to exercise 0.66 [0.42 to 1.03]	Patients who eventually underwent surgery: 5 in collar group, 3 in physiotherapy group, and 4 in control group.

						Exercise compared to no intervention 1.18 [0.78 to 1.77]	
2. Studies reporting on traction							
Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison / control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comments**
Bukhari, 2016	Type of study: RCT Setting and country: single hospital, Pakistan Funding and conflicts of interest: no funding received, conflict of interest not disclosed.	Inclusion criteria: Patients with evident radicular symptoms, cervical spine involvement, aged 20-70 years. Exclusion criteria: History of trauma, neck pain without radiculopathy N total at baseline: 42 Intervention: 15 (mechanical traction) Control: 21 (manual traction) Important prognostic factors: *age:* mean 45.8 years, not reported for both subgroups *Sex:* 66% M (not reported for both subgroups) *NRS score:* I: 6.26 (± 1.20) C: 6.80 (± 1.20) *NDI score:* I: 24.43 (± 8.64) C: 21.92 (± 8.89) Groups comparable at baseline? Unclear	Intervention treatment: Mechanical traction, applied on patient in supine position, with 10 second pull and 5 second rest for 10 minutes, with a traction force of 10-15% of body weight. In addition, segmental mobilisation of C3 to C7 by central posterior-anterior glide, 10 repetitions for 5 seconds was applied, and patients were advised to do a home exercise program with active range of motion, stretching, end isometric strengthening exercises 3 days a week for 6 weeks.	Control treatment: Manual traction, applied on patient in supine position at 25 degree neck flexion, with 10 second pull and 5 second rest for 10 times. In addition, segmental mobilisation of C3 to C7 by central posterior-anterior glide, 10 repetitions for 5 seconds was applied, and patients were advised to do a home exercise program with active range of motion, stretching, end isometric strengthening exercises 3 days a week for 6 weeks.	Length of follow-up: 6 weeks Loss-to-follow-up: 6 patients (unclear which group, no reasons provided) Incomplete outcome data: 6 (14.3%) *Same as above*	Outcome measures and effect size (95%CI): Pain on NRS (mean difference, 95%CI) -2.42 [-3.31 to -1.53] NDI (mean difference, 95%CI) -9.98 [-17.28 to -2.68]	Methodological weak study with single intervention session.
Ojoawo, 2019	Type of study: RCT Setting and country: Academic hospital, Nigeria Funding and conflicts of	Inclusion criteria: Neck pain that radiated distal from the elbow. Exclusion criteria: Main complaint of headache or facial pain, and having received manual therapy of the cervical region in the past 3 months. N total at baseline: 75	Intervention treatment: Group 1 (G1): cervical traction "over the door" with a water bat loaded to 10% of patient's body weight, for 15 minutes. This was administered twice a week for 6 weeks. Group 2 (G2): transverse	Control treatment: Patients performed active exercises: cervical spine retraction, rotation, extension, and side-bending stretching. In addition, ice packs were applied to the cervical region for 7 minutes, and massage. Both 2 times	Length of follow-up: 6 weeks Loss-to-follow-up: 3 Intervention: 1 (G1) and 0 (G2) (4%) *Reasons:* discontinued intervention Control: 2 (8%)	Outcome measures and effect size (95%CI): Pain on VAS (mean difference, 95%CI) Cervical traction compared to control -1.25 [-1.55 to -0.95] TOP compared to control -1.09 [-1.47 to -0.71]	Risk of selection bias. Unclear whether ITT (with unclear imputation methods) or PP was used for analysis.

	interest: none	Intervention: 50 (25 group 1 and 25 group 2) Control: 25 Important prognostic factors: *Age (mean ± SD):* I: 51.4 ± 6.5 (G1), 55.7 ± 5.4 (G2) C: 59.5 ± 2.6 *Sex:* I: 56% M (G1), 60% M (G2) C: 44% M *VAS score (mean ± SD):* I: 6.87 ± 1.0 (G1, 7.63 ± 2.30 (G2) C: 7.00 ± 0.8 *NDI score (mean ± SD)::* I: 42.1 ± 16.9 (G1), 58.7 ± 8.9 (G2) C: 55.3 ± 11.3 Groups comparable at baseline? NDI score varies relatively much at baseline, yet in general, yes.	oscillatory pressure (TOP) administered by the therapist manually, to the patient lying on his/her belly, on the side of the location of the pain. Administered 3 times for 20 seconds, with 2 min rest in between. TOP was given twice a week for 6 weeks. In addition, G1 and G2 patients performed active exercises: cervical spine retraction, rotation, extension, and side-bending stretching. Ice packs were applied to the cervical region for 7 minutes, and massage. Both 2 times per week for 6 weeks.	per week for 6 weeks.	*Reasons:* discontinued intervention Incomplete outcome data: 14 (13.9%) *Same as above*	Cervical traction compared to TOP -0.16 [-0.54 to 0.22] NDI (mean difference, 95%CI) Cervical traction compared to control -1.50 [-8.76 to 5.76] TOP compared to control -5.17 [-9.47 to -0.87] Cervical traction compared to TOP 3.67 [-4.29 to 11.63]	
Fritz, 2014	Type of study: RCT Setting and country: Several physical therapy offices, USA Funding and conflicts of interest: Non-commercial grant. Conflict of interests not disclosed.	Inclusion criteria: (1) Chief complaint of neck pain, with symptoms extending distal to acromioclavicular joingt or causal to the superior border of the scapula, (2) age 18-70 years, (3) NDI score ≥10. Exclusion criteria: (1) history of surgery to the neck or thoracic spine, (2) motor vehicle accident in past 2 weeks, (3) red flags indicative of possible nonmusculoskeletal condition, (4) diagnosis of cervical spinal stenosis on MRI or CT, (5) evidence of cervical myelopathy or CNS involvement N total at baseline: 86 Intervention: 58 (31 group 1 and 27 group 2) Control: 28	Intervention treatment: Group 1 (G1): Mechanical cervical traction, with angle of pull of 15 degrees. Intermittent traction was performed with 60 seconds pull force and 20 seconds relaxation, for 15 minutes. Group 2 (G2): Cervical traction using an over-the-door traction device for 15 minutes, used at home daily on days of no physiotherapy sessions. In addition, patients received 10 individual physiotherapy sessions for 4 weeks (3x/week in first 2	Control treatment: 10 individual physiotherapy sessions for 4 weeks (3x/week in first 2 weeks, 2x/week in final 2 weeks), plus an active exercise program, with cervical strengthening and scapula strengthening exercises, to be performed daily on the days between therapy sessions.	Length of follow-up: 12 months Loss-to-follow-up: 32 Intervention: 10 (G1) and 10 (G2) (34.5%) *Reasons:* various (unclear flow-diagram) Control: 12 (44.4%) *Reasons*: Various (unclear flow diagram) Incomplete outcome data: 32 (37.2%) *Same as above*	Outcome measures and effect size (95%CI): Pain on NRS (mean difference, 95%CI) Cervical traction as add-on to exercise -0.92 [-1.80 to -0.04] NDI (mean difference, 95%CI) Cervical traction as add-on to exercise -1.67 [-4.86 to 1.52] Adverse events no differences among treatment groups in number, type, duration or severity of adverse reactions	

		Important prognostic factors: *age:* I: 48.1 ± 10.0 (G1), 47.6 ± 10.9 (G2) C: 44.9 ± 11.3 *Sex:* I: 58% M (G1), 44% M (G2) C: 36% M *NRS score:* I: 3.8 ± 2.1 (G1), 4.5 ± 2.1 (G2) C: 4.4 ± 2.0 *NDI score:* I: 31 ± 15 (G1), 33 ± 14 (G2) C: 35 ± 14 Groups comparable at baseline? Yes	weeks, 2x/week in final 2 weeks), plus an active exercise program, with cervical strengthening and scapula strengthening exercises, to be performed daily on the days between therapy sessions.				
Moustafa, 2014	Type of study: RCT Setting and country: Single centre, Egypt Funding and conflicts of interest: none	Inclusion criteria: (1) Unilateral C5-6 or C6-7 disc herniation confirmed by CT or MRI, (2) dermatomal numbness C6 or C7, (3) current pain or discomfort for > 3 months, (4) radiation of pain in arm with diminished deep tendon reflexes, (5) increase in symptoms with cervical flexion or protrusion and decrease with retraction or side bending and rotation,(6) presence of 4 positive examination findings in provocation tests; all in patients recruited from outpatient physiotherapy department. Exclusion criteria: (1) presence of medical “red flags” (tumor, fracture, RA, osteoporosis, prolonged steroid use), (2) history of c- or t-spine surgery, (3) signs of upper motor neuron disease, (4) vestibulobasilar insufficiency, (5) amyothropic lateral sclerosis, (6) bilateral symptoms, (7) pregnancy, (8) complete loss of sensation along involved nerve root, (9) severe myelopathy from history taking of motor loss > 3 on MRC scale	Intervention treatment: Group 1 (G1): intermittent ventroflexion traction with increasing traction force, and an on/off cycle of 50/10 for 20 minutes, 3 times per week for 4 weeks. Group 2 (G2): FCR H-reflex-based traction, same as group 1 yet with different head posture. For 20 minutes, 3 times per week for 4 weeks. Both group 1 and 2 received in addition the multimodal treatment as described under the control treatment.	Control treatment: Multimodal program with - pain relief methods (infrared radiation for 15 minutes, interferential therapy for 20 minutes at 100Hz, and massage), • muscle strengthening via isometric contraction exercises increasing in time or resistance, twice daily • Thoracic spine manipulation through thrust manipulation. Duration of 4 weeks, 3 times per week.	Length of follow-up: 4 weeks, 12 months Loss-to-follow-up: Intervention: 7 (G1) and 13 (G2) (13.9%) *Reasons:* loss to follow-up for non-medical causes Control: 7 (9.7%) *Reasons:* loss to follow-up for non-medical causes Incomplete outcome data: 27 (12.5%) *Same as above*	Outcome measures and effect size (95%CI): Pain on NRS (mean difference, 95%CI) Traction as add-on to manual therapy -0.95 [-1.37 to -0.53] NDI (mean difference, 95%CI) Traction as add-on to manual therapy -19.00 [-21.05 to -16.95]	

		N total at baseline: 216 Intervention: 144 (72 group 1 and 72 group 2) Control: 72 Important prognostic factors: *age:* I: 40.2 ± 4.9 (G1), 41.5 ± 6.1 (G2) C: 41.7 ± 5.5 *Sex:* I: 43% M (G1), 61% M (G2) C: 56% M Groups comparable at baseline? Yes					
Young, 2009	Type of study: RCT Setting and country: Multi-centre, USA Funding and conflicts of interest: A grant from commercial company Saunders. Conflicts of interest not disclosed.	Inclusion criteria: Consecutive patients with unilateral upper-extremity pain, paraesthesia or numbness, aged 18-70 years, with at least 3 out of 4 provocation tests positive. Exclusion criteria: (1) History of c-spine or t-spine surgery, (2) bilateral upper-extremity symptoms, (3) signs of upper motor neuron disease, (4) medical "red flags"(tumor, fracture, RA, osteoporosis, prolonged steroid use), (5) cervical spine injections (steroidal) in past 2 weeks, (6) current use of steroidal medication for radiculopathy symptoms N total at baseline: 81 Intervention: 45 Control: 36 Important prognostic factors: *Age (mean ± SD):* I: 47.8 ± 9.9 C: 46.2 ± 9.4 *Sex:* I: 31% M C: 33% M *Duration of symptoms (> 3 months):*	Intervention treatment: Sessions including: - posture education (of the spine) - Manual therapy of upper and mid thoracic spine through thrust or nonthrust (posterior-anterior glides or other) manipulation. Thereafter, nonthrust manipulation of cervical spine (30 seconds or 15-20 repetitions) were performed. - Isometric and strengthening exercises of neck and shoulders - *Mechanical intermittent traction* for 15 minutes with an on/off cycle 50/10, with c-spine at 15 degrees flexion angle. Increasing traction force was	Control treatment: Sessions including: - posture education (of the spine) - Manual therapy of upper and mid thoracic spine through thrust or nonthrust (posterior-anterior glides or other) manipulation. Thereafter, nonthrust manipulation of cervical spine (30 seconds or 15-20 repetitions) were performed. - Isometric and strengthening exercises of neck and shoulders - *Sham intermittent traction* for 15 minutes with an on/off cycle 50/10, with c-spine at 15 degrees flexion angle. Max. 2.3 kg	Length of follow-up: 4 weeks Loss-to-follow-up: Intervention: 6 (13.3%) *Reasons:* - Control: 6 (16.7%) *Reasons:* - Incomplete outcome data: 12 (14.8%) *Same as above*	Outcome measures and effect size (95%CI): Pain on NRS (mean difference, 95%CI) Traction (as add-on to manual therapy and exercise) to control 0.20 [-1.23 to 1.63] NDI (mean difference, 95%CI) Traction (as add-on to manual therapy and exercise) to control 3.00 [-8.68 to 14.68] Psychosocial outcomes on FABQ (mean difference, 95%CI) Traction (as add-on to manual therapy and exercise) to control Physical activity subscale: -1.8 [-6.6 to 3.0] Work subscale: 2.9 [95% -8.1 to 13.9]	

		I: 40% C: 58% *NRS score (mean ± SD):* I: 6.3 ± 1.9 C: 6.5 ± 1.7 *NDI score (mean ± SD):* I: 19.8 ± 8.7 C: 17.1 ± 7.4 <u>Groups comparable at baseline?</u> Yes	applied per visit In addition, patients received a home exercise program.	of force was applied. In addition, patients received a home exercise program.			
3. Studies reporting on exercise*							
Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison / control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comments**
Dedering, 2018	<u>Type of study:</u> RCT <u>Setting and country:</u> Academic hospital, Sweden <u>Funding and conflicts of interest:</u> Non-commercial support and grant, no conflict of interests	<u>Inclusion criteria</u>: Patients with cervical radiculopathy were recruited from October 2010 to November 2012, with (1) verified cervical disc disease by MRI showing cervical nerve root compression, (2) neck and/or arm pain verified by neck extension test or neurodynamic provocation test. <u>Exclusion criteria</u>: Patients with (1) a previous cervical fracture, subluxation or surgery; (2) diagnosed psychiatric disorders; (3) spinal infection and malignancy; (4) other diseases or disorders contraindicating participation <u>N total at baseline</u>: 144 Intervention: 72 Control: 72 <u>Important prognostic factors</u>: *age± SD:* I: 46.8 ± 9.6 C: 49.7 ± 9.5 *Sex:* I: 47% M C: 35% M	<u>Intervention treatment:</u> Neck-specific training 3 sessions per week, for 3 months. This starts with gentle isometric neck movement, gradually progressing to low-load endurance training, individually tailored based on the patient's response. A continuous cognitive behavioural approach was adopted during the sessions. Additionally, patients received information folders with the elements of the intervention: pain physiology, consequences of stress and exercise, relaxation techniques, coping strategies, and ergonomic advice, plus a manual on the standardized neck-specific training program including instructions for progression.	<u>Control treatment:</u> Prescribed physical activity of 30 minutes, 3 times per week, for 3 month. This starts with one individual counselling session with a cognitive behavioural approach, after which patients receive written recommendations on aerobic and/or muscular physical activity (not neck-specific). Additionally, patients received information folders with the elements of the intervention: pain physiology, consequences of stress and exercise, relaxation techniques, coping strategies, and ergonomic advice	<u>Length of follow-up</u>: 24 months <u>Loss-to-follow-up</u>: Intervention: 0 Control: 4 (5.6%) *Reasons*: time restriction <u>Incomplete outcome data</u>: Intervention: 31 (43%) *Reasons:* discontinued intervention Control: 36 (50%) *Reasons* : discontinued intervention	Outcome measures and effect size (95%CI): <u>Pain on VAS (mean difference, 95%CI)</u> Neck-specific training to prescribed activity -0.30 [-1.42 to 0.82] <u>NDI (mean difference, 95%CI)</u> Neck-specific training to prescribed activity -1.00 [-9.99 to 7.99] <u>Quality of Life (EQ-5D) (mean difference, 95%CI)</u> Neck-specific training to prescribed activity Index: -0.03 [-0.15 to 0.09] VAS health state: -4 [-13 to 5] <u>Psychosocial outcomes (FABQ) (mean difference, 95%CI)</u> Neck-specific training to prescribed activity 6 [0 to 12]	

		Neck pain frequency (daily): I: 72% C: 72% Groups comparable at baseline? Yes					
Diab, 2012	Type of study: RCT Setting and country: Academic centre, Egypt Funding and conflicts of interest: None	Inclusion criteria: Patients with (1) a craniovertebral angle <50°, (2) unilateral radiculopathy due to spondylotic changes of C5-C6 or C6-C7, (3) side-to-side amplitude differences of ≥50% in dermatomal sensory-evoked potentials, (4) duration of symptoms >3 months. Inclusion was from September 2009 to July 2010. Exclusion criteria: (1) Spinal canal stenosis, (2) rheumatoid arthritis, (3) vestibulobasilar insufficiency N total at baseline: 96 Intervention: 48 Control: 48 Important prognostic factors: *Age ± SD:* I: 46.3 ± 2.05 C: 45.9 ± 2.1 *Sex:* I: 56% M C: 48% M Groups comparable at baseline? Yes	Intervention treatment: Posture corrective exercise programme of 10 weeks: 3 sets of 12 repetitions of 2 strengthening exercises, and 3 stretching exercises held for 30 seconds each, four times a week. Plus 10 weeks, 3 times a week infrared radiation on the neck for 10 minutes, followed by continuous ultrasound application on upper trapezius for 10 minutes (1.5 W/cm^2).	Control treatment: 10 weeks, 3 times a week infrared radiation on the neck for 10 minutes, followed by continuous ultrasound application on upper trapezius for 10 minutes (1.5 W/cm^2)	Length of follow-up: 6 months Loss-to-follow-up: Not reported Incomplete outcome data: not reported	Outcome measures and effect size (95%CI): Pain on VAS (mean difference, 95%CI) Exercise to control -0.70 [-1.24 to -0.16]	Selection bias through "conveniently selecting patients from our institution's outpatient clinic" Further risk of bias because no loss-of-follow up was reported: there might have been selective drop-out, or a per-protocol analysis performed.
4. Studies reporting on neurodynamic mobilisation							
Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison / control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comments**
Ayub, 2019	Type of study: RCT Setting and country: Single centre, Pakistan	Inclusion criteria: Female patients aged 30-50 years with chronic cervical radiculopathy and neck pain for ≥6 months, and positive provocation tests. Exclusion criteria:	Intervention treatment: Moist heat packs for 10 minutes followed by mechanical traction of the cervical spine for 15 minutes. Also 3 sets of slow gentle segmental	Control treatment: Moist heat packs for 10 minutes followed by mechanical traction of the cervical spine for 15 minutes. Also 3 sets of slow gentle segmental	Length of follow-up: 4 weeks Loss-to-follow-up: Intervention: 0 Control: 0	Outcome measures and effect size (95%CI): Pain on NRS (mean difference, 95%CI) 0.0 [-1.86to 1.86] NDI (mean difference, 95%CI)	Selection bias (convenience sampling)

	Funding and conflicts of interest: No conflict of interest, information on funding not disclosed.	(1) Recent neck trauma, (2) positive vertebrobasilar insufficiency signs, (3) receiving any form of physiotherapy or medical treatment for the last 6 weeks N total at baseline: 44 Intervention: 22 Control: 22 Important prognostic factors: *Age (median ± IQ):* I: 41 ± 12 C: 40 ± 11 *Sex:* not reported *Neck pain (median ± IQ):* I: 6 ± 2 C: 6 ± 2 *NDI (median ± IQ):* I: 10 ± 5 C: 10 ± 10 Groups comparable at baseline? Yes	mobilisation (unilateral posterior anterior glide) with at least 15 to 20 repetitions on the first session, thereafter modified based on patient response. Then active upper extremity neurodynamic mobilisation, for 6 to 8 repetitions. 3 sessions per week, for 4 weeks.	mobilisation (unilateral posterior anterior glide) with at least 15 to 20 repetitions on the first session, thereafter modified based on patient response. Then passive upper extremity neurodynamic mobilisation. 3 sessions per week, for 4 weeks.	Incomplete outcome data: 0	*No reporting of scale used* Cervical ROM (mean difference, 95%CI) *Reported in medians*	
Basson, 2020	Type of study: RCT Setting and country: Multicentre, South-Africa Funding and conflicts of interest: Funding received by orthopaedic research investment fund of South African society of physiotherapy and the faculty research	Inclusion criteria: (1) Aged > 18 years, (2) nerve related neck and arm pain by physical examination, (3) recent onset of pain (≤12 weeks), and (4) positive upper limb neurodynamic test Exclusion criteria: (1) Surgery or recent fractures of the cervical spine, (2) serious neurological signs, (3) RA, neurological disease, stroke, cerebral palsy, carcinoma, or any other red flags N total at baseline: 86 Intervention: 60 Control: 26 Important prognostic factors: *Age (mean ± SD):* I: 46.5 ± 14.1	Intervention treatment: neurodynamic mobilisation along the tract of the nerve, directly and indirectly, concentrating on areas where the nerve is mechano-sensitive to palpation. From hand or elbow up along the arm, first rib, scalene and into the neck, first in a non-tensioned position, progressing into a more tensioned position as pain and irritability improved. In addition, patient received usual care similar to patients in the usual	Control treatment: Usual care with (unilateral) posterior-anterior mobilisation of the cervical and thoracic spine, exercises, and advice to stay active. The number of treatments was determined by the treating physiotherapist.	Length of follow-up: 6 weeks, 6 months, 12 months Loss-to-follow-up: Intervention: 7 (11.7%) *Reasons:* could not be reached (of whom 2 had relocated) Control: 1 (3.8%) *Reasons*: could not be reached Incomplete outcome data: 0 Multiple imputation applied.	Outcome measures and effect size (95%CI): Pain on NRS (mean difference, 95%CI) -0.60 [-1.77 to -0.51] Function on PSFS (mean difference, 95%CI) (scale 0 to 30, high score is better) 0.05 [0-0.41 to 0.51] Quality of Life (EQ-5D) (mean difference, 95%CI) 1.1 [4.3 to 6.3]	

	committee of the University of Witwatersrand	C: 48.6 ± 13.6 *Sex:* not reported *Duration of pain (mean days* ± SD*):* I: 30.2 ± 27.4 C: 23.5 ± 22.9 <u>Groups comparable at baseline?</u> Yes	care group. The number of treatments was determined by the treating physiotherapist.				
Ibrahim, 2021	<u>Type of study:</u> RCT <u>Setting and country:</u> Single centre, Egypt <u>Funding and conflicts of interest:</u> No conflicts of interest, funding information not explicitly reported.	<u>Inclusion criteria</u>: Patients (1) 20-40 years of age, (2) history of pain >3 months, (3) radiating pain in one upper limb, (4) met at least 3 of Wainner criteria <u>Exclusion criteria</u>: (1) history of high level spinal cord injury, (2) malignancy, (3) any medical red flag (tumor, fracture, RA, osteoporosis, prolonged steroid use), (4) circulatory disturbances of upper extremity, (5) traumatic injuries of upper limb and cervical spine, (6) dizziness <u>N total at baseline</u>: 40 Intervention: 20 Control: 20 <u>Important prognostic factors</u>: *Pain (median ± range):* I: 3.75 ± 7 C: 3.75 ± 7 *Further no baseline characteristics reported* <u>Groups comparable at baseline?</u> No information	<u>Intervention treatment:</u> Tensioning neurodynamic mobilisation of brachial plexus, with the arm in neurodynamic testing position, 10 cycles of elbow extension and flexion (each 3 seconds) were administered Plus tradition physiotherapy (consisting of infrared radiation and manual traction), for 3 sessions per week, over the course of 3 weeks.	<u>Control treatment:</u> Traditional physiotherapy: - Infrared radiation 50/60 Hz for 20 minutes - Manual traction 15 seconds pull with 30 seconds rest, for 3 sets of 10 repetitions, with 60 seconds rest between sets. For 3 sessions per week, over the course of 3 weeks.	<u>Length of follow-up</u>: 3 weeks <u>Loss-to-follow-up</u>: Intervention: 0 Control: 0 <u>Incomplete outcome data</u>: 0	Outcome measures and effect size (95%CI): <u>Pain on VAS (mean difference, 95%CI)</u> 0.0 [-1.17 to 1.17]	Selection bias
Kayiran, 2021	<u>Type of study:</u> RCT <u>Setting and country:</u> Single centre, Turkey	<u>Inclusion criteria</u>: Patients for whom surgery was not recommended by the neurosurgeon, with (1) cervical disc herniation at C5/C6/C7/C8 confirmed by MRI, (2) aged 20-50 years, (3) cervicobrachial radicular pain for ≥6 weeks (4) pain severity ≥5 on VAS, (5) sensitivity and numbness in radial, median and/or	<u>Intervention treatment:</u> neurodynamic mobilisation on radial, median and ulnar nerves, 10 times 10 seconds for each nerve. For 10 sessions over 3 weeks.	<u>Control treatment:</u> Conservative physiotherapy: - Hotpack for 20 minutes - Transcutaneous electric nerve stimulation (TENS)	<u>Length of follow-up</u>: 3 weeks <u>Loss-to-follow-up</u>: Intervention: 6 (16.7%) *Reasons:* no belief in treatment (n = 3), no adaptation to treatment	Outcome measures and effect size (95%CI): <u>Pain on VAS (mean difference, 95%CI)</u> -1.04 [-1.57 to -0.51] NDI (mean difference, 95%CI) *No reporting of scale used*	

	Funding and conflicts of interest: None	ulnar nerve dynamic tests, (6) not receiving any other treatment or pharmacological agents. Exclusion criteria: (1) Spinal stenosis, (2) RA, (3) previous c-spine surgery, (4) severe neurological loss, (5) upper extremity vascular problems, (6) severe osteoporosis, (7) diabetes mellitus, (8) pregnant women. N total at baseline: 71 Intervention: 36 Control: 35 Important prognostic factors: *Age (mean ± SD):* I: 47.2 ± 12.5 C: 43.3 ± 12.0 *Sex:* not reported *Neck pain (mean* ± SD*):* I: 4.83 ± 1.12 C: 4.83 ± 1.23 NDI (mean ± SD) I: 18.93 ± 6.43 C: 18.93 ± 5.10 Groups comparable at baseline? Yes	Plus conservative physiotherapy (hotpacks, TENS, ultrasound and exercises) for 3 weeks, 5 sessions per week.	for 20 minutes at 100Hz - Continuous mode ultrasound for deep heating for 5 minutes at 1 MHz - Exercises for stretching and strengthening for 5 seconds with 10 repetitions For 3 weeks, 5 sessions per week	time (n = 2), relocation (n = 1) Control: 5 (14.3%) *Reasons:* no belief in treatment (n = 2), no adaptation to treatment time (n = 2), quit treatment because of poor health (n = 1) Incomplete outcome data: Intervention: 11 (15.5%) *Reasons:* as mentioned above.	Cervical ROM (mean difference, 95%CI) Flexion: 3.9 [1.1 to 6.7] Extension: 6.2 [3.0 to 9.5] Side bending right: 4.4 [1.5 to 7.3] Side bending left: 5.6 [2.6 to 8.6] Rotation right: -0.7 [-5.3 to 3.8] Rotation left: -0.3 [-5.4 to 4.8]	
Kim, 2017	Type of study: RCT Setting and country: Single centre, Korea Funding and conflicts of interest: No conflict of interest. Funding information not	Inclusion criteria: Patients with (1) a diagnosis of cervical radiculopathy ≥3 months, (2) aged 26 to 60 years, (3) unilateral pain, (4) ≥3 out of 4 positive provocation tests Exclusion criteria: *None reported* N total at baseline: 30 Intervention: 15 Control: 15 Important prognostic factors:	Intervention treatment: Similar treatment as control treatment group, yet during the manual cervical traction, another physiotherapist applied neurodynamic mobilisation using a slider technique for the median nerve in a smooth and rhythmic manner (with elbow extension/flexion and wrist flexion/extension), for 6	Control treatment: Conservative physiotherapy (total 35 minutes): - Hot pack for 20 minutes - TENS at 60Hz for 15 minutes Plus manual cervical traction for 6 repetitions of 1 minute pull with 30 seconds rest (total 10 minutes) For 8 weeks, 3 times per	Length of follow-up: 4 and 8 weeks Loss-to-follow-up: Intervention: 0 Control: 0 Incomplete outcome data: 0	Outcome measures and effect size (95%CI): Pain on NRS (mean difference, 95%CI) -1.0 [-1.69 to -0.31] NDI (mean difference, 95%CI) -6.92 [-11.41 to -2.43] Cervical ROM (mean difference, 95%CI) Flexion: 3.3 [0.3 to 6.4] Extension: 5.1 [2.2 to 8.0] Side bending right: 2.6 [0.7 to 4.5]	

	disclosed.	*Age (mean ± SD):* I: 29.3 ± 3.3 C: 29.3 ± 3.1 *Sex:* I: 40% M C: 33% M *NRS (mean ± SD):* I: 7.0 ± 0.85 C: 7.1 ± 0.80 *NDI (mean ± SD):* I: 21.7 ± 4.1 C: 22.1 ± 3.0 Groups comparable at baseline? Yes	times 1 minute with 30 seconds rest inbetween. For 8 weeks, 3 times per week.	week.		Side bending left: 2.4 [0.9 to 3.9] Rotation right: 2.4 [0.3 to 4.5] Rotation left: 3.6 [1.8 to 5.4]	
Rodriguez-sans, 2017	Type of study: RCT Setting and country: Single centre, Venezuela Funding and conflicts of interest: none	Inclusion criteria: Consecutive patients seeking treatment for cervicobrachial pain, who (1) had clinical signs of cervicobrachial pain (arm pain, paresthesia, numbness in upper limb), confirmed through MRI, (2) aged 18 to 45, (3) unilateral symptoms for at least 3 months, (4) 3 positive provocation tests Exclusion criteria: (1) Use of any type of treatment to relieve pain (therapy, procedures or drugs), (2) using anticonvulsant, antidepressant, or psychotropic medication, (3) vertebral instability, osteoporosis or spine infection, (4) neurologic diseases, (5) cervical stenosis myelopathy, (6) kinesiophobia, (7) pregnancy, (8) endocrine disorders and menopause, (9) history of spine surgery, (10) severe mental illness, (11) intoxication, (12) intellectual disability, (13) severe sleep deprivation, (14) Alzheimer's disease N total at baseline: 58 Intervention: 29 Control: 29	Intervention treatment: Cervical lateral glide (CLG) neural mobilisation administered by a physiotherapist, to the contralateral side of pain in a slow oscillating manner. CLG was applied continuously for two minutes in 5 consecutive applications, with one minute rest in between. For 5 days per week, for 6 weeks.	Control treatment: Waiting list for 6 weeks (did not receive an type of pain-modulating treatment)	Length of follow-up: 6 weeks (30 treatment days) Loss-to-follow-up: Intervention: 4 (13.8%) *Reasons:* did not complete treatment as allocated Control: 2 (6.9%) *Reasons*: did not complete treatment as allocated Incomplete outcome data: 6 (10.3%) *Reasons:* see above	Outcome measures and effect size (95%CI): Pain on NRS (mean difference, 95%CI) -2.96 [-3.54 to -2.38] Function (Quick DASH) -21.5 [-27.4 to -15.73] Function (ipsilateral cervical rotation) (mean difference, 95%CI) 8.0 [4.9 to 11.1]	

		Important prognostic factors: *Age(mean ± SD):* I: 33.3 ± 5.0 C: 32.5 ± 4.6 *Sex:* I: 56% M C: 44% M *NRS (mean ± SD):* I: 6.08 ± 0.99 C:6.44 ± 0.93 Groups comparable at baseline? As far as information is provided, yes					
Savva, 2016	Type of study: RCT Setting and country: Single centre, Cyprus Funding and conflicts of interest: None.	Inclusion criteria: Consecutive patients with unilateral cervical radiculopathy diagnosed by MRI or CT referred to the physiotherapy department, with (1) unilateral sharp pain, muscle weakness and numbness in upper arm, (2) ≥3 out of 4 positive provocation tests. Exclusion criteria: (1) current cervical myelopathy or signs of upper motor neuron disease, (2) bilateral complaints, (3) other musculoskeletal conditions in the affected limb, (4) use of analgesia or anti-inflammatory medication in the prior 2 weeks. N total at baseline: 42 Intervention: 21 Control: 21 Important prognostic factors: *Age (mean ± SD):* I: 45.2 ± 13.5 C: 49.2 ± 8.5 *Sex:* I: 38% M C: 62% M	Intervention treatment: Intermittent (pain-free) cervical traction with 1 minute pull and 1 minute rest for 6 sets. During the cervical traction, slider neurodynamic mobilisation using a median nerve bias were performed in slow and oscillatory fashion, with the patients' elbow, wrist and finger repositioning. 3 treatment sessions per week, for 4 weeks. In addition, patients received advice to avoid prescription or over-the-counter analgesia or anti-inflammatory medication.	Control treatment: Did not receive any type of treatment, with advice to avoid prescription or over-the-counter analgesia or anti-inflammatory medication, for the duration of 4 weeks.	Length of follow-up: 4 weeks Loss-to-follow-up: Intervention: 0 Control: 0 Incomplete outcome data: 0	Outcome measures and effect size (95%CI): Pain on NRS (mean difference, 95%CI) -3.36 [-4.56 to -1.96] NDI (mean difference, 95%CI) -15.33 [-23.26 to -7.40] Function on PSFS (mean difference, 95%CI) (scale 0 to 10) 1.62 [0.91 to 2.32] Cervical ROM (mean difference, 95%CI) Flexion: 5.7 [0.5 to 11.0] Extension: 8.8[-0.5 to 18.1] Side bending ipsilateral: 6.4 [1.6 to 11.1] Side bending contralateral: 6.0 [1.5 to10.4] Rotation ipsilateral: 7.9 [1.5 to 14.3] Rotation contralateral: 10.6 [3.6 to 17.6]	

		NRS (mean ± SD): I: 5.62 ± 2.52 C: 5.19 ± 2.11 NDI (mean ± SD): I:33.3 ± 17.6 C: 30.2 ± 16.4 <u>Groups comparable at baseline?</u> Yes					
Savva, 2021	<u>Type of study:</u> RCT <u>Setting and country:</u> Single centre, Cyprus <u>Funding and conflicts of interest:</u> None.	<u>Inclusion criteria</u>: Consecutive patients with unilateral cervical radiculopathy referred to the physiotherapy department, (1) aged 20 to 75 years, with (2) unilateral upper limb pain, sensory and/or motor symptoms, (3) ≥3 out of 4 positive provocation tests. <u>Exclusion criteria</u>: (1) bilateral complaints, (2) other musculoskeletal conditions in the affected limb, (3) evidence of central nervous system involvement, (4) history of medical red flags (tumor, metabolic disease, RA, osteoporosis), (5) use of analgesia or anti-inflammatory medication in the prior 2 weeks. <u>N total at baseline</u>: 66 Intervention: 22 (G1), 22 (G2) Control: 22 <u>Important prognostic factors</u>: *Age (mean ± SD):* I: 47.7 ± 10.8 (G1), 48.1 ± 11.9 (G2) C: 48.5 ± 12.3 *Sex:* I: 50% M (G1), 59% M (G2) C: 36% M *Duration of symptoms >3 months:* I: 54% (G1), 41% (G2) C: 55% *NRS (mean ± SD):*	<u>Intervention treatment:</u> *Group 1 (G1): Cervical traction with neurodynamic mobilisation* Intermittent (pain-free) cervical traction with 1 minute pull and 30 seconds rest for 10 sets. During the cervical traction, slider neurodynamic mobilisation of the median nerve was performed in slow and oscillatory fashion, with repeated passive flexion and extension of the patients' elbow, wrist and fingers. 3 treatment sessions per week, for 4 weeks. *Group 2 (G2): cervical traction with sham neurodynamic mobilisation* Intermittent (pain-free) cervical traction with 1 minute pull and 30 seconds rest for 10 sets. During the cervical traction, sham neurodynamic mobilisation with sustained position of	<u>Control treatment:</u> Waiting list without any type of treatment for 4 weeks.	<u>Length of follow-up</u>: 4 weeks <u>Loss-to-follow-up</u>: Intervention: 0 Control: 0 <u>Incomplete outcome data</u>: 0	Outcome measures and effect size (95%CI): <u>Pain on NRS (mean difference, 95%CI)</u> NM + cervical traction to waiting list -3.30 [-4.51 to -2.09] NM as add on to cervical traction to sham NM -2.4 [-3.75 to -1.05] <u>NDI (mean difference, 95%CI)</u> -32.60 [-47.56 to -17.64] <u>Function on PSFS (mean difference, 95%)</u> 1.39 [0.72 to 2.05] <u>Cervical ROM</u> Flexion: 5.9 [0.8 to 11.0] Extension: 5.8[-3.1 to 14.7] Side bending ipsilateral: 6.2 [1.4 to 11.1] Side bending contralateral: 6.3 [2.2 to10.4] Rotation ipsilateral: 8.7 [1.7 to 15.7] Rotation contralateral: 13.5 [6.7 to 20.3]	

		I: 6.1 ± 2.2 (G1), 6.1 ± 2.6 (G2) C: 5.4 ± 1.8 *NDI (mean ± SD):* I: 33.3 ± 17.6 (G1), 34.5 ± 14.2 (G2) C: 29.0 ± 15.9 Groups comparable at baseline? Gender seems to differ sligthly at baseline between intervention and control groups.	elbow and wrist, and repeated passive flexion and extension of the patients' fingers within the ROM. 3 treatment sessions per week, for 4 weeks.				
5. Studies reporting on manual therapy**							
Study reference	**Study characteristics**	**Patient characteristics**	**Intervention (I)**	**Comparison / control (C)**	**Follow-up**	**Outcome measures and effect size**	**Comments**
Hassan, 2020	Type of study: RCT Setting and country: single centre, Pakistan Funding and conflicts of interest: No conflicts of interest, funding information not disclosed.	Inclusion criteria: (1) Patients aged 30-70 with positive findings of cervical radiculopathy on X-ray, (2) decreased range of motion, (3) positive neurodynamic provocation tests, (4) neck pain <8 on NRS, and (5) numbness or paresthesia or pain in arm or hand Exclusion criteria: (1) Cervical myelopathy, (2) vertebrobasilar insufficiency, (3) recent history of trauma, (4) thoracic outlet syndrome, (5) carpal tunnel syndrome, (6) use of pain medications for cervical radiculopahty N total at baseline: 46 Intervention: 23 Control: 23 Important prognostic factors: *age± SD:* Overall: 43.1 ± 8.2 years *Sex:* I: 65% M C: 70% M *NRS score (median ± IQ):* I: 8.0 ± 0.75 C: 8.0 ± 1.75	Intervention treatment: Oscillatory mobilisation (Maitland), 3 sets of 15 repetitions of unilateral postero-anterior glide on the involved segment. For 7 treatment sessions over 2 weeks. Plus a home exercise plan (stretching and strengthening exercises), heat therapy and TENS for 10 minutes	Control treatment: Sustained stretch mobilisation (Kaltenborn): 3 sets of cervical traction and cervical segment flexion, coupled with side bending and rotation. For 7 treatment sessions over 2 weeks. Plus a home exercise plan (stretching and strengthening exercises), heat therapy and TENS for 10 minutes	Length of follow-up: 2 weeks Loss-to-follow-up: 6 Intervention: 3 (13%) Reasons: loss to follow up (n=3) Control: 3 (13%) *Reasons*: Loss to follow-up (n = 2), discontinued intervention (n = 1) Incomplete outcome data: 6 (13%) *See above.*	Outcome measures and effect size (95%CI): Pain on NRS (mean difference, 95%CI) -1.0 [-2.0 to 0.0] NDI (mean difference, 95%CI) *Not reported which scale used* Cervical range of motion (ROM, medians) Flexion: 47 to 24 Extension: 59 to 45 Side bending right: 45 to 45 Side bending left: 45 to 45 Right rotation: 80 to 50 Left rotation: 80 to 53.5	Selection bias Per protocol analysis

		NDI score (median ± IQ): I: 39.5 ± 4 C: 41.0 ± 10 <u>Groups comparable at baseline?</u> Insufficient information, yet seems so.					
Shafique, 2019	<u>Type of study:</u> RCT <u>Setting and country:</u> Single centre, Pakistan <u>Funding and conflicts of interest:</u> none	<u>Inclusion criteria</u>: (1) Cervical radiculopathy patients aged 20 to 60 years, (2) ≥3 out of 4 positive provocation tests; (3) pain and paraesthesia in the unilateral upper extremity and limited cervical ROM <u>Exclusion criteria</u>: (1) bilateral upper extremity symptoms, (2) previous C-spine or T-spine injury, (3) recent gracture or surgery in and around the shoulder, (4) any systemic disease, (5) unsTable spine <u>N total at baseline</u>: 38 Intervention: 19 Control: 19 <u>Important prognostic factors</u>: *age± SD:* I: 42.3 ± 10.4 C: 41.0 ± 9.3 *Sex:* I: 33% M C: 44% M *NRS score (mean ± SD):* I: 6.87 ± 1.06 C: 6.94 ± 0.85 *NDI score (mean ± SD):* I: 23.7 ± 7.9 C: 20.2 ± 6.8 <u>Groups comparable at baseline?</u> Yes	<u>Intervention treatment:</u> Spinal mobilisation with arm movement, through maintaining transverse glide with 10 repetitions in the first sessions, increasing to 30 repetitions in sets of 3 in further sessions. For 2 sessions per week, during 3 weeks. Plus treatment the control group received.	<u>Control treatment:</u> Conventional treatment, consisting of: - Hot pack applied for 10 minutes - active range of motion exercises with 3 sets of 10 repetitions and isometric exercises repeated 20x with a hold of 6 to 10 seconds - Sliding technique for 10 repetitions - Manual traction for 10 minutes with 10 second pull and 5 second rest. For 2 sessions per week, for 3 weeks.	<u>Length of follow-up</u>: 3 weeks <u>Loss-to-follow-up</u>: Intervention: 4 (21.1%) *Reasons*: drop-out Control: 3 (15.8%) *Reasons*: drop-out <u>Incomplete outcome data</u>: 7 (18.4%) *Reasons:* same as above	Outcome measures and effect size (95%CI): <u>Pain on NRS (mean difference, 95%CI)</u> -1.41 [-2.10 to -0.72] <u>NDI (mean difference, 95%CI)</u> *Not reported which scale used* <u>Cervical ROM (means)</u> Flexion: 41.06 to 45.93 Extension: 51.6 to 45.31 Side bending right: 51.6 to 29.94 Side bending left: 39.6 to 31.25 Right rotation: 69.27 to 61.5 Left rotation: 67.67 to 62.81 z	Unclear eligibility and exclusion criteria (unsTable spine?)
Young, 2019	<u>Type of study:</u> RCT	<u>Inclusion criteria</u>: Consecutive patients with unilateral upper extremity pain, paresthesia or numbness,	<u>Intervention treatment:</u> Thoracic spine manipulation: supine,	<u>Control treatment:</u> Sham manipulation: same position as	<u>Length of follow-up</u>: 48 to 72 hours after treatment	Outcome measures and effect size (95%CI):	

	Setting and country: Multicentre, United states of America Funding and conflicts of interest: none	(1) 18 to 65 years of age, (2) NDI score of ≥10/50, (3) ≥3 out of 4 positive provocation tests Exclusion criteria: (1) previous c- or t-spine surgery, (2) bilateral upper extremity symptoms, (3) signs of upper motor neuron disorder, (4) medical red flags (tumor, fracture, RA, osteoporosis, prolonged steroid use), (5) cervical steroidal injection or medication within past 2 weeks N total at baseline: 43 Intervention: 22 Control: 21 Important prognostic factors: *age± SD:* I: 48.8 ± 11.5 C: 43.1 ± 10.8 *Sex:* I: 23% M C: 43% M *Neck pain onset > 6 months:* I: 36% C: 52% Groups comparable at baseline? Moderately comparable; differences in gender, onset time, employment status, previous treatment	high-velocity, low-amplitude thrust manipulation technique, at exhalation of patient, directed bilaterally to the upper and mid thoracic spine, with audible cavitation.	intervention group, yet the physiotherapist's hand over the inferior vertebrae was open with fingers extended. No thrust manipulation delivered during exhalation.	Loss-to-follow-up: Intervention: 0 Control: 0 Incomplete outcome data: 0	Pain on NRS (mean difference, 95%CI) -3.1 [-4.5 to -1.7] NDI (mean difference, 95%CI) (scale 0 to 50) -8.0 [95%CI -11.6 to -4.5] Cervical ROM Reported in mean differences in change of score Adverse events No increase in neck, arm, or hand symptoms were reported, and no participants reported soreness lasting more than 3 hours after treatment	

Abbreviations (alphabetical): CI: confidence interval, CNS: central nervous system, c-spine: cervical spine, CT: computed tomography, EQ-5D: EuroQol-5D questionnaire, FABQ: Fear-avoidance beliefs questionnaire, GP: general practitioner, MCS: Mental Component Score, MRC scale: Medical Research Council scale for measurement of muscle power, MRI: magnetic resonance imaging, NDI: neck disability index, NRS: Numeric Rating Scale, NSAID: non-steroid anti-inflammatory drugs, PCS: Physical Component Score, PSFS: Patient-Specific Functional Scale, RA: rheumatoid arthritis, RCT: randomized controlled trial, ROM: range of motion, SF-36: Short Form 36, t-spine: thoracic spine, VAS: visual analog scale

*** Kuijper (2009) reports also on exercise as intervention, yet is already summarised in the collar-part of the Table.**

**** Ojoawo (2019) reports also on manual therapy, yet is already summarised in the cervical traction part of the Table**

Risk of Bias

Study reference	Was the allocation sequence adequately generated?	Was the allocation adequately concealed?	Blinding: Was knowledge of the allocated interventions adequately prevented? - Were patients blinded? - Were healthcare providers blinded? - Were data collectors blinded? - Were outcome assessors blinded? - Were data analysts blinded?	Was loss to follow-up (missing outcome data) infrequent?	Are reports of the study free of selective outcome reporting?	Was the study apparently free of other problems that could put it at a risk of bias?	Overall risk of bias If applicable/ necessary, per outcome measure
	Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	Definitely yes Probably yes Probably no Definitely no	**LOW** **Some concerns** **HIGH**
1. Studies reporting on the use of a collar							
Aksoy, 2018	Probably yes Reason: use of a computer-generated randomization Table, yet randomization process not described.	Probably no Reason: no allocation process described.	Probably no Reason: Patients, care provider not blinded. Outcome assessor was blinded, yet blinding of data analysts not reported.	Probably no Reason: Loss to follow-up was infrequent (max. 10%) in intervention and control group. However, no imputation methods were used.	Unclear Reason: No protocol available or previously published.	Probably no Reason: No ITT analysis. Possible selection bias. No sample size calculation, possibly underpowered.	**HIGH** - Inadequate allocation concealment - per protocol analysis - Unclear whether deviation from protocol occurred - possible selection bias
Kuijper, 2009	Definitely yes Reason: computer generated sequence per hospital.	Definitely yes Reason: sequentially numbered opaque, sealed envelopes.	Probably no Reason: Patients, physiotherapists and investigators not blinded (blinding of data analysts not reported)	Probably no Reason: Loss to follow-up was infrequent in intervention and control group. Inadequate imputation methods were used (last observation carried forward). Sample size not reached, possibly underpowered.	Definitely no Reason: secondary outcomes in protocol included time to work, persistent symptoms and surgery; in study report these are sick leave, satisfaction, and use of analgesics	Probably no Reason: patient selection might have occurred, as cervical radiculopathy is a clinical diagnosis, whereas all patients had to have MRI positive findings (which can be false negative)	**Some concerns** - No investigator blinding - Deviation from protocol in outcome reporting - possible selection bias - Underpowered
2. Studies reporting on cervical traction							
Bukhari, 2016	Definitely no	Probably no	Probably no	Probably no	Probably no	Probably no	**HIGH** - Inadequate

	Reason: described as "toss and trial method" without further explanation	Reason: no information on allocation concealment provided	Reason: Patients (self-reported outcome measures) and health care providers not blinded. Unclear whether data-analysts were blinded.	Reason: more than 10% loss to follow-up (can have impact on the intervention effect estimate), unclear in which groups it occurred	Reason: no protocol provided, scarce number of outcome measures.	Reason: no limitations of study mentioned in discussion, yet effect of traction compared to other treatment both groups received seems negligible. No sample size calculation, possibly underpowered.	randomization - Risk of selection bias - No blinding - Frequent and possible selective loss to follow-up - Underpowered
Ojoawo, 2019	Definitely yes Reason: patient drew opaque envelope with allocation	Probably yes Reason: opaque envelopes, yet unclear whether caregiver or data assessor was involved in process.	Probably no Reason: Patients (self-reported outcome measures) and health care providers not blinded. Unclear whether data-analysts were blinded.	Probably yes Reason: discontinuation of 3 persons has been reported. Unclear imputation method used (probably LOCF). Based on sample size calculation, study is underpowered.	Probably no Reason: no protocol provided, scarce number of outcome measures.	Definitely no Reason: Unclear whether ITT or PP analysis was done. Outcomes are reported in method section. Unclear inclusion and exclusion criteria	**HIGH** - High risk of selection bias - unclear allocation concealment - no research protocol - Unclear whether ITT or PP analysis has been performed - Underpowered
Fritz, 2014	Definitely yes Reason: opaque sealed envelopes prepared prior to enrolment, based on web-based randomization generator with allocation block sizes of 6, 8 or 10.	Probably yes Reason: research assistant opened randomization envelope	Probably yes Reason: patients and physiotherapists were not blinded, yet assessors and researchers were blinded.	Probably yes Reason: loss-to-follow up was frequent (37%), yet adequate imputation method through linear mixed models with repeated measurements, using maximum-likelihood estimation. However, imputation is not advised for >10% missing values.	Probably no Reason: as secondary outcome measure in protocol, "global rating of change" has been reported.	Probably no Reason: calculated required sample size not reached (underpowered), several baseline differences in treatment groups (e.g. duration of symptoms). Sample size calculation is not reached, underpowered.	**Some concerns** - Due to large loss to follow-up and crossover, results might be slightly biased - Deviation from protocol in outcome reporting - Underpowered
Moustafa, 2014	Definitely yes Reason: random number generator restricted to permuted blocks of different sizes, transferred to a sequence of consecutively numbered, sealed opaque envelopes	Definitely yes Reason: independent person picked next sealed opaque envelope	Definitely no Reason: Patients (self-reported outcome measures) and health care providers not blinded. Unclear whether data-analysts were blinded.	Probably yes Reason: loss to follow-up 12.5%, missing data imputed with linear mixed model with repeated measurements	Probably no Reason: protocol retrospectively registered. Patients included from 35-48 years of age not specified in manuscript.	Probably no Reason: highly selective inclusion criteria for study.	**Some concerns:** - Patients not random sample of population - Risk of further selection bias - No protocol available prior to study start
Young, 2009	Probably yes	Definitely yes	Probably yes	Probably yes	Unclear	Probably no	**Some concerns:** - possible selection

	Reason: numbered, sequential, sealed envelopes containing group allocation, stratified by clinic. Unclear generation of randomization sequence.	Reason: opaque sealed envelopes opened by evaluating therapist	Reason: Patients were -semi blinded (sham treatment. Health care providers were not blinded. Support staff unaware of group assignment administered self-report measures and testing. Data analysts not involved in treatment.	Reason: 15% loss to follow-up, yet repeated-measure linear mixed model analysis was performed for imputation.	Reason: no protocol available.	Reason: Possible selection bias due to patient selection through a clinical prediction rule. Home exercise adherence was not recorded.	bias - possible selective outcome reporting
3. Studies reporting on <u>exercise</u>							
Dedering, 2018	Definitely yes Reason: computer-generated randomized Table, randomizing patients in blocks of 8 with allocation ratio 1:1	Definitely yes Reason: treatment allocation put in opaque sealed envelope by statistician not involved in recruitment	Probably yes Reason: patients and care providers were not blinded (but difficult with regard to the intervention), but data entering and analysis were performed by different blinded individuals.	Definitely no Reason: large proportions in both groups (nearly 50%) discontinued intervention/control. Unclear imputation methods, imputation is not advised for >10% missing values.	Probably no Reason: in clinical trial registry additional secondary outcome measures are described	Probably yes Reason: ITT analysis performed (PP would be underpowered), no other problems mentioned.	**Some concerns** - High dropout rate - Selective outcome reporting
Diab, 2012	Probably yes Reason: random permuted size 4 blocks with equal allocation ratio, by the roll of a dice (odd/even)	Probably no Reason: end of block size prediction, resident blinded to research protocol operated the random assignment	Definitely no Reason: patients, care providers, and outcome assessors not blinded.	Probably no Reason: loss to follow-up not reported for outcomes after 6 months	Unclear Reason: all prespecified outcomes in methods were reported. No protocol available.	Probably no Reason: unclear whether ITT has taken place. Analysis was adjusted for baseline value.	**HIGH** - inadequate blinding - unclear dropout rate - high risk of biased analysis
4. Studies reporting on <u>neural mobilisation</u>							
Ayub, 2019	Probably no Reason: random allocation sequence was generated by one of the researchers	Definitely no Reason: inadequate randomization procedure	Probably yes Reason: data collector and analyst blinded for group allocation. Patients, health care professionals and data assessors not blinded.	Definitely yes Reason: No loss to follow-up, yet insufficient recruitment (underpowered)	Unclear Reason: No protocol available or previously published.	Definitely no Reason: selection bias through convenience sampling. Unclear interventions. Unclear choice for only female patients.	**HIGH** - Selection bias - inadequate randomization and allocation concealment - Underpowered
Basson, 2020	Definitely yes Reason: blocked randomization with a 2:1 ratio in blocks of 6 with a computer random numbet	Definitely yes Reason: Administrative research assistant informed participating physiotherapist of	Probably yes Reason: Patients and physiotherapists were not blinded. Follow-up measurements were taken by blinded physiotherapist	Definitely yes Reason: multiple imputation applied for missing data (larger in intervention group).	Probably no Reason: Global Rating of Change Scale reported in protocol, yet not in article.	Probably no Reason: early stop of recruitment, reducing power to 85%. Possible underpowered for detecTable difference.	**LOW**

	generator	allocation after baseline measurements					
Ibrahim, 2021	Probably yes Reason: opaque sealed envelopes containing the name of one of the groups	Definitely yes Reason: envelopes were picked by investigator not participating in the study	Probably no Reason: Patients and physiotherapists not blinded. No reporting of data collector, assessor, or analyst blinding.	Definitely yes Reason: no loss to follow-up.	Probably no Reason: no baseline data provided. No protocol available.	Probably no Reason: high risk of selection bias. Sample size calculated for disability, yet no disability outcome measure was taken.	**HIGH** - High risk of selection bias - No blinding of data collectors or analysts - unclear sample size calculation
Kayiran, 2021	Probably no Reason: no information available	Probably no Reason: no information available	Probably yes Reason: patients and physiotherapists were not blinded. Pre- and post-treatment evaluation by blinded physiotherapists. Unclear whether data analysts were blinded.	Definitely no Reason: >10% loss to follow-up without the use of adequate imputation methods (per protocol analysis).	Unclear Reason: no protocol available	Definitely no Reason: no sample size calculation available (underpowered?)	**HIGH** - Possible selection bias - high risk of inadequate randomization - Unclear sample size calculation
Kim, 2017	Probably no Reason: no information available	Probably no Reason: no information available	Probably no Reason: no information available.	Definitely yes Reason: no loss to follow-up.	Unclear Reason: no protocol available	Probably no Reason: risk of selection bias.	**HIGH** - possible selection bias - Lacking relevant information for methodological assessment of study
Rodriguez-sans, 2017	Definitely yes Reason: restricted block randomization with 1:1 allocation ratio through computerized randomization software	Definitely yes Reason: printed cards in consecutively numbered opaque sealed envelopes	Definitely yes Reason: subjects, physiotherapists and outcome assessors were blinded to the hypothesis tested and the existence of a second group (unethical?). Data analyst were blinded.	Probably no Reason: loss-to-follow-up was >10%, has impact on intervention effect estimate. As basis for sample size calculation unclear, risk for being underpowered.	Unclear Reason: protocol registered after recruitment of patients had started.	Probably yes Reason: no other problems reported, though authors state themselves that generalization of results is difficult.	**Some concerns** - Per protocol analysis (with risk of underpower) - Possible selective outcome reporting (
Savva, 2016	Definitely yes Reason: block randomization with blocks of 4 in sealed envelopes	Definitely yes Reason: researcher responsible for participant allocation (not involved in data collection or treatment) was blinded to block size	Probably yes Reason: Patients blinded to group assignment. Physiotherapists not blinded. Data collectors and assessors were blinded.	Definitely yes Reason: no loss to follow-up. Sample size calculation powered on NDI.	Unclear Reason: no protocol available	Probably yes Reason: no other issues reported. Patients unaware of other treatment group seems unethical.	**LOW**

Savva, 2021	Probably yes Reason: block randomization with block size of 4, yet sequence generation not described	Definitely yes Reason: researcher responsible for participant allocation (not involved in data collection or treatment) was blinded to block size	Probably yes Reason: Patients were blinded to group assignment. Data collectors were blinded to nature and purpose of study.	Definitely yes Reason: no loss to follow-up. Sample size calculation powered on NDI.	Unclear Reason: protocol registered after recruitment of patients had started.	Probably yes Reason: no other issues reported.	**LOW**
5. Studies reporting on <u>manual therapy</u>							
Hassan, 2020	Probably yes Reason: lottery method	No information Reason: specifics of lottery method not described	Probably yes Reason: patient and data analyst were blinded. Caregiver not blinded (not possible).	Probably no Reason: 13% loss to follow-up, has impact on intervention effect estimate (underpowered).	Probably yes Reason: all prespecified outcomes in methods were reported. No protocol available.	Definitely no Reason: selection bias through purposive sampling. Per protocol analysis.	**HIGH:** - Selection bias - Unclear allocation concealment - Per protocol analysis - Underpowered
Shafique, 2019	Probably yes Reason: lottery method	No information Reason: specifics of lottery method not described	Probably no Reason: no information provided on blinding of subjects, caregivers, data collectors or data analysts.	Definitely no Reason: Nearly 20% loss to follow up, current per protocol analysis has impact on effect estimate of intervention	Probably yes Reason: all prespecified outcomes in methods were reported. No protocol available.	Definitely no Reason: unclear eligibility and exclusion criteria. Unclear sample size calculation (likely underpowered). Unclear choice for statistical analysis.	**HIGH** - risk of selection bias - Unclear allocation concealment - Possibly underpowered - Per protocol analysis
Young, 2019	Definitely yes Reason: numbered, sequential, sealed opaque envelopes, stratified in blocks of 2 and 4 by clinic.	Definitely yes Reason: opaque sealed envelopes	Probably yes Reason: patients were blinded. Caregiver collected baseline outcomes, while another clinician blinded to allocation collected follow-up outcomes	Definitely yes Reason: due to short follow-up time (72 hours), no loss to follow-up occurred	Probably yes Reason: no deviations from published protocol, yet protocol was registered after inclusion start	Probably no Reason: trial stopped early due to exceeded effect sizes (larger than estimate)	**LOW**

Table of excluded studies

Reference	Reason for exclusion
Afzal 2019	<15 patients per treatment arm
Akkan 2018	Wrong comparator
Allison 2002	<15 patients per treatment arm
Alshami 2021	<15 patients per treatment arm
Anwar 2015	Wrong outcome
Aydin 2012	<15 patients per treatment arm
Borrella-Andrés 2021	Wrong intervention
Boyles 2011	Wrong study type included
Cheng 2015	Wrong patient population
Colombo 2020	Too broad PICO
Coppieters 2003(a)	Wrong outcome
Coppieters 2003(b)	Duplicate study population (Coppieters)
Costello 2016	<15 patients per treatment arm
Elnaggar 2009	Insufficient reporting of outcome of interest
Graham 2008	Wrong patient population
Gross 2015	Wrong patient population
Gross 2016	wrong study type
Halvorsen 2016	Duplicate study population (Dedering), wrong study design
Jellad 2009	<15 patients per treatment arm
Kuligowski 2021	wrong intervention, wrong outcome presentation (narrative)
Langevin 2015	wrong intervention
Leininger 2011	Incomplete study inclusion, not up to date
Liang 2019	wrong intervention, wrong language
Marks 2011	Wrong intervention
Ojoawo 2016	Possible duplicate patient population with Ojoawo 2018 (included in analysis)
Pandey 2021	Unclear presentation of outcome
Rajalaxmi 2020	Wrong intervention/unclear intervention
Rodine 2012	wrong study type included
Rodríguez-Sanz 2018	Duplicate patient population with 2017
Romeo 2018	More recent SR available
Salt 2011	Wrong intervention
Thoomes 2016	Wrong study type included
Thoomes 2013	Wrong controls (including surgery)
Xiao 2021	Insufficient reporting of outcome of interest
Yadav 2020	No full text available
Zhu 2016	Foreign language
Zronek 2016	Wrong patient population

5

Literature search strategy

Algemene informatie

Richtlijn: Cervicaal radiculair syndroom	
Uitgangsvraag: *Wat is de rol van fysiotherapie bij de behandeling van patiënten met CRS?*	
Database(s): Ovid/Medline, Embase.com	Datum: 25-04-2022
Periode: 2000 - heden	Talen: Engels, Nederlands
Literatuurspecialist: Miriam van der Maten	
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting: → Voor deze vraag is gezocht op de elementen cervical radiculopathy en fysiotherapeutische interventies → Het sleutelartikel wordt gevonden met de zoekopdracht.	
Te gebruiken voor richtlijnen tekst: In de databases Embase.com en Ovid/Medline is op 25 april 2022 met relevante zoektermen gezocht naar systematische reviews en RCTs over fysiotherapeutische interventies bij de behandeling van patiënten met CRS. De literatuurzoekactie leverde 339 unieke treffers op.	

5 ***Zoekopbrengst***

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SRs	161	124	167
RCT	150	114	172
Observationele studies			
Totaal	311	238	339

Zoekstrategie

Embase.com

No.	**Query**	**Results**
#14	#12 OR #13	311
#13	#9 AND #11 NOT #12 = RCT	150
#12	#9 AND #10 = SR	161
#11	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	1902585
#10	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR	733409

	metasynthes*:ti,ab OR 'meta synthes*':ti,ab	
#9	#7 AND #8 AND ([english]/lim OR [dutch]/lim) AND [2000-2022]/py NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	1350
#8	'physiotherapy'/exp OR physiotherap*:ti,ab,kw OR 'physio therap*':ti,ab,kw OR 'physical therap*':ti,ab,kw OR 'kinesiotherapy'/exp OR kinesiotherap*:ti,ab,kw OR kinesitherapeutic*:ti,ab,kw OR 'occupational therapy'/exp OR 'occupation* therap*':ti,ab,kw OR ergotherapy*:ti,ab,kw OR 'exercise'/exp OR exercise*:ti,ab,kw OR 'manipulative medicine'/exp OR chiropract*:ti,ab,kw OR manual*:ti,ab,kw OR manipulation*:ti,ab,kw OR collar:ti,ab,kw OR 'mobilisation'/exp OR mobili*ation:ti,ab,kw OR 'traction therapy'/exp OR traction:ti,ab,kw OR 'conservative treatment'/exp OR conservative:ti,ab,kw OR noninvasive:ti,ab,kw OR 'non invasive':ti,ab,kw OR nonsurg*:ti,ab,kw OR 'non surg*':ti,ab,kw OR nonoperati*:ti,ab,kw OR 'non operati*':ti,ab,kw	2266399
#7	'cervicobrachial neuralgia'/exp/mj OR cervicobrachialgia:ti,ab,kw OR ((radiculalgia:ti,ab,kw OR radiculitis:ti,ab,kw OR radiculitides:ti,ab,kw OR radiculopath*:ti,ab,kw OR polyradiculopath*:ti,ab,kw OR neuralgia:ti,ab,kw OR 'herniated disc*':ti,ab,kw OR hernia:ti,ab,kw OR ((radicular NEAR/3 (pain* OR neuralgia* OR symptom*)):ti,ab,kw) OR (('nerve root' NEAR/3 (pain* OR inflammation* OR disorder* OR compression* OR avulsion* OR impingement)):ti,ab,kw)) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('radicular pain'/exp/mj OR 'radiculopathy'/exp/mj) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw))	10643

Ovid/Medline

#	Searches	Results
9	7 or 8	238
8	(4 and 6) not 7 = RCT	114
7	4 and 5 = SR	124
6	(exp randomized controlled trial/ or randomized controlled trials as topic/ or random*.ti,ab. or rct?.ti,ab. or ((pragmatic or practical) adj "clinical trial*").ti,ab,kf. or ((non-inferiority or noninferiority or superiority or equivalence) adj3 trial*).ti,ab,kf.) not (animals/ not humans/)	1369026
5	(meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	560304
4	limit 3 to ((english language or dutch) and yr="2000 -Current")	906
3	1 and 2	1205
2	exp Physical Therapy Modalities/ or exp Occupational Therapy/ or physiotherap*.ti,ab,kf. or 'physio therap*'.ti,ab,kf. or 'physical therap*'.ti,ab,kf. or kinesiotherap*.ti,ab,kf. or kinesitherapeutic*.ti,ab,kf. or 'occupation*	1227076

	therap*'.ti,ab,kf. or ergotherapy*.ti,ab,kf. or exp Conservative Treatment/ or conservative.ti,ab,kf. or noninvasive.ti,ab,kf. or 'non invasive'.ti,ab,kf. or nonsurg*.ti,ab,kf. or 'non surg*'.ti,ab,kf. or nonoperati*.ti,ab,kf. or 'non operati*'.ti,ab,kf. or exp Exercise/ or exercise*.ti,ab,kf. or exp Musculoskeletal Manipulations/ or chiropract*.ti,ab,kf. or manual*.ti,ab,kf. or manipulation.ti,ab,kf. or collar.ti,ab,kf. or mobile*ation.ti,ab,kf. or exp Traction/ or traction.ti,ab,kf.	
1	((exp Radiculopathy/ or radiculalgia.ti,ab,kf. or radiculitis.ti,ab,kf. or radiculitides.ti,ab,kf. or radiculopath*.ti,ab,kf. or polyradiculopath*.ti,ab,kf. or neuralgia.ti,ab,kf. or 'herniated disc*'.ti,ab,kf. or hernia.ti,ab,kf. or (radicular adj3 (pain* or neuralgia* or symptom*)).ti,ab,kf. or ('nerve root' adj3 (pain* or inflammation* or disorder* or compression* or avulsion* or impingement)).ti,ab,kf.) and (exp Cervical Vertebrae/ or exp Neck/ or cervical.ti,ab,kf. or cervico*.ti,ab,kf. or neck.ti,ab,kf.)) or cervicobrachialgia.ti,ab,kf.	6515

Module 2.2. Epidurale corticosteroïde-injecties

Uitgangsvraag

Wat is de rol van epidurale corticosteroïde-injecties (ECSI) bij de behandeling van patiënten met een cervicaal radiculair syndroom?

Inleiding

Veelal heeft het voorkeur om patiënten met een cervicaal radiculair syndroom (CRS) primair te behandelen met conservatieve (niet-operatieve) therapieën. Als onderdeel van een conservatief traject kunnen zorgverleners naast bewegingsadviezen, fysiotherapie en pijnmedicatie ook een interventionele pijnbehandeling geven. Een interventionele pijnbehandeling kan bestaan uit epidurale corticosteroïde-injecties. Door pijnverlichting probeert men een operatieve interventie te voorkomen, aangezien het natuurlijk beloop van een CRS meestal gunstig is.

De achtergrond voor epidurale corticosteroïde-injecties is gebaseerd op de veronderstelling dat CRS gepaard gaat met een ontstekingsreactie, welke bijdraagt aan de radiculaire pijnklachten. De aanname is dat de injecties pijnstillend en ontstekingsremmend werken. Injecties kunnen transforaminaal of interlaminair toegediend worden.

Epidurale corticosteroïde-injecties worden in de praktijk veelvuldig toegepast. Momenteel is echter de (toegevoegde) waarde van epidurale corticosteroïde-injecties, als behandeling of als add-on therapie, voor patiënten met CRS onduidelijk. Vanwege mogelijke complicaties, dienen zowel effectiviteit als veiligheid in kaart gebracht te worden, alvorens aanbevelingen kunnen worden geformuleerd.

Deze module gaat over patiënten met cervicaal radiculair syndroom. Raadpleeg bij nekpijn zonder radiculaire pijn de betreffende richtlijn.

Search and select.

A systematic review of the literature was performed to answer the following question: *What is the efficacy of epidural steroid injections compared to care as usual in patients with cervical radiculopathy?*

P: Patients with cervical radiculopathy (acute or sub-acute)
I: (Add on) epidural corticosteroid injections with or without local anaesthetic injection (transforaminal/midline or interlaminar)
C: Other conservative treatment possibilities
O: Pain, patient satisfaction, complications, use of medication, functioning, disability, quality of life, surgery sparing effect

<u>Relevant outcome measures</u>

The guideline development group considered pain, patient satisfaction, and complications as a critical outcome measure for decision making; and use of medication, functioning (return to work), quality of life and surgery sparing effect as important outcome measures for decision making.

The working group defined the outcome measures as follows:

- Patient satisfaction: Likert-scale or global perceived effect (GPE)
- Functioning: Return to work
- Quality of life: Validated questionnaires

A priori, the working group did not define other outcome measures but used the definitions from the studies.

The working group defined a 10% difference for both continuous outcome measures and dichotomous outcome measures informing on relative risk (RR ≤ 0.91 and ≥ 1.1), and standardized mean difference (SMD=0,2 (small); SMD=0,5 (medium); SMD=0,8 (large)) as minimal clinically (patient) important differences.

Search and select (Methods)

The databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms from 1990 until 25 April 2022. The detailed search strategy is depicted under the tab Methods. The systematic literature search resulted in 382 hits. Studies were selected based on the following criteria:

- Systematic review (searched in at least two databases, and detailed search strategy, risk of bias assessment and results of individual studies available), randomized controlled trial comparing epidural steroid injections with other conservative treatment possibilities;
- Patients aged ≥ 18 years;
- Full-text English or Dutch language publication;
- Studies including ≥ 20 patients (ten in each study arm); and
- Studies according to PICO

Initially, 37 studies were selected based on title and abstract screening. After reading the full text, 32 studies were excluded (see the table with reasons for exclusion under the tab Methods), and five studies were included.

Results

Five studies were included in the analysis of the literature. A comprehensive overview of study characteristics is depicted in Table 1. Important study characteristics and results are summarized in the evidence table. The assessment of the risk of bias is summarized in the risk of bias table.

Summary of literature

Description of studies

Anderberg (2007) performed an RCT to determine the short-term effect of a single dose corticosteroid injection on cervical radiculopathy with radicular pain. Participants were 27 to 65 years of age, and underwent prior MRI investigation of the cervical spine, evaluated by three medical specialists, and a diagnostic selective nerve root block (SNRB). All patients responding with a significant pain reduction to SNRB's, were randomized into treatment with transforaminal epidural injections with mepivacaïne (carbocain) and methylprednisolone acetate (n= 20), or with transforaminal epidural injections with mepivacaïne (carbocain) with saline (n= 20). Patients whose MRI documented degenerative pathology at two levels received SNRB at two levels. If the response to SNRB was positive, they received the at random selected treatment at two levels. Otherwise, the patient received the random treatment at one level. A total of 40 (100%) participants completed the three-week follow-up.

Bureau (2014) performed an RCT to test the effectiveness of intra-articular facet steroid injections (IFSI) compared with transforaminal corticosteroid injections (TFSI) in participants with cervical radiculopathy. Participants were adults with a history of at least one month radiculopathy, refractory to medical treatment, with motor weakness due to degenerative spondylosis and/or disk herniation, and a pain score of at least 6 or higher on a verbal analogue scale (VAS). A total of 56 (100%) participants completed the 4-week follow-up.

Cohen (2014) performed an RCT to determine the effectiveness of cervical interlaminar epidural steroid injections compared to conservative care (pharmacotherapy and physical therapy) or combination-treatment (epidural steroid injection with physical therapy). Participants had a minimal age of 18 years and had a history of cervical radicular pain of more than 4/10 on a numerical rating scale. Participants had complaints longer than one month, but not over 4 years.
A total of 58 (98%) participants in the conservative treatment-group, 54 (98%) participants in the interlaminar epidural steroid-group and 51 (93%) participants in the combined-group completed the one-month follow-up. For 3- and 6-month follow up data, the last observation carried forward method was used.

Manchikanti (2012) performed an RCT to determine the effectiveness of cervical interlaminar epidural injections of local anaesthetics with or without steroids for the treatment of patients with herniation and radiculitis. Participants had a minimal age of 18 years, had a history of chronic, function-limiting neck and upper extremity pain (at least for six months), and failed to respond to conservative treatment. Participants were blinded to group assignment, and a total of 56 (93%) participants in the intervention group, and 59 (98%) in the group receiving local anaesthetic completed 12-month follow-up. All participants were included in analysis.

Stav (1993) performed an RCT to determine the effectiveness of cervical epidural steroid injections for treatment of cervical pain syndrome. It was not reported whether an interlaminar or transforaminal approach was used. Participants were 20 to 75 years of age and had chronic refractory cervicobrachialgia. Participants were not blinded to group assignment, and a total of 25 (100%) participants in the intervention group, and 17 (68%) in the control group, receiving an intramuscular injection of lidocaine and steroid, completed 1 year follow-up. In the control group, 8 participants were excluded from all analyses due to a process of litigation of insurance claims.

***Table 1**. Description of included studies*

Study	Intervention		Comparator		Follow-up	Outcomes
	Characteristics	**Intervention type/ dose**	**Characteristics**	**Type of control group**		
Anderberg, 2007	Mean age (SD): 49.5 (8.7) Female (%): 11 (55) Duration of pain, months (SD): 34.5 (26.9) Level of injection: C5-C6 (n= 3), C6 (n= 7), C6-C7 (n=3), C7 (n=6), C7-C8 (n= 1) Diagnosis: foraminal stenosis (n= 15), hard disc (n=4), soft disc (n= 1)	Transforaminal steroids/local anaesthetics (n= 20) 0.5 ml Carbocain (Mepivacaine) and 1 ml Depo Medrol (40 mg methylprednisolone acetate) per injection (either on one or two levels (roots) of the cervical spine)	Mean age (SD): 52.5 (7.0) Female (%): 9/20 (45) Duration of pain, months (SD): 27.0 (25.8) Level of injection: C4 (n= 1) C5 (n= 3), C6 (n= 8), C6-C7 (n=4), C7 (n=3), C8 (n= 1) Diagnosis: foraminal stenosis (n= 11), hard disc (n= 8), soft disc (n= 1)	Transforaminal saline/local anaesthetic (n= 20) 0.5 ml Carbocain (Mepivacaine) and 1 ml saline per injection (either on one or two levels (roots) of the cervical spine)	1, 2, and 3 weeks after injections.	Pain (significant subjective reduction of radicular pain/neurological deficits (yes/no))
Bureau, 2014	Mean age (SD): 52 (11) Female (%): 13 (46) Duration of pain, months (SD): 17 (21) Level of injection: C4-C5 (n= 3), C5-C6 (n= 15), C6-C7 (n= 10) Imaging findings: disc herniation (n= 7), spondylosis (n= 20), spondylosis/disc herniation (n= 1)	TFSI (n= 28) 1 ml of dexamethasone sodium phosphate, 10 mg/ml, with 0.5-1.0 mL of contrast material, the needle is positioned in the posterolateral aspect of the foramen.	Mean age (SD): 44 (8.3) Female (%): 20 (71) Duration of pain, months (SD): 14 (20) Level of injection: C3-C4 (n= 1), C4-C5 (n= 1), C5-C6 (n= 16), C6-C7 (n=10) Imaging findings: disc herniation (n= 12), spondylosis (n= 14), spondylosis/disc herniation (n= 2)	IFSI (n= 28) 1 ml of dexamethasone sodium phosphate, 10 mg/ml, with 0.5-1.0 mL of contrast material, the needle is positioned in the facet joint.	4 weeks after injections.	Pain (VAS), medication use (MSQ), disability (NDI)
Cohen, 2014	Median age (IQR): 44.0 (41.0-54.0) Female (%): 28 (50.9) Duration of pain, years (median, IQR): 0.8 (0.3-2.0)	Epidural steroid injection (n= 59) 3 ml solution, 60 mg depo-methylprednisolone and saline. At least one injection with fluoroscopic guidance, ipsilateral to midline (when symptoms were unilateral) or midline (bilateral symptoms).	Median age (IQR): 45.0 (41.0-54.0) Female (%): 33 (55.9) Duration of pain, years (median, IQR): 1.0 (0.5-2.0)	Conservative treatment (n= 55) Pharmacotherapy (gabapentin/nortriptyline) and physical therapy as indicated.	1, 3, and 6 months after injections	Pain (NRS arm, NRS neck), successful treatment outcome (yes/no), medication use, positive global perceived effect (yes/no), disability (NDI), surgery sparing effect
	Median age (IQR): 49.0 (41.0-59.0) Female (%): 25 (45.5) Duration of pain, years (median, IQR): 0.7 (0.3-2.5)	Combined treatment (n= 55) Conservative treatment (pharmacotherapy) with				

Study	Intervention		Comparator		Follow-up	Outcomes
	Characteristics	**Intervention type/ dose**	**Characteristics**	**Type of control group**		
		additional epidural steroid injection.				
Manchikanti, 2012	Mean age (SD): 45.6 (10.4) Female (%): 35 (58) Duration of pain, months (SD): 91.9 (94.5) Level of disc herniation: C3-C4 (n= 8), C4-C5 (n= 12), C5-C6 (n= 36), C6-C7 (n= 28), C7-T1 (n= 7)	Betamethasone (n= 60) Cervical interlaminar epidural injections, 4 ml with 0.5% lidocaine, mixed with 1 ml or 6 mg non-particulate betamethasone	Mean age (SD): 46.2 (10.3) Female (%): 32 (53) Duration of pain, months (SD): 118.3 (98.6) Level of disc herniation: C3-C4 (n= 8), C4-C5 (n= 18), C5-C6 (n= 30), C6-C7 (n= 24), C7-T1 (n= 6)	Anaesthetic (n= 60) Cervical interlaminar injections 5 ml with lidocaine 0.5%	3, 6, and 12 after injections	Pain (NRS), medication use (opioid intake), functioning (employment characteristics), disability (NDI)
Stav, 1993	Mean age (SD): 52.3 (12.2) Female (%): 14 (56) Duration of pain, months (SD): 16.2 (10.5)	Cervical epidural steroid/lidocaine injection (n= 25)	Mean age (SD): 49.3 (12.4) Female (%): 9 (53) Duration of pain, months (SD): 14.2 (8.3)	Steroid/lidocaine injections into posterior neck muscles (n= 17)	1 week and 1 year after injections	Pain (VAS), functioning (recovery of capacity for work), medication use (decreased daily dose of analgesics), complications (worse pain (yes/no))

MSQ, Medication Quantitative Scale; NDI, Neck Disability Index; NRS, Numeric Rating Scale; VAS, Visual Analogue Scale

Results

1. Pain (critical)

Five studies reported on pain (Anderberg, 2007; Bureau, 2014; Cohen, 2014; Manchikanti, 2012; Stav, 1993). Results are presented in three post-intervention terms: a) short term: until 30 days, b) mid-term: >30 days to 3 months, and c) long term: >3 months to 1 year. A brief overview of the main characteristics is provided in Table 2.

***Table 2**. Overview on post-intervention terms*

Study	Follow-up	Term	Scale
Anderberg, 2007	1, 2 and 3 weeks	Short term	Arm pain and/or neurological deficits (VAS-scale, yes/no)
Bureau, 2014	4 weeks	Short term	Mean change from baseline score of 62.4 (VAS-scale, 0-100)
Cohen, 2014	1, 3 and 6 months	Short term, mid-term, long term	Mean score on numerical rating pain scale for arm and neck-pain (NRS-scale, 0-10)
			Decrease of ≥2 points on arm pain (NRS-scale, yes/no)
Manchikanti, 2012	3, 6 and 12 months	Mid-term, long term	Pain relief (NRS-scale, 0-10)
Stav, 1993	1 week and 12 months	Short term, long term	Pain decrease of ≥50% (VAS-scale, yes/no)

NRS: Numeric rating scale; VAS: Visual Analogue Scale

1a. Short term arm pain (post-treatment: 30 days)

Four studies reported on pain up to 30 days (Anderberg, 2007; Bureau, 2014; Cohen, 2014; Stav, 1993).

Local anaesthetic with steroids vs. local anaesthetic alone

Anderberg (2007) reported results for one, two and three weeks after injection. One week after injection, eight out of twenty (40%) participants in the intervention group and seven out of twenty (35%) participants in the control group reported a reduction. This resulted in a risk ratio of 1.14 (95%CI 0.51 to 2.55). Two weeks after injection, in seven (35%) participants in the steroid treatment group, and in six (30%) participants in the control group the effect was maintained. This resulted in a risk ratio of 1.17 (95%CI 0.48 to 2.86). These effects were not clinically relevant. Three weeks after injection, in six participants in the intervention group (30%) and six participants in the control group (30%) the effect was maintained. This resulted in a risk ratio of 1.00 (95%CI 0.39 to 2.58). Results are depicted in figure 1.

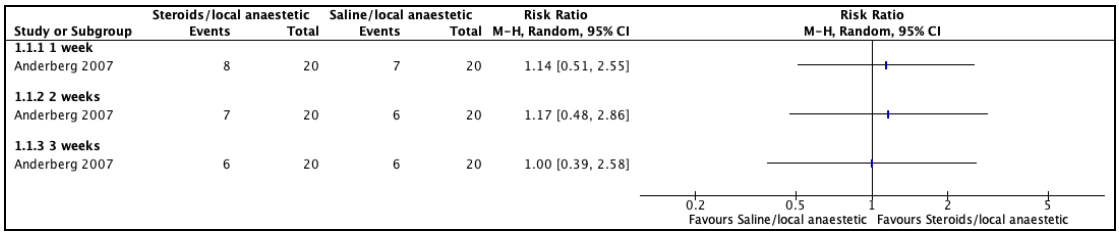

***Figure 1**. Mean differences for arm pain, local anaesthetic with steroids versus anaesthetic alone (follow-up: 1-3 weeks)*

Transforaminal vs. intra-articular facet corticosteroid injections

Bureau (2014) reported results for four weeks after baseline. In the TFSI-group, mean VAS-scores reduced with 9.8% (95%CI -11.5 to 31.2). In the IFSI-group, VAS-scores reduced with 45.3% (95%CI 21.4 to 69.2). The analysis resulted in a mean difference of -35.50 (95%CI -66.1 to -4.89) favouring the IFSI-group. This difference was clinically relevant. Results are depicted in figure 2.

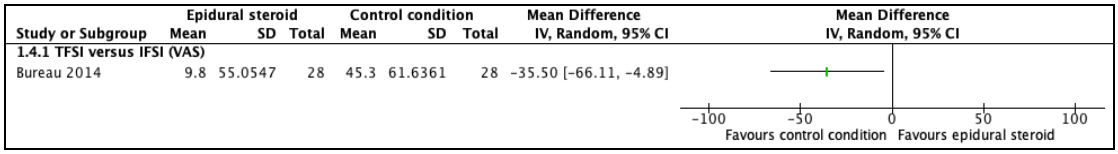

***Figure 2**. Mean differences in pain, transforaminal versus intra-articular facet corticosteroid injections.*

Epidural steroids with or without conservative treatment vs. conservative treatment alone

Cohen (2014) reported results for arm pain one month after injection. In the epidural steroid injection group, the mean score was 4.2 (SD 2.59). In the combined group, mean score was 3.5 (SD 2.59). In the group with conservative treatment, the mean score was 4.3 (SD 2.69). The mean difference between the epidural steroid group and the conservative treatment group was 0.1 (95%CI -0.87 to 1.07). The mean difference between the combination group and the conservative treatment group was 0.80 (95%CI -0.17 to 1.77). Results are depicted in figure 3.

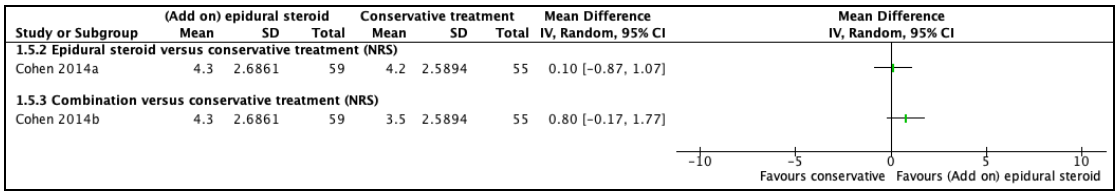

***Figure 3**. Mean differences in arm pain, epidural steroids with hand without conservative treatment versus conservative treatment alone.*

After 1 month, 29 (53.7%) of the participants in the epidural steroid group, 30 (51.7%) participants in the conservative treatment group and 33 (64.7%) participants in the combined group reported a successful treatment outcome. The risk ratio between the group receiving conservative treatment and the group receiving epidural steroids was 1.04 (95%CI 0.73 to 1.47). The risk ratio between the group receiving conservative treatment and combination treatment was 1.25 (95%CI 0.91 to 1.72) are depicted in figure 4.

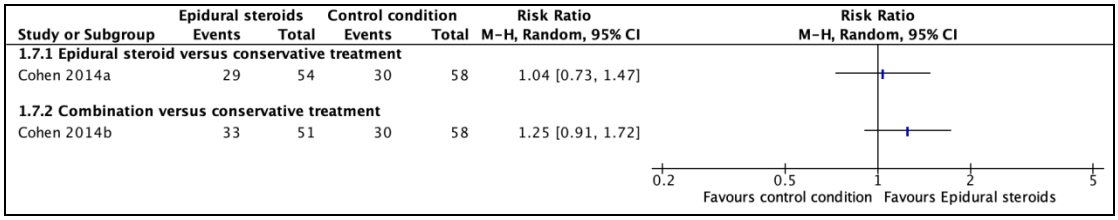

***Figure 4**. Risk ratios for successful treatment outcome, epidural steroids with and without conservative treatment versus conservative treatment alone*

Cervical epidural steroid injection vs. steroid injections into posterior neck muscles

Stav (1993) reported results for one week after injection. Very good and good scores were considered as pain relief.

After one week, in the cervical epidural steroid group 19 out of 25 participants (76%) experienced pain relief, compared to 6 out of 17 participants (35%) in the posterior neck-muscle steroid group. This resulted in a risk ratio of 2.15 (95%CI 1.09 to 4.25), favouring the cervical epidural group. This difference was clinically relevant. Results are depicted in figure 5.

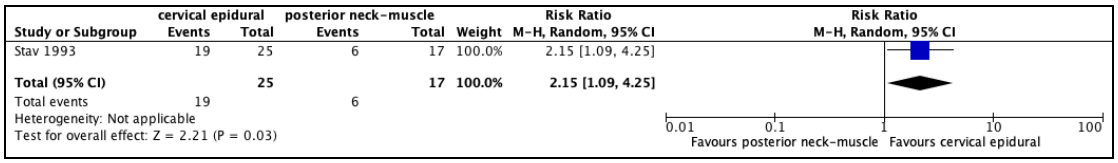

***Figure 5**. Risk ratios for pain relief, cervical epidural steroid injection versus steroid injection into posterior neck muscles*

1b. Mid-term arm pain (post-treatment: >30 days to 3 months)

Two studies reported on pain after 30 days up to 3 months (Cohen, 2014; Manchikanti, 2012).

Epidural steroids with or without conservative treatment vs. conservative treatment alone

Cohen (2014) reported results for 3 months after injection. 18 (36.7%) of the participants in the epidural steroid group, 15 (26.8%) participants in the conservative treatment group and 29 (56.9%) participants in the combined group reported a successful treatment outcome. This resulted in a risk ratio of 1.37 (95%CI 0.78 to 2.42).

The risk ratio between the group receiving conservative treatment and combination treatment was 2.12 (95%CI 1.29 to 3.48), favouring the combined group. These differences were clinically relevant. Results are depicted in figure 6.

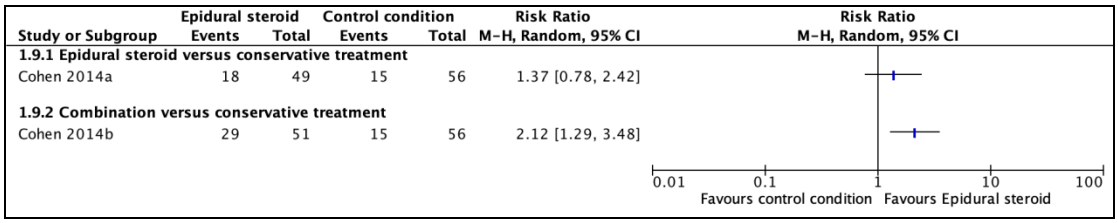

Figure 6*. Mean differences for arm pain 3 months after injection, Epidural steroids with or without conservative treatment versus conservative treatment alone.*

Cervical interlaminar injections with anaesthetic and betamethasone vs. anaesthetic alone

Manchikanti (2012) reported results for three months after injection. After 3 months, the mean difference between anaesthetic with betamethasone group and the anaesthetic group was 0.1 (95%CI -0.40 to 0.60). Results are depicted in figure 7.

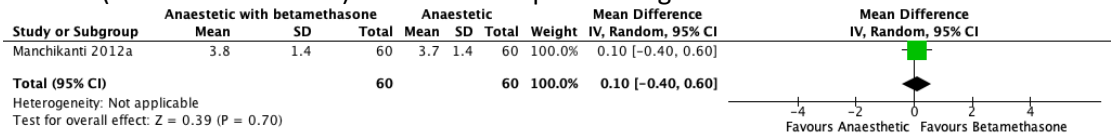

Figure 7*. Mean difference for pain 3 months after injection, Cervical interlaminar injections with anaesthetic and betamethasone versus anaesthetic alone*

1c. Long term arm pain (post-treatment: >3 months to 1 year):

Three studies reported on pain over 3 months up to one year after injection (Cohen, 2014; Manchikanti, 2012; Stav, 1993).

Epidural steroids with or without conservative treatment vs. conservative treatment alone

Cohen (2014) reported results for 6 months after injection. 12 (25.5%) of the participants in the epidural steroid group, 13 (23.6%) participants in the conservative treatment group and 22 (44%) participants in the combined group reported a successful treatment outcome. The risk ratio between the epidural steroid group and the conservative treatment group was 1.08 (95%CI 0.55 to 2.13).

The risk ratio between the group receiving conservative treatment and combination treatment was 1.86 (95%CI 1.05 to 3.29), favouring the combined group. This difference was clinically relevant. Results are depicted in figure 8.

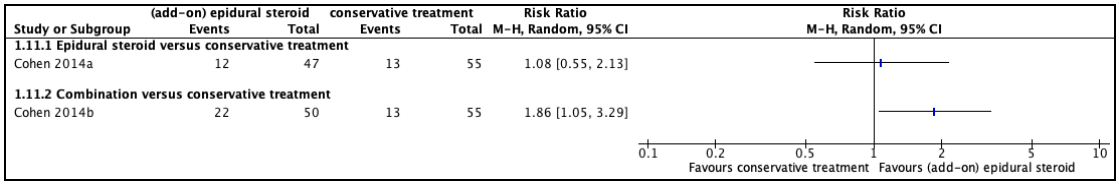

***Figure 8**. Risk ratio for successful treatment outcome, Epidural steroids with or without conservative treatment versus conservative treatment alone*

Cervical interlaminar injections with anaesthetic and betamethasone vs. anaesthetic alone

Manchikanti (2012) reported results for 6 months after injection. After 6 months, the mean difference between the anaesthetic group and the group receiving betamethasone plus anaesthetic was -0.40 (95%CI -0.92 to 0.12). After 12 months, the mean difference was -0.20 (95%CI -0.74 to 0.34). Results are depicted in figure 9.

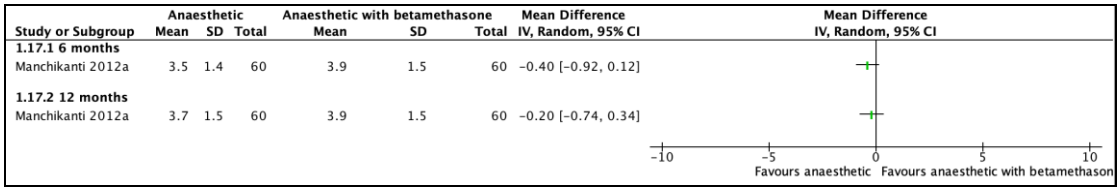

***Figure 9**. Mean difference for pain, Cervical interlaminar injections with anaesthetic and betamethasone versus anaesthetic alone.*

Cervical epidural steroid injection vs. steroid injections into posterior neck muscles

Stav (1993) reported results for one year after injection. Very good and good scores were considered as pain relief.

After one year, in the cervical epidural group 17 out of 25 participants (68%) experienced pain relief, compared to 2 out of 17 (12%) participants in the posterior neck-muscle group. This resulted in a risk ratio of 5.78 (95%CI 1.53 to 21.84), favouring the cervical epidural group. This difference was clinically relevant. Results are depicted in figure 10.

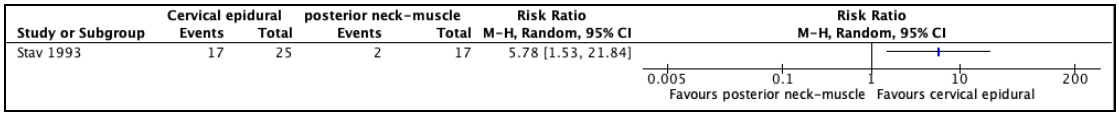

***Figure 10**. Risk ratio for pain relief, Cervical epidural steroid injection versus steroid injections into posterior neck muscles*

1d. Short term neck pain (post-treatment: 30 days)

Epidural steroids with or without conservative treatment vs. conservative treatment alone

Cohen (2014) reported results for neck pain one month after injection. In the epidural steroid injection group, the mean score was 4.6 (SD 2.59). In the combined group, mean score was 3.5 (SD 2.77). In the group with conservative treatment, the mean score was 4.7 (SD 2.49). The mean difference between the epidural steroid group and the conservative treatment group was 0.10 (95%CI -0.83 to 1.03).

The mean difference between the combination group and the conservative treatment group was 1.20 (95%CI 0.23 to 2.17), favouring the combined group. This difference was clinically relevant. Results are depicted in figure 11.

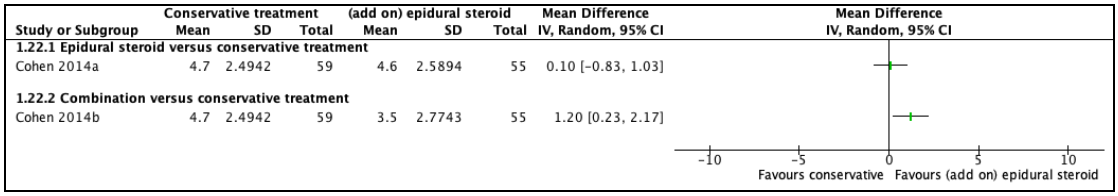

***Figure 11**. Mean differences for neck pain 30 days after injection, Epidural steroids with or without conservative treatment versus conservative treatment alone.*

2. Patient satisfaction (critical)

One study reported on patient satisfaction (Cohen, 2014).

Epidural steroids with or without conservative treatment vs. conservative treatment alone

Cohen (2014) reported on patient satisfaction using the global perceived effect (GPE). The GPE was considered positive when both, arm pain was reduced since baseline for two points or more, and the participant was satisfied with the treatment. This was measured with the two statements "my pain has improved/worsened/stayed the same since my last visit" and "I am satisfied/not satisfied with the treatment I received and would/would not recommend it to others". A positive GPE was reported in 33 (61.1%) participants in the epidural steroid group, in 37 participants (72.6%) in the combined group and in 35 (60.3%) participants in the conservative group.

The risk ratio between the epidural steroid group and the conservative group was 1.01 (95%CI 0.75 to 1.37). The risk ratio between the combined group and the conservative treatment group was 1.07 (95%CI 0.87 to 1.32). Results are depicted in figure 12.

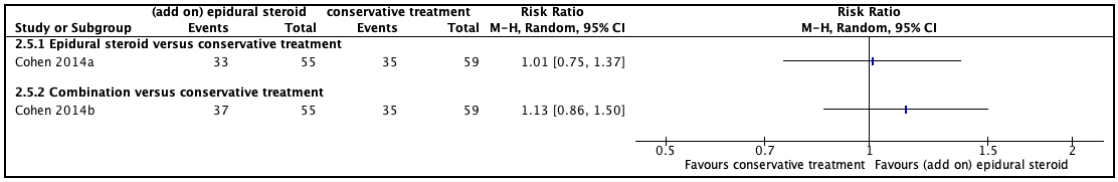

***Figure 12.** Risk ratio for positive Global Perceived Effect, Epidural steroids with or without conservative treatment versus conservative treatment alone.*

3. Complications (critical)

Five studies reported on complications (Anderberg, 2007; Bureau, 2014; Cohen, 2014; Manchikanti, 2012; Stav, 1993).

Local anaesthetic with steroids vs. local anaesthetic alone

Anderberg (2007) reported no serious complications. Five out of 40 patients reported minor complications. One participant experienced an allergic skin reaction, and four participants experienced increase in radicular pain for some days after injections. None of the participants reported any persisting negative effects three weeks after the intervention.

Transforaminal vs. intra-articular facet corticosteroid injections

Bureau (2014) reported that one participant in the TFSI-group had tinnitus and vertigo after the intervention. In both groups, one participant reported having headaches in the two days following the injections. For adverse events, results were presented for participants as treated. The participant reporting headache in the IFSI-group actually received TFSI. Thus, all participants reporting adverse events received TFSI.

Epidural steroids with or without conservative treatment vs. conservative treatment alone
Cohen (2014) reported that ten complications occurred in eight participants receiving epidural steroids or combined treatment. Two headaches were reported, one wet-tap (not associated with neurological sequalae), one participant experienced prolonged post procedure pain, and in two participants the neurological symptoms worsened for less than two weeks. Furthermore, one rash, two vasovagal episodes and one case of tachycardia (resolved with assurance) were reported.

Cervical interlaminar injections with anaesthetic and betamethasone vs. anaesthetic alone
Manchikanti (2012) did not report on complications per arm. One participant had a subarachnoid puncture, intravascular penetrations appeared in three participants, and one participant reported soreness for seven days.

Cervical epidural steroid injection vs. steroid injections into posterior neck muscles
In Stav (1993), two participants in the intervention-group and two participants in the control-group experienced worse pain after one week. This did not change after 1 year.

Outcomes for complications were not pooled, because complications were often not reported per group, the low number of events, and definitions of complications were not similar enough to ensure a clinical meaningful answer.

4. Use of medication (important)
Four studies reported on use of medication (Bureau, 2014; Cohen, 2014; Manchikanti, 2012; Stav, 1993).

Transforaminal vs. intra-articular facet corticosteroid injections
Bureau (2014) reported pain outcomes using the Medication Quantitative Scale-scale (MQS-scale) at four weeks after injection. At baseline, subjects were instructed continuing with their usual medication. However, mean differences were presented for different groups by baseline VAS-score. For this reason, this outcome could not be graded.

Epidural steroids with or without conservative treatment vs. conservative treatment alone
Cohen (2014) reported use of medication in whether a participant reduced their opioid use with ≥20%, or completely quit using non-opioids. The study did not provide information on whether changed intake of opioids was based on prescription or initiative of the participant. Reduced medication use was reported in 15 (34.9%) participants in the epidural steroid group, 16 (35.6%) participants in the conservative treatment group, and in 23 (54.8%) participants in the combined group. The risk ratio between the epidural steroid group and the conservative group was 1.01 (95%CI 0.55 to 1.83).

The risk ratio between the combined group and the conservative group was 1.54 (95%CI 0.86 to 1.89). Results are depicted in figure 13.

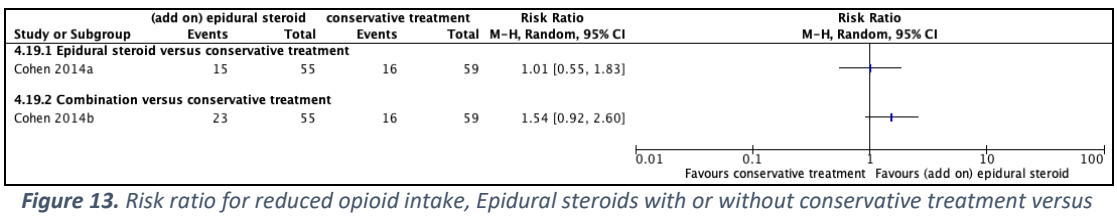

Figure 13. *Risk ratio for reduced opioid intake, Epidural steroids with or without conservative treatment versus conservative treatment alone.*

Cervical interlaminar injections with anaesthetic and betamethasone vs. anaesthetic alone

Manchikanti (2012) reported medication use in changes in intake of morphine equivalents. The study did not provide information on whether changed intake of opioids was based on prescription or initiative of the participant. Baseline morphine intake was 53.8 (SD 36.1) in the betamethasone group, and 57.0 (SD 46.1) in the anaesthetic group. At 3 months, mean difference in medication use was -0.80 (95%CI -7.67 to 6.07). At 6 months, mean difference in medication use was -2.50 (95%CI -9.49 to 4.49). At 12 months, mean difference in medication use was -0.80 (95%CI -8.04 to 6.44). Results are depicted in figure 14.

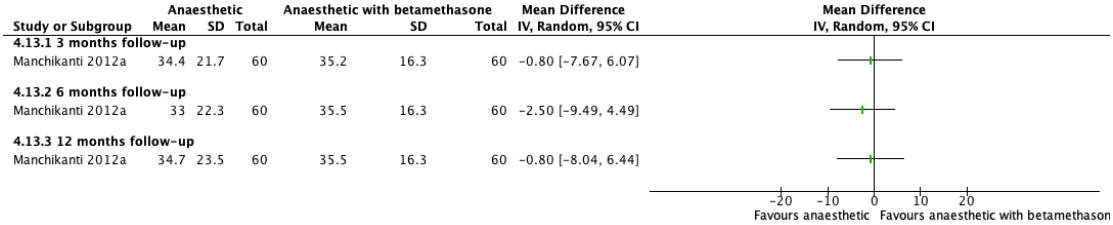

***Figure 14**. Mean differences for intake of morphine equivalents Cervical interlaminar injections with anaesthetic and betamethasone versus anaesthetic alone.*

Cervical epidural steroid injection vs. steroid injections into posterior neck muscles

Stav (1993) reported on medication use in whether a participant reduced their daily dose of analgesics. The study did not provide information on whether changed intake of medication was based on prescription or initiative of the participant. After one-week, reduced use of analgesics was reported in 81.7% of the participants in the cervical epidural steroid group, and in 8.6% of the participants in the posterior neck-muscle group. After one year 63.9% participants in the cervical epidural steroid group reduced their use of analgesics compared to 9.4% of the participants in the posterior neck-muscle group. Upon subsequent calculation, these percentages could not be translated to risk ratios. These results were therefore not graded.

5. Functioning (important)

Cervical interlaminar injections with anaesthetic and betamethasone vs. anaesthetic alone

Manchikanti (2012) reported on functioning using employment characteristics. Results are presented in (table 3), however these results could not be evaluated using GRADE.

***Table 3**. Employment characteristics*

	Group 1		**Group 2**	
Employment status	Baseline	12 months	Baseline	12 months
Total employed/eligible for employment at baseline	11/13	11/13	15/22	17/22
Unemployed due to pain/eligible for employment at baseline	0/13	0/13	2/22	1/22
Disabled/total	37/60	37/60	33/60	33/60
Retired/total	7/60	7/60	4/60	4/60

Cervical epidural steroid injection vs. steroid injections into posterior neck muscles

Stav (1993) reported on functioning using recovery of capacity for work. After one week, recovered capacity for work was reported in 69.4% of the participants in the cervical epidural steroid group and in 12.8% of the participants in the posterior neck-muscle group. After one year, 61.3% participants in the cervical epidural steroid group recovered capacity for work, compared to 15.9% of the participants in the posterior neck-muscle group. Upon subsequent calculation, these percentages could not be translated to risk ratios. These results were therefore not evaluated using GRADE.

6. Disability

Three studies reported on disability (Bureau, 2013; Cohen, 2014; Manchikanti, 2012) using the Neck Disability Index (NDI).

6a. Short term disability (post-treatment: 30 days)

Transforaminal vs. intra-articular facet corticosteroid injections

Bureau (2014) reported results for four weeks after baseline, using the NDI range 0-50. In the TFSI-group, mean NDI-scores reduced with 9.6% (SD 64.0). In the IFSI-group, NDI-scores reduced with 24.3% (SD 70.1). This corresponds with a decrease of 4.8 points in the TFSI-group (95%CI -17.2 to 7.6) and a decrease of 12.15 points in the IFSI-group (95%CI -25.75 to 1.45). The analysis resulted in a mean difference of -14.7 (95%CI -49.9 to 18.4).

Epidural steroids with or without conservative treatment vs. conservative treatment alone

Cohen (2014) reported results for disability one month after injection, using the NDI range 0-100. In the epidural steroid injection group, the mean score was 33.4 (SD 13.8). In the group with conservative treatment, the mean score was 32.0 (SD 12.2). In the combined group, mean score was 28.4 (SD 13.3). The mean difference between the epidural steroid group and the conservative treatment group was -1.40 (95%CI -6.18 to 3.38).

The mean difference between the combination group and the conservative treatment group was 3.60 (95%CI -1.17 to 8.37).

6b. Mid-term disability (post-treatment: >30 days to 3 months)

Cervical interlaminar injections with anaesthetic and betamethasone vs. anaesthetic alone

Manchikanti (2012) reported results for 3 months after baseline using the NDI range 0-100. At baseline, mean score in the anaesthetic group was 29.6 (SD 5.3) and 29.2 (SD 6.1) in the betamethasone group. In the anaesthetic group, mean score after 3 months was 14.7 (SD 5.5) and mean score in the betamethasone group was 15.6 (SD 6.3). The analysis resulted in a mean difference of 0.90 (95%CI -1.33 to 3.13).

6c. Long term disability (post-treatment: >3 months to 1 year)

Cervical interlaminar injections with anaesthetic and betamethasone vs. anaesthetic alone

Long term results were reported by Manchikanti (2012). After 6 months, the mean score in the anaesthetic group was 13.8 (SD 5.4) and the mean score in the betamethasone group was 15.3 (SD 6.9). The mean difference between the anaesthetic group and the betamethasone group was 1.50 (95%CI 0.73 to 3.72). After 12 months, the mean score in the anaesthetic group was 13.8 (SD 5.7) and the mean score in the betamethasone group was 15.1 (SD 7.0). The mean difference between the anaesthetic group and the betamethasone group was 1.30 (95%CI -0.98 to 3.58). Results are depicted in figure 15.

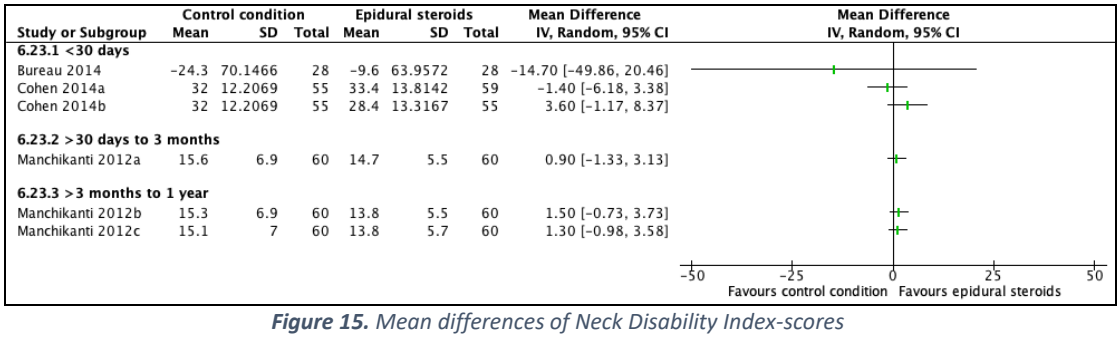

Figure 15. *Mean differences of Neck Disability Index-scores*

7. Quality of life (important)

The outcome quality of life was not reported in the included studies.

8. Surgery sparing effect (important)

One study reported on cervical surgery sparing effect (Cohen, 2014).

Epidural steroids with or without conservative treatment vs. conservative treatment alone

Cohen (2014) reported whether a participant proceeded for surgery within one year of treatment. Surgery within one year of treatment was reported in 3 (5.5%) participants in the epidural steroid group, in 4 (6.8%) participants in the conservative treatment group and in 3 (5.5%) participants in the combined group. Both risk ratios comparing epidural steroids or combined treatment with conservative treatment, were 1.24 (95%CI 0.29 to 5.30).

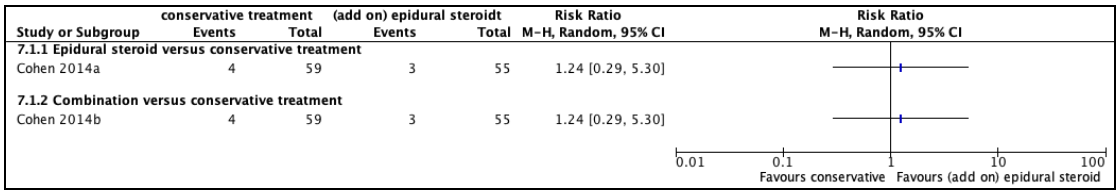

Figure 17. *Risk ratio's for proceeding for surgery within one year of treatment, Epidural steroids with or without conservative treatment versus conservative treatment alone.*

Level of evidence of the literature

1. Pain (critical)

1.1 Short term

The level of evidence regarding the outcome measure pain (short term) started as high because it was based on RCTs and was downgraded by three levels to very low because lack of blinding (Cohen, 2014) (-1, risk of bias), clinical heterogeneity (-1, inconsistency), and crossing of both thresholds of clinical decision-making (Cohen, 2014; Anderberg; 2007) (-1, imprecision).

1.2 Mid term

The level of evidence regarding the outcome measure pain (mid-term) started as high because it was based on RCTs and was downgraded by three levels to very low because lack of blinding (Cohen, 2014) (-1, risk of bias), clinical heterogeneity (-1, inconsistency) and crossing of one threshold of clinical decision-making (Cohen, 2014) (-1, imprecision).

1.3 Long term

The level of evidence regarding the outcome measure pain (long-term) started as high because it was based on RCTs and was downgraded by three levels to very low because lack of blinding (Cohen, 2014; Stav, 1993) (-1, risk of bias) clinical heterogeneity (-1, inconsistency) and crossing of one threshold of clinical decision-making (Cohen, 2014; Stav, 1993) (-1, imprecision).

2. Patient satisfaction (critical)

The level of evidence regarding the outcome measure patient satisfaction started as high because it was based on RCTs and was downgraded by three levels to very low because lack of blinding in a self-reported outcome without any compensating RCTs of adequate quality (Cohen, 2014) (-2, risk of bias) and crossing of both thresholds of clinical decision-making (-1, imprecision).

3. Complications (critical)

The level of evidence regarding the outcome measure complications started as high because it was based on RCTs and was downgraded by three level to very low because of methodological shortcomings (Cohen, 2014 and Stav, 1993) (-1, risk of bias), strong heterogeneity in outcome-definition (-1, inconsistency) and a low number of events (-1, imprecision).

4. Use of medication (important)

The level of evidence regarding the outcome measure medication use started as high because it was based on RCTs and was downgraded by three levels to very low because lack of blinding (Cohen, 2014) (-1, risk of bias) and intervals crossing borders of clinical relevance (Cohen, 2014; Manchikanti, 2012) (-2, imprecision).

5. Functioning (important)

The level of evidence regarding the outcome measure functioning was not assessed.

6. Disability

The level of evidence regarding the outcome measure disability started as high because it was based on RCTs and was downgraded by three levels to very low because lack of blinding (Cohen, 2014) (-1, risk of bias), clinical and statistical heterogeneity (-1, inconsistency) confidence intervals crossing borders of clinical relevance (Bureau, 2014; (-1, imprecision).

7. Quality of life (important)

The level of evidence regarding the outcome measure quality of life was not assessed.

8. Surgery sparing effect (important)

The level of evidence regarding the outcome measure cervical surgery started as high because it was based on an RCT and was downgraded by three levels to very low because lack of blinding (Cohen, 2014) (-1, risk of bias) and confidence interval crossing both borders of clinical relevance (-2, imprecision).

Conclusions

1. Pain (critical)

Very low GRADE	The evidence is very uncertain about the effect of (add on) epidural corticosteroid injections with or without local anaesthetic injection on pain (any term) compared with usual care in patients with cervical radiculopathy. *Sources: Anderberg, 2007; Cohen, 2014; Manchikanti, 2012; Stav, 1993*

2. Patient satisfaction (critical)

Very low GRADE	The evidence is very uncertain about the effect of (add on) epidural corticosteroid injections with or without local anaesthetic injection on patient satisfaction compared with usual care in patients with cervical radiculopathy. *Sources: Cohen, 2014*

3. Complications (critical)

Very low GRADE	The evidence is very uncertain about the effect of (add on) epidural corticosteroid injections with or without local anaesthetic injection on complications compared with usual care in patients with cervical radiculopathy. *Sources: Anderberg, 2007; Cohen, 2014; Manchikanti, 2012; Stav, 1993*

4. Use of medication (important)

Very low GRADE	The evidence is very uncertain about the effect of (add on) epidural corticosteroid injections with or without local anaesthetic injection on medication use compared with usual care in patients with cervical radiculopathy. *Sources: Cohen, 2014; Manchikanti, 2012; Stav, 1993*

5. Functioning (important)

- GRADE	No evidence was found regarding the effect of epidural steroid injections on functioning, compared with usual care in patients with cervical radiculopathy. *Sources: -*

6. Disability

Very low GRADE	The evidence is very uncertain about the effect of (add on) epidural corticosteroid injections with or without local anaesthetic injection on disability compared with usual care in patients with cervical radiculopathy. *Sources: Bureau, 2014; Cohen, 2014; Manchikanti, 2012*

7. Quality of life (important)

- GRADE	No evidence was found regarding the effect of epidural steroid injections on quality of life, compared with usual care in patients with cervical radiculopathy. *Sources: -*

8. Surgery sparing effect (important)

Very low GRADE	The evidence is very uncertain about the effect of (add on) epidural corticosteroid injections with or without local anaesthetic injection on cervical surgery compared with usual care in patients with cervical radiculopathy. *Sources: Cohen, 2014*

Overwegingen – van bewijs naar aanbeveling

Voor- en nadelen van de interventie en de kwaliteit van het bewijs

Het doel van de uitgangsvraag was om de waarde van cervicale epidurale corticosteroïde-injecties (ECSI) met of zonder lokaal anestheticum te evalueren in de behandeling van een cervicaal radiculair syndroom (CRS). Corticosteroïden zijn niet geregistreerd voor epidurale toediening, wat betekent dat deze behandeling een off-label gebruik is. In totaal zijn vijf RCT's gevonden die ECSI vergeleken met een andere conservatieve behandeling.

De bewijskracht voor de kritieke uitkomstmaten (pijn, patiënttevredenheid en complicaties) was zeer laag. Deze zeer lage bewijskracht wordt veroorzaakt door verschillende methodologische beperkingen, variërende behandelingen en relatief kleine studiepopulaties waarvan de duur van de klachten varieert (van subacuut tot chronisch) en/of niet altijd duidelijk is. Dit betekent dat andere studies waarschijnlijk leiden tot nieuwe inzichten. Er kunnen op basis van alleen de literatuur geen sterke aanbevelingen geformuleerd worden.

Toekomstige studies zouden zich vooral moeten richten op patiënten met een 'subacuut' CRS (<3 maanden) waarbij ECSI wordt vergeleken met 'usual care'. Terwijl ECSI tot doel heeft de ontstekingsreactie rondom de zenuw te verminderen, wat vooral in de (sub)acute fase voorkomt, worden in de meeste studies ook patiënten geïncludeerd met chronische klachten (>3 maanden). Tevens verschilt de controlegroep sterk in de vijf RCT's (fysiotherapie, lokaal anestheticum, intra-articulaire facet-injectie, intramusculaire injectie). Bij formuleren van aanbevelingen baseerde de werkgroep zich daarom ook op de onderstaande overwegingen.

Complicaties

Complicaties van ECSI komen voor in RCT's, maar meestal zijn de studie populaties zeer klein (Hong, 2021; Schneider, 2016). Zeldzame complicaties worden daarom hoofdzakelijk beschreven in case reports (van Boxem, 2019; Peene, 2023). De minder ernstige complicaties (zoals nekpijn, gevoeligheid op de injectieplaats, complicaties door het gebruik van glucocorticoïden, subjectieve zwakte van de armen en slapeloosheid) lijken veelal van kortdurende aard. Het risico op een epiduraal hematoom na ECSI lijkt voornamelijk verhoogd bij patiënten die al behandeld worden met bloedverdunners. Voor het beleid omtrent antistolling verwijst de werkgroep naar de richtlijn Neuraxisblokkade en antistolling (NVA, 2014). Voor meer ECSI specifieke informatie verwijst de werkgroep naar de internationale richtlijn (Narouze, 2018). Het bijwerkingenprofiel voor interlaminaire en transforaminale toediening lijkt verschillend van aard (Peene, 2023), en wordt hieronder nader beschreven.

Interlaminair

Bij interlaminaire toediening worden zeldzame ernstige complicaties gerapporteerd, zoals epiduraal hematomen, infecties, accidentele subdurale injectie, en direct naaldtrauma (Peene, 2023). Subdurale injectie kan leiden tot post-punctionele hoofdpijn en in uitzonderlijke gevallen tot hypoventilatie en hypotensie (Vallejo, 2022). Post-punctionele hoofdpijn is veelal te verhelpen met conservatieve behandeling en/of een epidurale bloedpatch. Complicaties ten gevolge van direct naaldtrauma kunnen vermeden worden door een correcte techniek met beeldvorming (van Boxem, 2019).

Transforaminaal

Bij transforaminale toediening komen verschillende ernstige complicaties voor. De meest voorkomende zijn letsels aan het ruggenmerg door anterieure spinale arterie injectie en mogelijke schade aan het centrale zenuwstelsel door embolisatie van de aanvoerende

arteriën (Van Boxem, 2019; Peene, 2023). Dergelijke complicaties lijken niet altijd technisch te voorkomen.

Gezien het lager risico op ernstige complicaties bij de interlaminaire benadering, adviseert de werkgroep hier de voorkeur aan te geven indien, ondanks het ontbreken van bewijs van effectiviteit, toch wordt gekozen voor het geven van een cervicale epidurale injectie.

Dexamethason

Mocht toch de voorkeur liggen bij een transforaminale ESCI, dan adviseert de werkgroep dexamethason zonder bewaarmiddelen te gebruiken, een non-particulate corticosteroïde. Dit wordt onderbouwd in een consensuspaper van US stakeholders (Benzon, 2015; Rathmell, 2015). In Nederland is dexamethason zonder bewaarmiddelen als farmaceutische specialiteit echter niet beschikbaar. Daarom is in 2019 het Benelux "Safe Use Initiative" geüpdatet op basis van de beschikbare producten in de Benelux (Van Boxem, 2019). Hierin wordt aanbevolen om dexametason zonder bewaarmiddelen te gebruiken op basis van generieke producten (ook wel "compound" genoemd).

Toediening

In geval van interlaminaire toediening wordt een ECSI bij voorkeur op niveau C7-T1 geplaatst. Meer naar craniaal neemt de diameter van de epidurale ruimte af. Het verdient aanbeveling om radiologische evaluatie vooraf middels MRI (tweede voorkeur: CT) uit te voeren om de beschikbare epidurale ruimte voorafgaand te evalueren.

Voor de interlaminaire injectie zijn geen vasculaire complicaties gemeld, daarom kan een partikel houdend steroïde (of dexamethason 10 mg) toegediend worden. Indien nodig kan 0.9% NaCl of 1-2% lidocaïne gebruikt worden als verdunning. Beperk hierbij het totale volume tot maximum 4 ml.

Indien na de eerste injectie onvoldoende verbetering optreedt, kan een tweede of derde injectie nuttig zijn na enkele weken (Joswig, 2018). Bij het bepalen van een minimaal interval tussen twee injecties, baseert de werkgroep zich op de huidige praktijk, waarin een tweede injectie kan worden toegediend wanneer nodig (i.e. na enkele weken of maanden).

<u>Waarden en voorkeuren van patiënten (en evt. hun verzorgers)</u>

De meeste patiënten die voor ECSI in aanmerking komen hebben al een conservatieve behandeling ondergaan met onvoldoende resultaat. Aangezien de epidurale toediening van corticosteroïden een off-label toepassing is, moeten de mogelijke voor- en nadelen van ECSI goed met de patiënt worden besproken. De werkgroep geeft de voorkeur aan een beslissing in samenspraak met de patiënt.

<u>Kosten (middelenbeslag)</u>

Een Amerikaanse studie vergeleek de kosten-effectiviteit van patiënten die ECSI kregen met patiënten die conservatieve behandeling (fysiotherapie en analgetica) kregen. ECSI was kosten-effectiever dan de conservatieve behandeling (Alvin, 2019). Patiënten met ECSI hadden ongeveer 50% minder ziekteverzuim in vergelijking met de controlegroep. Ook in een andere internationale kosteneffectiviteitsstudie werd ECSI kosteneffectief bevonden (Manchikanti, 2019).

De verschillen tussen het Amerikaanse en Nederlandse zorgsysteem moeten bij de interpretatie van deze resultaten goed in overweging genomen worden. De werkgroep verwacht echter dat de richting van de resultaten ook zullen gelden voor het Nederlandse zorgsysteem.

Aanvaardbaarheid, haalbaarheid en implementatie

De werkgroep concludeert op basis van verschillende studies dat beeldvorming essentieel is om ECSI goed en veilig uit te voeren (Hochberg, 2021; Park, 2016; Ulusoy, 2018; van Zundert, 2010; Peene, 2023). Bij de keuze van de beeldvormingstechniek dient rekening gehouden te worden met de stralingsbelasting, waarbij deze voor de CT scan het hoogst is. De werkgroep geeft daarom de voorkeur aan toediening van ECSI onder controle van beeldvorming met fluoroscopie/doorlichting als standaard ("Real time" bij de transforaminale benadering). In het licht van het bovenstaande vergt het uitvoeren van de ECSI een grondige kennis van de (vasculaire) anatomie en ervaring met de interpretatie van de medische beeldvorming. Een goede training en opleiding voor deze techniek is daarom essentieel.

Patiënten worden doorgaans verwezen door de neuroloog die de patiënt met een CRS heeft gezien op verzoek van de huisarts. ECSI zijn relatief laagdrempelig toegankelijk voor iedereen die zich naar een pijncentrum kan begeven. De interventie duurt gemiddeld rond 30 minuten. Daarna wordt de patiënt in observatie gehouden gedurende enkele uren. Veelal wordt een speciale dag gepland voor de ECSI toedieningen.

Aanbevelingen

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventies

De bewijskracht voor ECSI is beperkt, aangezien het bewijs gebaseerd is op relatief kleine RCT's van wisselende methodologische kwaliteit. De werkgroep raadt in het licht van het risico op complicaties voorzichtigheid aan bij het gebruik van ECSI. Alhoewel de werkgroep transforaminale ECSI niet aanbeveelt, zijn er weinig argumenten tegen het uitvoeren van transforaminale toediening mits dexamethason zonder bewaarstoffen wordt gebruikt.

Overweeg het toedienen van cervicale epidurale steroïde-injecties (ECSI) bij patiënten met een subacuut CRS die ernstige pijnklachten ervaren ondanks adequate pijnmedicatie/fysiotherapie.

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Bijlagen bij module 'Epidurale corticosteroïde-injecties'

Implementatieplan

Aanbeveling	Tijdspad voor implementatie: < 1 jaar, 1 tot 3 jaar of > 3 jaar	Verwacht effect op kosten	Randvoorwaarden voor implementatie (binnen aangegeven tijdspad)	Mogelijke barrières voor implementatie[1]	Te ondernemen acties voor implementatie[2]	Verantwoordelijken voor acties[3]	Overige opmerkingen
Alle aanbevelingen	< 1 jaar	Beperkt	• Zorgverleners moeten adequate expertise hebben om ECSI toe te passen. • Bekendheid met richtlijn.	• Meer kennis over herhaalde injecties en toedieningswijze (qua veiligheid, effectiviteit, interval).	• Voldoende kennis bij / scholing voor zorgverleners. • Afspraken met zorgverzekeraars. • Onderzoek naar herhaalde injecties en toedieningswijze initiëren. • Verspreiden van richtlijn.	• Beroepsverenigingen (o.a. NVN, NVvN, NVA). • CRS onderzoekers.	Niet van toepassing.

[1] Barrières kunnen zich bevinden op het niveau van de professional, op het niveau van de organisatie (het ziekenhuis) of op het niveau van het systeem (buiten het ziekenhuis). Denk bijvoorbeeld aan onenigheid in het land met betrekking tot de aanbeveling, onvoldoende motivatie of kennis bij de specialist, onvoldoende faciliteiten of personeel, nodige concentratie van zorg, kosten, slechte samenwerking tussen disciplines, nodige taakherschikking, etc.

[2] Denk aan acties die noodzakelijk zijn voor implementatie, maar ook acties die mogelijk zijn om de implementatie te bevorderen. Denk bijvoorbeeld aan controleren aanbeveling tijdens kwaliteitsvisitatie, publicatie van de richtlijn, ontwikkelen van implementatietools, informeren van ziekenhuisbestuurders, regelen van goede vergoeding voor een bepaald type behandeling, maken van samenwerkingsafspraken.

[3] Wie de verantwoordelijkheden draagt voor implementatie van de aanbevelingen, zal tevens afhankelijk zijn van het niveau waarop zich barrières bevinden. Barrières op het niveau van de professional zullen vaak opgelost moeten worden door de beroepsvereniging. Barrières op het niveau van de organisatie zullen vaak onder verantwoordelijkheid van de ziekenhuisbestuurders vallen. Bij het oplossen van barrières op het niveau van het systeem zijn ook andere partijen, zoals de NZA en zorgverzekeraars, van belang.

Risk of bias table for intervention studies

Study reference	Was the allocation sequence adequately generated?	Was the allocation adequately concealed?	Blinding: Was knowledge of the allocated interventions adequately prevented?	Was loss to follow-up (missing outcome data) infrequent?	Are reports of the study free of selective outcome reporting?	Was the study apparently free of other problems that could put it at a risk of bias?	Overall risk of bias If applicable/necessary, per outcome measure
Anderberg, 2007	Probably yes; Reason: No information	Probably yes; Reason: No information	Probably yes; Reason: Patients were blinded. The healthcare provider (neuroradiologist) was not blinded, all other persons involved in the study were declared blinded.	Probably yes; Reason: No loss to follow-up appeared, all patients available for outcome assessment.	Definitely yes; Reason:	Definitely yes; Reason:	Some concerns (all outcomes)
Bureau, 2014	Probably yes; Reason: Randomization was computer-generated	Definitely yes; Reason: Envelopes were sealed.	Probably yes; Reason: Patients were blinded. The healthcare provider (radiologist) was not blinded, research assistant, also outcome assessor/data collector, was blinded. Not mentioned whether data-analysts were blinded.	Probably yes Reason: No subjects were lost to follow-up and patients were analysed according to randomization (ITT). Two TFSI subjects received IFSI. One subject randomized to IFSI received TFSI by mistake.	Definitely yes Reason: No registration in on Clinical Trials.gov was found. However, all predefined outcomes were reported in the publication.	Definitely yes; Reason: The study was not suspected of any other biases.	**LOW** (all outcomes)
Cohen, 2014	Definitely yes; Reason: Randomization was computer-generated	Probably yes; Reason: No information, but estimated low risk	Defenitely no; Reason: Probably due to the nature of the control group (conservative treatment), blinding participants was not pursued/possible. Blinding of healthcare providers, data collectors, outcome assessors or data analysts was not reported.	Probably yes; Reason: Slightly imbalanced drop-out between epidural steroid group and conservative group, however it did probably not bias the effect estimates. For 3 and 6 month follow-up, the last-observation carried forward method was used.	Defenitely yes; Reason: No registration in on Clinical Trials.gov was found. However, all predefined outcomes were reported in the publication.	Probably yes; Reason: The study was not suspected of any other biases.	**HIGH** (pain, use of medication, patient satisfaction, cervical surgery)
Manchikanti, 2012	Defenitely yes; Reason: Allocation sequence was computer-generated	Probably yes; Reason: No information, but estimated low risk	Probably no; Reason: patients were blinded, as were healthcare providers. Data collector was	Probably yes; Reason: Drop-out rate 5/120 not perceived to bias the effect estimates.	Probably yes; Reason: Study registered at NCT01071369. No outcomes were predefined in the	Probably yes; Reason: The study was not suspected of any other biases.	**LOW** (all outcomes)

			not blinded, but did not reveal any allocation-information.		protocol. All outcomes predefined in the method-section were reported in the publication.		
Stav, 1993	Probably no; Reason: No information	Probably no; Reason: no information	Defenitely no Reason: Blinding was not described in either person involved in the study.	Defenitely no; Drop out seems to be related to treatment, since litigation of insurance claims from 8 patients in control-group.	Probably no; No registration found. All predefined outcomes were described in results.	Probably no; Reason: All assessments were only briefly described, patients were excluded from analysis for policy-reasons and outcomes were described in a limited way.	HIGH (all outcomes)

Table of excluded studies

Reference	Reasons
Pountos 2016	Reported on incidence of AE, not compared with comparison group (wrong comparison)
Bush 1996	results not stratified according to type of injection (wrong control)
Kumar 2008	all participants received injections with corticosteroids (wrong control)
Lin 2006	all participants received epidural injections with corticosteroids (wrong control)
Persson 2012	all participants received epidural injections with corticosteroids (wrong control)
Shakir 2013	all participants received epidural injections with corticosteroids (wrong control)
Vallee 2001	all participants received epidural injections with corticosteroids (wrong control)
Lee 2009	all participants received epidural injections with corticosteroids (wrong control)
Lee 2022	Stellate ganglion block (Jan+Germine: no usual care) versus cervical epidural steroid injection (wrong control)
Jang 2020	Selective Nerve Root Block (Jan+Germine: no usual care) versus Fluoroscopy-Guided Interlaminar Epidural Block versus Fluoroscopy-Guided Transforaminal Epidural Bloc
Abdi 2005	SR, maar op Stav (1993) na, geen relevante vergelijkende studies, veelal over lumbar (wrong population, no recent review)
Abdi 2007	SR, maar op Stav (1993) na, geen relevante vergelijkende studies, veelal over lumbar (wrong population, no recent review)
Benyamin 2009	SR, maar op Stav (1993) na, geen relevante vergelijkende studies (wrong control, no recent review)
Boswell 2007	SR, maar op Stav (1993) na, geen relevante vergelijkende studies (wrong control, no recent review)
Benditz 2017	All participants received epidural injections with corticosteroids (wrong control)
Huston 2005	All participants received selective nerve root blocks (wrong control)
Jang 2020	Letter to editor, and all participants received epidural injections with corticosteroids (wrong control)
Kim 2018	All participants received epidural injections with corticosteroids (wrong control)
Park 2019	Interlaminar epidural steroid injections versus selective nerve root block (Jan: selective nerve root block is geen usual care, zelfs soms gelijk aan epidurale corticosteroïden injectie, en chronische populatie (wrong control, wrong participants)
Boswell 2003	SR, maar op Stav (1993) na, geen relevante vergelijkende studies (wrong control, no recent review)
Boswell 2005	SR, maar op Stav (1993) na, geen relevante vergelijkende studies (wrong control, no recent review)
Diwan 2012	SR, maar op Stav (1993), Manchikanti (2010, 2012) na geen relevante vergelijkende studies (wrong control, no recent review)
Conger 2012	SR, but only within group differences presented (wrong control)
Binder 2008	SR, but only Persson 1997 en Castagnera1994 concerning radiculopathy, both no match for inclusion (wrong intervention, wrong control, old review)
Engel 2014	SR, maar op Anderberg (2007) na geen relevante vergelijkende studies (wrong control, old review)
Mesregah 2020	SR, maar includeerde 1 trial met patienten met radiculitis (Manchicanti 2012), verder alleen cervical central spinal stenosis, or patients without radiculitis (wrong population)
Manchikanti 2015	SR, maar op Stav (1993) na, geen relevante vergelijkende studies (wrong control, wrong population)
Bureau 2020	Outcome: Association between injectate dispersal patterns and clinical outcome (wrong outcome)
Jee 2012	All participants received epidural injections with corticosteroids (wrong control)
Manchikanti 2010	Preliminary results of Manchikanti (2012), less participants and no additional information
Kaye 2015	SR, but only with outcomes for pain relief/function (Stav (1993) and Cohen (2014)).
Alvin 2019	Observational comparative study (wrong study design)

Literature search strategy

Zoekverantwoording

Algemene informatie

Richtlijn: Cervicaal Radiculair Syndroom	
Uitgangsvraag: Wat is de rol van corticosteroïd-injecties bij de behandeling van patiënten met CRS?	
Database(s): Ovid/Medline, Embase.com	Datum: 25-04-2022
Periode: 1990 – heden	Talen: Engels, Nederlands
Literatuurspecialist: Miriam van der Maten	
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting: → Voor deze vraag is gezocht op de elementen cervical radiculopathy en corticosteroïden injecties → De sleutelartikelen wordt gevonden met de zoekopdracht.	
Te gebruiken voor richtlijnen tekst: In de databases Embase.com en Ovid/Medline is op 25 april 2022 met relevante zoektermen gezocht naar systematische reviews, RCT en observationele studies over de rol van corticosteroïd-injecties bij de behandeling van patiënten met CRS De literatuurzoekactie leverde 382 unieke treffers op.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SRs	62	51	64
RCT	54	57	61
Observationele studies	208	203	257
Totaal	324	311	**382**

Zoekstrategie

Embase.com

No.	**Query**	**Results**
#16	#13 OR #14 OR #15	324
#15	#9 AND #12 NOT (#13 OR #14) **= observationeel**	208
#14	#9 AND #11 NOT #13 **= RCT**	54
#13	#9 AND #10 **= SR**	62
#12	'major clinical study'/de OR 'clinical study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'comparative study'/de OR 'cohort analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti) OR 'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR	14781024

	'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	
#11	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	1902585
#10	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	818766
#9	#7 AND #8 AND ([english]/lim OR [dutch]/lim) AND [1990-2022]/py NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	630
#8	'steroid'/exp/mj OR 'corticosteroid'/exp/mj OR corticosteroid*:ti,ab,kw OR glucocorticoid*:ti,ab,kw OR 'adrenal cortex hormone*':ti,ab,kw OR corticoid*:ti,ab,kw OR steroid*:ti,ab,kw OR 'epidural drug administration'/exp/mj OR epidural:ti,ab,kw OR esi:ti,ab,kw OR transforaminal:ti,ab,kw OR interlaminar:ti,ab,kw OR ctfesi:ti,ab,kw	1168892
#7	'cervicobrachial neuralgia'/exp/mj OR cervicobrachialgia:ti,ab,kw OR ((radiculalgia:ti,ab,kw OR radiculitis:ti,ab,kw OR radiculitides:ti,ab,kw OR radiculopath*:ti,ab,kw OR polyradiculopath*:ti,ab,kw OR neuralgia:ti,ab,kw OR 'herniated disc*':ti,ab,kw OR hernia:ti,ab,kw OR ((radicular NEAR/3 (pain* OR neuralgia* OR symptom*)):ti,ab,kw) OR (('nerve root' NEAR/3 (pain* OR inflammation* OR disorder* OR compression* OR avulsion* OR impingement)):ti,ab,kw)) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('radicular pain'/exp/mj OR 'radiculopathy'/exp/mj) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw))	10643

Ovid/Medline

#	Searches	Results
11	8 or 9 or 10	311
10	(4 and 7) not (8 or 9) **= observationeel**	203
9	(4 and 6) not 8 **= RCT**	57
8	4 and 5 **= SR**	51
7	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/ or Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. Or	6812447

	(confounding adj6 adjust*).ti,ab. Or (versus or vs or compar*).ti. or ((exp cohort studies/ or epidemiologic studies/ or multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. Or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.))	
6	(exp randomized controlled trial/ or randomized controlled trials as topic/ or random*.ti,ab. Or rct?.ti,ab. Or ((pragmatic or practical) adj "clinical trial*").ti,ab,kf. Or ((non-inferiority or noninferiority or superiority or equivalence) adj3 trial*).ti,ab,kf.) not (animals/ not humans/)	1369026
5	(meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. Or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. Or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. Or (systemic* adj1 review*).ti,ab,kf. Or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. Or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. Or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. Or (("data extraction" or "data source*") and "study selection").ti,ab,kf. Or ("search strategy" and "selection criteria").ti,ab,kf. Or ("data source*" and "data synthesis").ti,ab,kf. Or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	560304
4	limit 3 to ((english language or dutch) and yr="1990 -Current")	596
3	1 and 2	673
2	exp *Steroids/ or exp *Adrenal Cortex Hormones/ or corticosteroid*.ti,ab,kf. Or glucocorticoid*.ti,ab,kf. Or 'adrenal cortex hormone*'.ti,ab,kf. Or corticoid*.ti,ab,kf. Or steroid*.ti,ab,kf. Or exp *Injections, Epidural/ or exp *Analgesia, Epidural/ or (epidural or esi or ctfesi or transforaminal or interlaminar).ti,ab,kf.	889447
1	((exp Radiculopathy/ or radiculalgia.ti,ab,kf. Or radiculitis.ti,ab,kf. Or radiculitides.ti,ab,kf. Or radiculopath*.ti,ab,kf. Or polyradiculopath*.ti,ab,kf. Or neuralgia.ti,ab,kf. Or 'herniated disc*'.ti,ab,kf. Or hernia.ti,ab,kf. Or (radicular adj3 (pain* or neuralgia* or symptom*)).ti,ab,kf. Or ('nerve root' adj3 (pain* or inflammation* or disorder* or compression* or avulsion* or impingement)).ti,ab,kf.) and (exp Cervical Vertebrae/ or exp Neck/ or cervical.ti,ab,kf. Or cervico*.ti,ab,kf. Or neck.ti,ab,kf.)) or cervicobrachialgia.ti,ab,kf.	6515

Module 2.3. Pulsed Radiofrequency (PRF)

Uitgangsvraag

Wat is de plaats van Pulsed Radiofrequency (PRF)-behandelingen bij patiënten met CRS?

Introductie

Een Pulsed Radiofrequency (PRF)-behandeling bestaat uit een radiofrequente stroom die via een speciale naald met kleine stootjes wordt gegeven. Daardoor wordt de geleidingscapaciteit van de zenuwwortel beïnvloed, waardoor in veel gevallen de pijn vermindert. Een PRF-behandeling is gericht op de uitstralende pijn (radiculaire of zenuwwortelpijn) en niet zozeer op rug- of nekklachten zelf. Deze behandelingen worden op steeds grotere schaal toegepast. Meestal niet in de acute fase, maar veelal bij patiënten met chronische (>3 maanden) CRS.

Momenteel is het onduidelijk wanneer PRF-behandelingen precies overwogen dienen te worden. De achterliggende gedachte is dat een PRF-behandeling veiliger is dan een injectie met epidurale corticosteroïde (ECSI), vooral die via de transforaminale route. Deze module evalueert de inzet van PRF-behandelingen bij patiënten met CRS.

Search and select

A systematic search of the literature was performed to answer the following question: *What is the effectiveness of Pulsed Radiofrequency (PRF) compared to other interventions in patients with chronic CRS?*

P = Patients with chronic CRS (not myelopathy)
I = Pulsed radiofrequency (PRF)
C = Any comparator, usual care, PRF with corticosteroid injections, corticosteroid injections, sham intervention
O = Pain, patient satisfaction, complications, medication use, functioning, quality of life, cervical surgery

<u>Relevant outcome measures</u>

The guideline development group considered pain, patient satisfaction and complications as *critical* outcome measures for decision making and medication use, functioning, quality of life and cervical surgery as *important* outcome measures for decision making.

A priori, the working group did not define the outcome measures listed above but used the definitions used in the studies.

The working group defined a 10% difference for continuous outcome measures (weighted mean difference), 10% for dichotomous outcome measures informing on relative risk ($0.91 \leq RR \geq 1.1$), and standardized mean difference (≤ -0.5 SMD ≥ 0.5) as minimal clinically (patient) important differences.

<u>Search and select (Methods)</u>

The databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms until 10 February 2023. The detailed search strategy is depicted under the tab Methods. The systematic literature search resulted in 124 hits. Studies were selected based on the following criteria:

- Systematic reviews (searched in at least two databases, and detailed search strategy, risk of bias assessment and results of individual studies available) or randomized controlled trials;
- Adults (≥18 years);
- Publication date ≥1998;
- Studies including ≥20 (ten in each study arm) patients;
- Full-text English or Dutch language publication; and
- Studies according to the PICO.

Twenty-seven studies were initially selected based on title and abstract screening. After reading the full text, 22 studies were excluded (see the table with reasons for exclusion under the tab Methods), and five studies were included.

Results

Five studies were included in the analysis of the literature. Important study characteristics and results are summarized in the evidence tables. The assessment of the risk of bias is summarized in the risk of bias tables.

Summary of literature

Description of studies

Van Zundert (2007) performed a double-blind RCT to evaluate the efficacy of PRF treatment in patients with chronic cervical radicular pain. A total of 23 patients with cervical radicular pain for at least 6 months were included. Note: Of the 114 patients who met the inclusion criteria, 63 (55%) gave no informed consent. Patients were randomly assigned to either the PRF treatment group (n=11, mean age ± SD: 42 ± 12 years, %male: 46%, mean pain duration ± SD: 54 ± 40 months) or the sham treatment group (n=12, mean age ± SD: 53 ± 12 years, %male: 42%, mean pain duration ± SD: 60 ± 65 months). Patients in the PRF treatment group received PRF stimulation at 0.5V during 120s adjacent to the cervical dorsal root ganglion. Sham treatment consisted of the same preparation procedure as the intervention group, however, instead of passing current through the electrode the generator was merely manipulated without starting the procedure. The following outcome measures were reported: pain, patient satisfaction, complications, medication use, functioning, quality of life, and cervical surgery.

Lee (2016) performed a RCT to compare the effectiveness of PRF with a second transforaminal epidural steroid injection (TFESI) *after* failure of a first TFESI for the treatment of radicular pain due to disc herniation. In total, 38 patients with cervical or lumbar radicular pain were included. Patients were randomly assigned to either the PRF group (n=19, mean age ± SD: 54 ± 12 years, mean pain duration: 5.1 weeks, cervical pain n=10, lumbar pain n=9) or the TFESI group (n=19, mean age ± SD: 51 ± 13 years, mean pain duration: 4.8 weeks, cervical pain n=8, lumbar pain n=11). PRF treatment was administered at 5 Hz and a 5 ms pulsed width for 240 seconds at 45V. Patients in the TFESI group received 2 mL of 0.125% bupivacaine mixed with 5 mg dexamethasone. The following outcome measures were reported: pain, complications, and functioning. Subgroup analyses were performed for patients undergoing cervical and lumbar procedures.

Halim (2017) conducted an RCT to evaluate the efficacy of PRF compared to percutaneous nucleoplasty (PCN) in patients with contained cervical disc herniation. A total of 34 patients with single level contained cervical disc herniation were included. Patients were randomized to either PCN treatment (n=17, mean age: 50 years, %male: 41%, mean duration of symptoms: 12 months) or PRF treatment (n=17, mean age: 52 years, %male: 53%, mean

duration of symptoms: 12 months). Patients in the PRF treatment group received PRF stimulation of the dorsal root ganglion at 45V, 2 Hz (20ms) for six minutes. PCN treatment consisted of decompression of the herniated disc, using a 52°C thermal reaction. The following outcome measures were reported: pain, patient satisfaction, complications, and functioning.

Wang (2016) performed an RCT to compare the efficacy of cervical nerve root block (CNRB) with betamethasone, PRF, and CNRB + PRF in patients with chronic cervical radicular pain. In total, 62 patients with moderate to severe chronic cervical radicular pain were included. Patients were randomized into three groups and received treatment with CNRB (n=21, mean age ± SD: 59 ± 14 years, %male: 43%, mean pain duration ± SD: 9.5 ± 5.2 months), PRF (n=20, mean age ± SD: 58 ± 16 years, %male: 55%, mean pain duration ± SD: 10.1 ± 5.1 months), or a combination of CNRB and PRF (n=21, mean age ± SD: 58 ± 15 years, %male: 38%, mean pain duration ± SD: 8.6 ± 3.9 months). Data on the CNRB + PRF group is not considered in this module because it is beyond the scope of this module. PRF treatment consisted of a PRF stimulus that was applied for 4 minutes followed by radiculography. CNRB treatment consisted of a mixture of corticosteroids containing betamethasone dipropionate and betamethasone disodium phosphate, NaCl, and lidocaine after radiculography. The following outcome measures were reported: pain, patient satisfaction, and complications.

Chalermkitpanit (2023) conducted an RCT to evaluate the efficacy of PRF for patients with cervical radicular pain for at least 3 months. A total of 41 patients with moderate to severe cervical radicular pain were included. Patients were randomly assigned to either PRF treatment and steroid (n=20, mean age ± SD: 49 ± 16 years, %male: 40%, mean pain duration ± SD: 6.5 ± 6.4 months) or transforaminal steroid treatment (n=21, mean age ± SD: 56 ± 15 years, %male: 38%, mean pain duration ± SD: 7 ± 7.4 months). After a sensory stimulation, PRF treatment was performed between 0.3-0.5 volts at 42°C for 4 minutes. Thereafter, patients got injected a mixture of lidocaine and dexamethasone. Patients in the steroid group received sensory stimulation with a short bevel stimulating 22G-needle followed by the same injectate. The following outcome measures were reported: pain, complications, medication use, and functioning.

Results

1. Pain

Five studies reported on pain (Van Zundert, 2007; Lee, 2016; Halim, 2017; Wang, 2016; Chalermkitpanit, 2023). Results are presented in *Table 1*. Data could not be pooled because of the diversity in presentation of the data (dichotomous/continuous), missing absolute values (Wang, 2016), or dispersion measures (SE/SD) (Halim, 2017).

Van Zundert (2007) reported on pain, defined as a 20-points reduction in pain intensity measured by VAS score three months after treatment. Authors reported that pain improvement was achieved in 82% (9/11) of patients in the PRF treatment group (VAS score pre-treatment mean ± SD: 55.7 ± 17.3) and in 25% (3/12) in the sham treatment group (VAS score pre-treatment mean ± SD: 76.2 ± 14.2). The risk ratio was 3.27 (95%CI 1.18 to 9.07) in favour of PRF treatment, which was considered clinically relevant.

Lee (2016) reported on pain intensity measured by VAS (0-10 mm) three months after treatment. Subgroup analyses were performed based on the presentation of radicular pain (cervical or lumbar). For patients with cervical radicular pain, they reported a mean ± SD VAS score of 2.0 ± 0.8 for the PRF treatment group (n=10) and 2.4 ± 2.3 for the TFESI treatment

group (n=8). Mean difference was 0.40 (95%CI -2.07 to 1.27) in favour of PRF treatment. This difference was not considered clinically relevant.

Halim (2017) reported on pain measured by VAS (0-100 mm) three months after treatment. They reported a mean VAS score of 35.5 for the PRF treatment group (n=17) and 27.6 for the PCN treatment group (n=17). Effect measures were not reported and could not be calculated due to missing dispersion measures.

Wang (2016) reported on pain defined as pain intensity measured by a 11-point NRS six months after treatment. They reported that the mean NRS in each group was reduced at all time intervals (1 week, 1 month, 3 months and 6 months) compared to baseline. Effect measures were not reported and could not be calculated due to missing dispersion measures.

Chalermkitpanit (2023) reported on pain measured by NRS (0-10) three months post procedure. They reported a mean ± SD NRS score of 2.8 ± 2.7 for the PRF + steroid treatment group (n=20) and 5.5 ± 2.6 for the steroid treatment group (n=21). Mean difference was 2.70 (95%CI -4.32 to -1.08) in favour of PRF treatment. This difference was clinically relevant.

Table 1. Outcome Pain: comparison VAS/NRS scores

Study	Comparison	PRF (mean ± SD)		Control (mean ± SD)	
		Baseline	follow-up 3 months	Baseline	follow-up 3 months
Van Zundert, 2007 (n=11/12 VAS 0-100mm)	PRF vs sham	55.7 ± 17.3	43* ± nr	76.2 ± 14.2	62* ± nr
Lee, 2016 (n=10/8, VAS 0-10mm)	*PRF vs 2nd TFESI 2-6wks after failure TFESI*	5.3 ± 1.2	2.0 ± 0.8	4.9 ± 0.8	2.4 ± 2.3
Wang, 2016 (n=20/21, NRS 0-10)	*PRF vs TFESI*	6.2 ± 1.0	4.0* ± nr	6.0 ± 0.08	4.0* ± nr
Halim, 2017 (n=17/17, VAS 0-100mm)	*PRF vs PCN*	69.5 ± nr	35.5 ± nr	71.0 ± nr	27.6 ± nr
Chalermkitpanit, 2023 (n=20/21, NRS 0-10)	*PRF+steroid vs TFESI*	7.5* ± nr	2.8 ± 2.7	7.9* ± nr	5.5 ± 2.6
**estimated from figure; nr: not reported*					

2. Patient satisfaction

Three studies reported on patient satisfaction (Van Zundert, 2007; Halim, 2017; Wang, 2016). Data could not be pooled because of missing dispersion measures (SE/SD) (Halim, 2017).

Van Zundert (2007) reported on patient satisfaction defined as the global perceived effect (GPE), measured using a 7-point Likert scale. Authors reported the number of patients with >50% improvement in GPE (6 or 7 on Likert scale) three months after treatment. In the PRF treatment group, this was achieved in 82% (9/11) of patients, whereas in the sham treatment group it was achieved in 33% (4/12) of patients. The risk ratio was 2.45 (95%CI 1.05 to 5.73) in favour of PRF treatment, which was considered clinically relevant.

Halim (2017) reported on patient satisfaction using a VAS for satisfaction three months after treatment. They reported a mean VAS satisfaction score of 63.5 for the PRF treatment group (n=17) and 58.4 for the PCN treatment group (n=17). Effect measures were not reported and could not be calculated due to missing dispersion measures.

Wang (2016) reported on patient satisfaction defined as positive GPE (+2 or +3 points) six months after treatment, measured using a 7-point scale. Authors reported positive GPE in 11% (2/19) of patients in the PRF treatment group and in 5% (1/19) of patients in the CNRB

treatment group. The risk ratio was 2.00 (95%CI 0.20 to 20.24) in favour of PRF treatment, which was considered clinically relevant.

3. Complications

Five studies reported on complications (Van Zundert, 2007; Lee, 2016; Halim, 2017; Wang, 2016, Chalermkitpanit, 2023). Van Zundert (2007), Lee (2016), Halim (2017) and Wang (2016) reported on the proportion of patients with complications. Chalermkitpanit (2023) reported on procedure-related complications.

Data of Chalermkitpanit (2023) could not be pooled because no absolute values were described. Authors reported that there was no difference the number of procedure-related complications between both groups.

The pooled data show a risk ratio of 1.21 (95%CI 0.32 to 4.53) in favour of control treatment (Figure 1), which was considered clinically relevant.

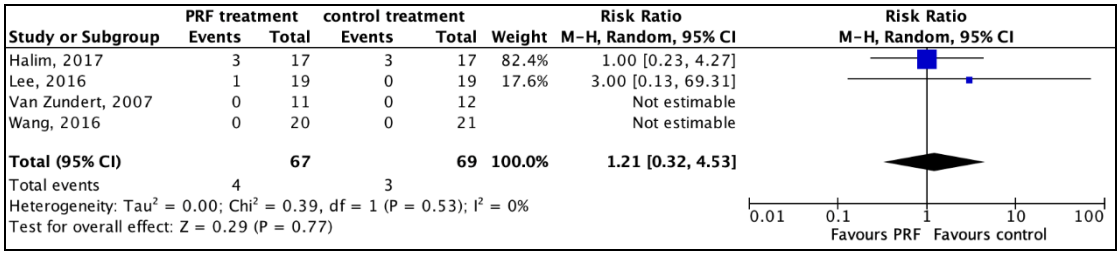

Figure 1: The effect of PRF treatment on complications.

Z: p-value of the pooled effect; df: degrees of freedom; I2: statistic heterogeneity; CI: confidence interval.

4. Medication use

Two studies reported on medication use (Van Zundert, 2007; Chalermkitpanit, 2023).

Van Zundert (2007) reported on medication use, defined as a reduction in the intake of pain medication from baseline to three months (Van Zundert, 2007). A reduction in the intake of pain medication was reported in 55% (6/11) of patients in the PRF treatment group and in 33% (4/12) of patients in the sham treatment group. The risk ratio was 1.64 (95%CI 0.62 to 4.30) in favour of PRF treatment, which was considered clinically relevant.

Chalermkitpanit (2023) reported on the amount of rescue pain medication. They reported that there was no difference in the amount of rescue pain medication between both groups. Effect measures were not reported and could not be calculated due to missing dispersion measures.

5. Functioning

Four studies reported on functioning (Van Zundert, 2007; Lee, 2016; Halim, 2017; Chalermkitpanit, 2023). Results are presented in *Table 2*. Data could not be pooled because of the diversity in presentation of the data (mean difference/mean value), and because of missing dispersion measures (SE/SD) (Halim, 2017).

Van Zundert (2007) reported on functioning, defined as physical functioning after 3 months of treatment, measured using the Short Form 36 (SF-36). They reported a mean difference ± SD in physical functioning score between baseline and three months of 9.0 ± 16.6 in the PRF treatment group (n=11) and 6.9 ± 15.0 in the sham treatment group (n=12).

Lee (2016) reported on functioning, defined as functional disabilities associated with cervical radicular pain after three months of treatment, assessed using the Neck Disability Index

(NDI) (0-50). They reported a mean ± SD NDI score of 14.0 ± 7.0 in the PRF treatment group (n=10) and 17.0 ± 14.3 in the TFESI treatment group (n=8). Mean difference was 3.0 (95%CI -13.82 to 7.82) in favour of PRF treatment. This difference was not considered clinically relevant.

Halim (2017) reported on neck and limb functioning three months after treatment, measured using the NDI (0-50). They reported a mean NDI score of 10.8 for the PRF treatment group (n=17) and 11.1 for the PCN treatment group (n=17). Effect measures were not reported and could not be calculated due to missing dispersion measures.

Chalermkitpanit (2023) reported on functioning measured using the NDI. After three months, they reported a mean difference of 23.0 (95%CI 9.6 to 36.4) between the PRF treatment group (n=20) and the steroid treatment group (n=21). After six months, they reported a mean difference of 23.8 (95%CI 4.2 to 43.3) between the PRF treatment group and the steroid treatment group.

Table 2. Outcome Functioning: comparison NDI scores

Study	Comparison	PRF (mean ± SD)		Control (mean ± SD)	
		Baseline	follow-up 3 months	Baseline	follow-up 3 months
Lee, 2016 (n=10/8, VAS 0-10mm)	*PRF vs 2nd TFESI 2-6wks after failure TFESI*	38.7 ± 8.3	14.0 ± 7.0	39.1 ± 11.6	17.0 ± 14.3
Halim, 2017 (n=17/17, VAS 0-100mm)	*PRF vs PCN*	19.4 ± 10.8	10.8 ± nr	21.1 ± nr	11.1 ± nr
Chalermkitpanit, 2023 (n=20/21, NRS 0-10)	*PRF+steroid vs TFESI*	49* ± 20*	20* ± nr	48* ± nr	40* ± nr
**estimated from figure; nr: not reported*					

6. Quality of life

One study reported on quality of life, by using SF-36 and Euroqol (Van Zundert, 2007). *Table 3* shows mean differences in SF-36 and Euroqol scores between baseline and three months for both treatment groups. Quality of life indicated a trend towards a better result after three months in the PRF group compared to the sham treatment group.

Table 3. *Results of the SF-36 and Euroqol (Van Zundert, 2007)**

Item	PRF group (n=11)	Sham group (n=12)
Euroqol	12.6 ± 19.7	4.7 ± 30.8
SF-36		
Physical functioning	9.0 ± 16.6	6.9 ± 15.0
Social functioning	12.5 ± 28.0	-1.0 ± 28.4
Physical role restriction	23.5 ± 48.6	24.3 ± 26.9
Emotional role restriction	24.2 ± 36.8	0.0 ± 53.7
Mental health	6.9 ± 12.9	0.3 ± 22.2
Vitality **	17.3 ± 17.1	2.1 ± 16.0
Pain	9.8 ± 20.5	9.3 ± 25.8
General health	4.1 ± 10.0	2.3 ± 19.0

**Data are presented as mean difference ± SD between baseline and three months. ** Statistically significant, p=0.04*

7. Cervical surgery

One study reported on cervical surgery, defined as the number of patients requiring neck surgery (Van Zundert, 2007). Authors reported that 9.1% (1/11) of patients in the PRF treatment group required neck surgery and 25% (3/12) of patients in the sham treatment group. The risk ratio was 0.36 (95%CI 0.04 to 3.00) in favour of PRF treatment, which was considered clinically relevant.

Level of evidence of the literature

1. Pain

The level of evidence regarding pain was downgraded by three levels to *very low* because of study limitations (risk of bias: -1), differences in PRF and control treatment between the studies (indirectness: -1), and because the confidence interval is crossing the border of clinical relevance (imprecision: -1).

2. Patient satisfaction

The level of evidence regarding patient satisfaction was downgraded by three levels to *very low* because of study limitations (risk of bias: -1), differences in PRF and control treatment between the studies (indirectness: -1), and because the confidence interval is crossing the border of clinical relevance (imprecision: -1).

3. Complications

The level of evidence regarding complications was downgraded by three levels to *very low* because of study limitations (risk of bias: -1), differences in PRF and control treatment between the studies (indirectness: -1), and because the confidence interval is crossing the border of clinical relevance and the low number of events (imprecision: -1).

4. Medication use

The level of evidence regarding medication use was downgraded by three levels to *very low* because of study limitations (risk of bias: -1), differences in PRF and control treatment between the studies (indirectness: -1), and because the confidence interval is crossing the borders of clinical relevance (imprecision: -1).

5. Functioning

The level of evidence regarding functioning was downgraded by three levels to *very low* because of study limitations (risk of bias: -1), differences in PRF and control treatment between the studies (indirectness: -1), and because the confidence interval is crossing the border of clinical relevance (imprecision: -1).

6. Quality of life

The level of evidence regarding quality of life was downgraded by three levels to *very low* because of study limitations (risk of bias: -1), and because of the very low number of patients and inclusion from only one study (imprecision: -2).

7. Cervical surgery

The level of evidence regarding cervical surgery was downgraded by three levels to *very low* because of study limitations (risk of bias: -1), the very low number of patients and events from one study, and because the confidence interval is crossing both borders of clinical relevance (imprecision: -2).

Conclusions

1. Pain (critical)

Very low GRADE	The evidence is very uncertain about the effect of PRF treatment on pain when compared with control treatment in patients with chronic cervical radicular syndrome. *Source: Van Zundert, 2007; Lee, 2016; Halim, 2017; Wang, 2016; Chalermkitpanit, 2023.*

2. Patient satisfaction (critical)

Very low GRADE	The evidence is very uncertain about the effect of PRF treatment on patient satisfaction when compared with control treatment in patients with chronic cervical radicular syndrome. *Source: Van Zundert, 2007; Halim, 2017; Wang, 2016.*

5

3. Complications (critical)

Very low GRADE	The evidence is very uncertain about the effect of PRF treatment on complications when compared with control treatment in patients with chronic cervical radicular syndrome. *Source: Van Zundert, 2007; Lee, 2016; Halim, 2017; Wang, 2016; Chalermkitpanit, 2023.*

4. Medication use (important)

Very low GRADE	The evidence is very uncertain about the effect of PRF treatment on medication use when compared with control treatment in patients with chronic cervical radicular syndrome. *Source: Van Zundert, 2007; Chalermkitpanit, 2023.*

10 **5. Functioning (important)**

Very low GRADE	The evidence is very uncertain about the effect of PRF treatment on functioning when compared with control treatment in patients with chronic cervical radicular syndrome. *Source: Van Zundert, 2007; Lee, 2016; Halim, 2017; Chalermkitpanit, 2023.*

6. Quality of life (important)

Very low GRADE	PRF treatment likely results in little to no difference in quality of life when compared with control treatment in patients with chronic cervical radicular syndrome. *Source: Van Zundert, 2007.*

7. Cervical surgery

Very low GRADE	The evidence is very uncertain about the effect of PRF treatment on cervical surgery when compared with control treatment in patients with chronic cervical radicular syndrome. *Source: Van Zundert, 2007.*

Overwegingen – van bewijs naar aanbeveling

Voor- en nadelen van de interventie en de kwaliteit van het bewijs

In de literatuur is gekeken naar de effectiviteit van PRF-behandeling bij mensen met een cervicaal radiculair syndroom. Er werden vijf RCT's gevonden die PRF-behandeling vergeleken met een controle behandeling, waaronder epidurale corticosteroïde-injecties (ECSI), percutane nucleoplastie en schijnbehandeling. De studiepopulaties in deze studies zijn echter klein, met enkele methodologische beperkingen (risico op bias, imprecisie). De bewijskracht voor de cruciale uitkomstmaten pijn, patiënttevredenheid en complicaties en de overall bewijskracht komt daarmee op *zeer laag*. Dit betekent dat nieuwe studies kunnen leiden tot nieuwe inzichten. Derhalve kunnen er op basis van de literatuur geen sterke conclusies worden getrokken over de effectiviteit van PRF-behandeling bij mensen met cervicaal radiculair syndroom ten opzichte van controle behandelingen.

Met het vaststellen van een zeer lage bewijskracht, is echter niet gezegd dat er geen bewijs is (Huygen, 2019). Hierbij neemt de werkgroep twee facetten in overweging:

- Ondanks de lage patiëntaantallen, toont Van Zundert (2007) een effect van PRF-behandeling op pijn, patiënttevredenheid, medicatie-gebruik en zelfs voorkómen van nekchirurgie.
- Behandelvoorkeur bij de patiënt lijkt een grote rol te spelen op de haalbaarheid van het uitvoeren van een RCT bij PRF-behandelingen. Zo gaf bijvoorbeeld 50% in Van Zundert (2007) geen informed consent voor deelname aan de sham-controle groep.
  Verschillende artikelen en case series concluderen dat PRF-behandeling aanbevolen kan worden (Kwak, 2018; Huygen, 2019; Peene, 2023).

Daarbij is het belangrijk dat het bewijs voor effect van PRF-behandeling zich beperkt tot een chronisch (>3 maanden) CRS. Er lijkt geen verschil in effect te zijn tussen PRF-behandeling en epidurale corticosteroïde-injecties (Wang, 2016; Lee, 2016). Een argument voor PRF-behandeling is dat er geen ernstige complicaties zijn gemeld tijdens de procedure zoals bij het gebruik van epidurale corticosteroïde-injecties (Peene, 2023). Vervolgonderzoek op dit gebied is wenselijk. Een argument tegen PRF-behandeling is dat het werkingsmechanisme minder duidelijk is dan van epidurale corticosteroïde-injecties.

De werkgroep doet geen uitspraak of het geven van een gecombineerde behandeling van PRF én epidurale corticosteroïde-injecties zinvol is.

De werkgroep is van mening dat bij een chronisch CRS, in samenspraak met de patiënt en afhankelijk van het beloop na eerdere epidurale corticosteroïde-injecties, er gekozen kan worden voor een herhaalde epidurale corticosteroïde-injectie dan wel PRF-behandeling. Indien de eerste PRF-behandeling effectief is gebleken, kan de PRF-behandeling tot één á twee keer bij dezelfde pijn episode herhaald worden (expert opinion).

Waarden en voorkeuren van patiënten (en evt. hun verzorgers)

De meeste patiënten die voor PRF-behandeling in aanmerking komen hebben al een conservatieve behandeling ondergaan, met onvoldoende resultaat of (ernstige) complicaties. De werkgroep geeft de voorkeur aan een beslissing in samenspraak met de patiënt, waarbij de voor- en nadelen worden afgewogen.

Kosten (middelenbeslag)

Er is weinig bekend over de kosteneffectiviteit van PRF-behandelingen bij patiënten met CRS. De werkgroep verwacht dat de PRF-behandelingen als interventie bescheiden kosten met zich meebrengt.

Aanvaardbaarheid, haalbaarheid en implementatie

Op het gebied van aanvaardbaarheid, haalbaarheid en implementatie voorziet de werkgroep geen grote uitdagingen. De behandeling wordt op diverse plekken in Nederland uitgevoerd. De werkgroep voorziet geen grote haalbaarheid en implementatie barrières.

Aanbevelingen

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventies

Hoewel de bewijskracht zeer laag is, acht de werkgroep op basis van praktijkervaring, expert opinion en overige literatuur dat een PRF-behandeling te overwegen is bij patiënten met chronische CRS.

Overweeg Pulsed Radiofrequency (PRF)-behandeling toe te passen bij patiënten met chronisch CRS (>3 maanden), met als doel om pijnverlichting te bewerkstelligen, indien:

- eerdere conservatieve therapie onvoldoende effectief is,
- chirurgie besproken is, en
- de patiënt persisterende arm-pijn ervaart.

Literatuur

Chalermkitpanit P, Pannangpetch P, Kositworakitkun Y, Singhatanadgige W, Yingsakmongkol W, Pasuhirunnikorn P, Tanasansomboon T. Ultrasound-guided pulsed radiofrequency of cervical nerve root for cervical radicular pain: a prospective randomized controlled trial. Spine J. 2023 May;23(5):651-655. Doi: 10.1016/j.spinee.2023.01.004. Epub 2023 Jan 12. PMID: 36641034.

Halim W, van der Weegen W, Lim T, Wullems JA, Vissers KC. Percutaneous Cervical Nucleoplasty vs. Pulsed Radio Frequency of the Dorsal Root Ganglion in Patients with Contained Cervical Disk Herniation; A Prospective, Randomized Controlled Trial. Pain Pract. 2017 Jul;17(6):729-737. Doi: 10.1111/papr.12517. Epub 2016 Oct 14. PMID: 27611826.

Huygen F, Kallewaard JW, van Tulder M, Van Boxem K, Vissers K, van Kleef M, Van Zundert J. "Evidence-Based Interventional Pain Medicine According to Clinical Diagnoses": Update 2018. Pain Pract. 2019 Jul;19(6):664-675. Doi: 10.1111/papr.12786. Epub 2019 May 2. PMID: 30957944; PMCID: PMC6850128.

Kwak SY, Chang MC. Effect of intradiscal pulsed radiofrequency on refractory chronic discogenic neck pain: A case report. Medicine (Baltimore). 2018 Apr;97(16):e0509. Doi: 10.1097/MD.0000000000010509. PMID: 29668635; PMCID: PMC5916694.

Lee DG, Ahn SH, Lee J. Comparative Effectivenesses of Pulsed Radiofrequency and Transforaminal Steroid Injection for Radicular Pain due to Disc Herniation: a Prospective Randomized Trial. J Korean Med Sci. 2016 Aug;31(8):1324-30. Doi: 10.3346/jkms.2016.31.8.1324. Epub 2016 Jun 24. PMID: 27478346; PMCID: PMC4951565

Peene L, Cohen SP, Brouwer B, James R, Wolff A, Van Boxem K, Van Zundert J. 2. Cervical radicular pain. Pain Pract. 2023 Jun 4. Doi: 10.1111/papr.13252. Epub ahead of print. PMID: 37272250.

Van Zundert J, Patijn J, Kessels A, Lamé I, van Suijlekom H, van Kleef M. Pulsed radiofrequency adjacent to the cervical dorsal root ganglion in chronic cervical radicular pain: a double blind sham controlled randomized clinical trial. Pain. 2007 Jan;127(1-2):173-82. Doi: 10.1016/j.pain.2006.09.002. Epub 2006 Oct 18. PMID: 17055165.

Wang F, Zhou Q, Xiao L, Yang J, Xong D, Li D, Liu L, Ancha S, Cheng J. A Randomized Comparative Study of Pulsed Radiofrequency Treatment With or Without Selective Nerve Root Block for Chronic Cervical Radicular Pain. Pain Pract. 2017 Jun;17(5):589-595. Doi: 10.1111/papr.12493. Epub 2016 Oct 14. PMID: 27739217.

Bijlagen bij module 'PRF'

Implementatieplan

Aanbeveling	Tijdspad voor implementatie: < 1 jaar, 1 tot 3 jaar of > 3 jaar	Verwacht effect op kosten	Randvoorwaarden voor implementatie (binnen aangegeven tijdspad)	Mogelijke barrières voor implementatie[1]	Te ondernemen acties voor implementatie[2]	Verantwoordelijken voor acties[3]	Overige opmerkingen
Alle aanbevelingen	< 1 jaar	Zeer beperkt.	Bekendheid met de richtlijn.	Overtuiging dat PRF-behandelingen een plek heeft bij subacute CRS.	*Verspreiden van richtlijn. *Voldoende kennis bij zorgverleners.	*Beroepsverenigingen. *Zorginstellingen.	n.v.t.

[1] Barrières kunnen zich bevinden op het niveau van de professional, op het niveau van de organisatie (het ziekenhuis) of op het niveau van het systeem (buiten het ziekenhuis). Denk bijvoorbeeld aan onenigheid in het land met betrekking tot de aanbeveling, onvoldoende motivatie of kennis bij de specialist, onvoldoende faciliteiten of personeel, nodige concentratie van zorg, kosten, slechte samenwerking tussen disciplines, nodige taakherschikking, etc.

[2] Denk aan acties die noodzakelijk zijn voor implementatie, maar ook acties die mogelijk zijn om de implementatie te bevorderen. Denk bijvoorbeeld aan controleren aanbeveling tijdens kwaliteitsvisitatie, publicatie van de richtlijn, ontwikkelen van implementatietools, informeren van ziekenhuisbestuurders, regelen van goede vergoeding voor een bepaald type behandeling, maken van samenwerkingsafspraken.

[3] Wie de verantwoordelijkheden draagt voor implementatie van de aanbevelingen, zal tevens afhankelijk zijn van het niveau waarop zich barrières bevinden. Barrières op het niveau van de professional zullen vaak opgelost moeten worden door de beroepsvereniging. Barrières op het niveau van de organisatie zullen vaak onder verantwoordelijkheid van de ziekenhuisbestuurders vallen. Bij het oplossen van barrières op het niveau van het systeem zijn ook andere partijen, zoals de NZA en zorgverzekeraars, van belang.

Evidence tables

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Van Zundert, 2007	Type of study: RCT Setting and country: Patients that were referred to the pain centers of the University Hospital Maastricht, Maastricht, The Netherlands; Ziekenhuis Oost-Limburg, Genk, Belgium, and Catharina Hospital, Eindhoven, The Netherlands, were screened for inclusion. Funding and conflicts of interest: None declared.	Inclusion criteria: - Neck pain radiating over the posterior shoulder area to the arm for >6 months. - Conventional therapy, including medication, physical therapy, and transcutaneous electrical nerve stimulation, was not effective. - Symptoms should suggest involvement of the cervical spinal nerve and be perceived along the affected nerve root. - Positive Spurling test. - Average pain intensity (VAS) > 35. Exclusion criteria: - Age <20 years or >75 years. - History of cancer. - Fractures of the cervical vertebrae. - Myelopathy. - Previous cervical fusion or laminectomy. - Systemic diseases or connective tissue diseases. - Diabetes mellitus. - Coagulation disorders and use of anticoagulants. - Multiple sclerosis. - Pregnancy. - Shoulder pathology. - Presence of a cardiac	Describe intervention: PRF treatment - Stimulation was started at 50 Hz to obtain a sensory stimulation threshold. - The PRF current was applied during 120 s from the lesion generator.	Describe control: Sham treatment during which the identification of the target point, electrode placement, and the sensory stimulation was performed in the same way as for the patients in the intervention group.	Length of follow-up: 6 months Loss-to-follow-up: Intervention: none before 3 months Reasons: - Control: 1 before 3 months Reasons: surgical treatment Incomplete outcome data: Not reported, except loss-to-follow-up as above.	Outcome measures and effect size: **Pain** *Defined as a 20-points reduction in pain intensity measured by VAS after 3 months* I: 82% (9/11) C: 25% (3/12) **Patient satisfaction** *Defined as at least 50% pain improvement of the GPE* *4 weeks* I: 64% (7/11) C: 42% (5/12) *3 months* I: 82% (9/11) C: 33% (4/12) *6 months* I: 64% (7/11) C: 17% (2/12) **Complications** *Defined as the number of participants that reported side effects or complications over the study period* I: 0 C: 0 **Medication use** *Defined as the change in intake of pain medication*	*Authors conclusion*: PRF treatment of the cervical dorsal root ganglion might provide pain relief for a limited number of patients with chronic cervical radicular pain. *Limitations*: - Difference in baseline demographic characteristics. - Low inclusion rate, resulting in not enough power for different parameters.

		pacemaker or spinal cord stimulator. - Previous RF or PRF treatment of the cervical DRG. <u>N total at baseline</u>: *I*: 11 *C*: 12 <u>Important prognostic factors</u>: *Age ± SD:* *I:* 42 ± 12.2 *C:* 52.9 ± 11.9 *Sex (%male):* *I:* 46% *C:* 42% <u>Groups comparable at baseline</u>? No, patients in the control group were older and started with a higher VAS score.				*from baseline to 3 months* *Higher* I: 9.1% (1/11) C: 41.7% (5/12) *Equal* I: 36.4% (4/11) C: 25.0% (3/12) *Lower* I: 54.5% (6/11) C: 33.3% (4/12) **Functioning** *SF-36, defined as the mean difference (SD) at 3 months* Physical functioning I: 9.0 (16.6) C: 6.9 (15.0) Social functioning I: 12.5 (28.0) C: -1.0 (28.4) **Quality of life** *Euroqol, defined as the mean difference (SD) at 3 months* I: 12.6 (19.7) C: 4.7 (30.8) *SF-36, defined as the mean difference (SD) at 3 months* Physical role restriction I: 23.5 (48.6) C: 24.3 (26.9) Emotional role restriction I: 24.2 (36.8) C: 0.0 (53.7) Mental health I: 6.9 (12.9) C: 0.3 (22.2) Vitality	

						I: 17.3 (17.1) C: 2.1 (16.0) Pain I: 9.8 (20.5) C: 9.3 (25.8) General health I: 4.1 (10.0) C: 2.3 (19.0) **Cervical surgery** *Defined as the number of participants that were referred for neck surgery* I: 9% (1/11) C: 25% (3/12)	
Lee, 2016	Type of study: RCT Setting and country: Department of Physical Medicine & Rehabilitation, Dongsan Medical Center, Keimyung University School of Medicine, Daegu, Korea, Department of Physical Medicine & Rehabilitation, Yeungnam University School of Medicine, Daegu, Korea. Funding and conflicts of interest: The study was supported by the	Inclusion criteria: - Age between 20 and 70 years. - Presentation with symptomatic cervical or lumbar radicular pain. - Imaging findings of a cervical or lumbar intervertebral disc pathology compatible with pain symptoms. - Severe cervical or lumbar radicular pain than cervical or lumbar axial pain. - Presentation with a VAS of >4 and an ODI or Neck Disability Index of >30% after first TFESI. Exclusion criteria: - Severe allergy to injectants. - History of spine surgery. - Spinal instability. - Spinal stenosis or degenerative spondylolisthesis. - Infection on the spine.	Describe intervention: PRF therapy: - The catheter needle was inserted, and a sensory stimulation test was carried out using an RF generator. - Treatment was administered at 5 Hz and a 5 ms pulsed width for 240 seconds at 45V.	Describe control: Transforaminal epidural steroid injection: - Patients received 2 mL of 0.125% bupivacaine mixed with 5 mg dexamethasone.	Length of follow-up: 3 months Loss-to-follow-up: Total: 6 Reasons: drop-out (n=5), flare up pain (n=1). Incomplete outcome data: Not reported, except loss-to-follow-up as above.	Outcome measures and effect size: **Pain** *Defined as pain intensities, assessed by VAS, mean (SD)* Pre-treatment I: 5.3 (1.2) C: 4.9 (0.8) 2 weeks I: 4.2 (1.3) C: 3.6 (1.2) 4 weeks I: 3.3 (1.1) C: 2.8 (1.3) 8 weeks I: 2.4 (0.9) C: 2.5 (2.1) 3 months I: 2.0 (0.8) C: 2.4 (2.3) **Complications** I: 5.3% (1/19) C: 0% (0/19) **Functioning**	*Authors conclusion*: PRF treatment can be considered as a useful option for the control of radicular pain that helps reduce or avoid the possible adverse effects of TFESI. *Limitations*: - Small sample size *Other remarks:* Subgroup analyses for cervical radicular patients are available.

	2015 Yeungnam University Research Grant. The authors had no potential conflicts of interest to disclose.	- Tumor or tumor metastasis in the involved spinal area. - Pregnancy. N total at baseline: *I*: 19 *C*: 19 Important prognostic factors: *Age ± SD:* *I:* 54.3 ± 12.1 *C:* 50.8 ± 12.7 *Sex (%male):* *I:* 16% *C:* 58% Groups comparable at baseline? No, percentage male differed between the two groups.				*Defined as functional disabilities associated with cervical radicular pain, assessed by NDI, mean (SD)* Pre-treatment I: 38.7 (8.3) C: 39.1 (11.6) 2 weeks I: 28.3 (14.7) C: 28.6 (9.7) 4 weeks I: 22.2 (11.6) C: 19.4 (11.2) 8 weeks I: 17.6 (6.8) C: 18.8 (15.7) 3 months I: 14.0 (7.0) C: 17.0 (14.3)	
Halim, 2017	Type of study: RCT Setting and country: Anna Hospital, Geldrop, The Netherlands, Radboud UMC Medical Center, Nijmegen, The Netherlands. Funding and conflicts of interest: No funding reported. The institution one author works for	Inclusion criteria: - Patients with a contained, single-level cervical disk herniation diagnosed on recent MRI (<4 weeks) who failed conservative treatment. - Presentation with a 100 mm VAS of ≥50 mm with or without neck pain corresponding to the herniated level. - Disk height over 50% of adjacent level. Exclusion criteria: - Patients who did not respond to a diagnostic nerve block placed with local anesthetic at the level	Describe intervention: PRF treatment: - A 45 V, 2 Hz (20 ms) PRF stimulus was applied for 6 minutes.	Describe control: Percutaneous nucleoplasty treatment	Length of follow-up: 3 months Loss-to-follow-up: Intervention: 7 Reasons: no reason provided Control: 3 Reasons: no reason provided Incomplete outcome data: No other than loss-to-follow-up reported above.	Outcome measures and effect size: **Pain** Baseline I: 69.5 C: 71.0 1 month I: 41.0 C: 29.3 2 months I: 38.0 C: 31.5 3 months I: 35.5 C: 27.6 **Patient satisfaction** 1 month I: 52.8 C: 68.9	*Authors conclusion*: Both PRF and PCN treatment show significant pain improvement in patients with contained cervical disk herniation, but none of the treatments is superior to the other. Both treatment options are shown to be effective and safe for use in clinical practice. *Limitations*: - Comparison of two active treatments. - Limited follow-up of 3 months. - Small sample size.

	receives study grants from Cotera Inc and Zimmer Biomet Inc, and he is a consultant for Zimmer Biomet, but this is unrelated to the current study.	identified with history taking and MRI. - Extruded disk fragmentation. - Cervical spondylolisthesis. - Spinal canal stenosis. - Previous surgery at the index cervical disk herniation level. N total at baseline: *I*: 17 *C*: 17 Important prognostic factors: *Age ± SD:* *I:* 49.5 *C:* 52.4 *Sex (%male):* *I:* 53% *C:* 41% Groups comparable at baseline? Yes.				2 months I: 60.9 C: 67.8 3 months I: 63.5 C: 58.4 **Complications** I: 18% (3/17) C: 18% (3/17) **Functioning** Baseline I: 19.4 C: 21.1 1 month I: 14.9 C: 15.9 2 months I: 12.2 C: 12.3 3 months I: 10.8 C: 11.1	
Wang, 2016	Type of study: Randomized comparative study Setting and country: Pain Management Department of Shenzhen Nanshan Hospital in China. Funding and conflicts of	Inclusion criteria: - Age ≥20 years - Males and females - Moderate to severe chronic cervical radicular pain (NRS ≥ 5) - Resistance to conservative management - No indication for open surgical intervention - MRI evidence of nerve root compression - Absence of progressive motor deficit Exclusion criteria:	Describe intervention: PRF treatment: - At 42 degrees Celsius, the PRF stimulus was applied for 4 minutes, and then radiculography was carried out.	Describe control: The control (CNRB) group received a mixture of 1 mL corticosteroids containing 5 mg betamethasone dipropionate and 2 mg betamethasone disodium phosphate, 1 mL 0.9% NaCl, and 1 mL of 2% lidocaine after radiculography.	Length of follow-up: 6 months Loss-to-follow-up: Intervention: 1 Reasons: NR Control: 2 Reasons: NR Incomplete outcome data: Not reported, except loss-to-follow-up as above.	Outcome measures and effect size: **Patient satisfaction** Defined as rates of positive GPE (+2 or +3) 1 week I: 20% (4/20) C: 23.8% (5/21) 1 month I: 40% (8/20) C: 14.3% (3/21) 3 months I: 5.3% (1/19) C: 14.3% (3/21) 6 months I: 10.5% (2/19)	*Authors conclusion*: Combining PRF and CNRB achieved superior outcomes to those accomplished by either CNRB or PRF alone. *Limitations*: - Small sample size - Short follow-up to determine long-term effects

	interest: No conflicts of interest to declare. Nothing is mentioned about funding.	- Uncorrected coagulopathy - Infection - Cervical myelopathy - Malignancy - Bilateral or more than one level radicular pain - Previous cervical fusion or laminectomy - Significant psychopathology N total at baseline: I: 20 C: 21 Important prognostic factors: *Age ± SD:* *I:* 58.4 ± 16.2 *C:* 59.0 ± 13.8 *Sex (%male):* *I:* 55% *C:* 43% Groups comparable at baseline? Yes.				C: 5.3% (1/19) **Complications** Defined as the number of patients with complications I: 0 C: 0	
Chalermkitpanit, 2023	Type of study: RCT Setting and country: King Chulalongkorn Memorial Hospital (KCMH), Bangkok, Thailand Funding and conflicts of	Inclusion criteria: - Age between 30-80 years. - Diagnosis of cervical spondylosis with radicular pain by an orthopaedic surgeon and a pain specialist. - Clinical examination compatible with MRI. - Moderate to severe cervical radicular pain rated by a NRS at least 4 out of 10. - Chronic pain >3 months despite conservative treatment.	Describe intervention: PRF treatment: - Treatment was done for 4 minutes following a positive sensory stimulation between 0.3 and 0.5 volts. After the PRF treatment, 1.5 mL of 2% lidocaine with 10 mg of dexamethasone was injected.	Describe control: Steroid treatment: - A short bevel stimulating 22G-needle was placed and the sensory stimulation was confirmed. Then the same injectate was administered.	Length of follow-up: 9 months Loss-to-follow-up: Intervention: 1 Reasons: not reported. Control: - Reasons: - Incomplete outcome data: No other than loss-to-follow-up reported	Outcome measures and effect size: **Pain** NRS, mean (SD) I: 2.8 (2.7) C: 5.5 (2.6) **Functioning** *NDI, mean differences between PRF and steroid group* 3 months: 23.0 (95%CI 9.6 to -36.4) 6 months: 23.8 (95%CI 4.2 to 43.3)	*Authors conclusion*: PRF treatment exhibited a neuromodulation effect and is shown to be effective for patients with cervical radicular pain. *Limitations*: - Small sample size.

	interest: The study was funded by a grant from Ratchadapisek-sompotch Fund, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. The authors had no potential conflicts of interest to disclose.	Exclusion criteria: - Cervical radiculopathy with progressive weakness. - Radicular pain secondary to spinal tumor. - Patients with cardiac device implantation. - Ongoing local infection at the injection area or systemic infection. - Patients with bleeding disorders. - History of allergy to study medications. N total at baseline: *I*: 20 *C*: 21 Important prognostic factors: *Age ± SD:* *I:* 48.9 ± 15.8 *C:* 56.3 ± 14.6 *Sex (%male):* *I:* 40% *C:* 38% Groups comparable at baseline? Yes.			above.		

Risk of Bias

Study reference (first author, publication year)	**Was the allocation sequence adequately generated?**	**Was the allocation adequately concealed?**	**Blinding: Was knowledge of the allocated interventions adequately prevented? Were patients/healthcare providers/data collectors/outcome assessors/data analysts blinded?**	**Was loss to follow-up (missing outcome data) infrequent?**	**Are reports of the study free of selective outcome reporting?**	**Was the study apparently free of other problems that could put it at a risk of bias?**	**Overall risk of bias** **If applicable/necessary, per outcome measure**
Van Zundert, 2007	Definitely yes Reason: A computer-generated randomization list was used.	Definitely yes Reason: Independent observer provided the treating physician with a sealed envelope numbered in advance, which was opened in the operating room.	Definitely yes Reason: Patients, independent observer, data manager and neurologist were blinded. The healthcare provider was not blinded.	Definitely yes Reason: Only one (8%) participant was lost to follow-up before three months from the control group for a valid reason (surgery).	Probably yes Reason: No registration in register of clinical trials mentioned, but no reason to doubt that the report is free of selective outcome reporting.	Definitely no Reason: - Differences in baseline demographic characteristics. - Underpowering for different parameters, due to the low number of included participants.	**Some concerns (underpowering due to small sample size)**
Lee, 2016	Unknown	Unknown	Unknown	Probably no Reason: five patients (12%) were lost to follow-up (no reason reported) and one patient dropped out due to a pain flare-up.	Probably yes Reason: No registration in register of clinical trials known. Study protocol has been written but is not available.	Probably yes Reason: - Small sample size.	**Some concerns (information is missing)**
Halim, 2017	Unknown	Unknown	Unknown	Definitely no Reason: three patients (15%) were lost to follow-up from PCN group (no reason reported), and seven (29%) patients were lost to follow-up from	Probably no Reason: No registration in register of clinical trials mentioned. Some outcomes mentioned in the methods section are not reported in the	Probably yes Reason: - Small sample size.	**High**

				PRF group (no reason reported).	results section.		
Wang, 2016	Definitely no Reason: Patients were randomized according to the last number of their medical record number, which was generated by two research fellows.	Definitely no Reason: The same research fellows assigned participants to interventions.	Definitely no Reason: Data collectors (two nurses) were the only ones blinded.	Probably yes Reason: two patients (10%) were lost to follow-up from CNRB group (no reason), and one patient (5%) was lost to follow-up from PRF group (no reason).	Probably yes Reason: No registration in register of clinical trials known. Study protocol has been written but is not available.	Probably yes Reason: - Small sample size.	**High**
Chalermkitpanit, 2023	Unknown	Unknown	Probably yes Reason: Double-blinded RCT; patients and pain assessors were blinded.	Probably yes Reason: Only one (5%) participant was lost to follow-up at 1 month, but no reason was reported.	Probably yes Reason: No registration in register of clinical trials mentioned, but no reason to doubt that the report is free of selective outcome reporting.	Probably yes Reason: - Small sample size.	**Some concerns (information is missing)**

Table of excluded studies

Reference	Reason for exclusion
Van Zundert J, Huntoon M, Patijn J, Lataster A, Mekhail N, van Kleef M; Pain Practice. 4. Cervical radicular pain. Pain Pract. 2010 Jan-Feb;10(1):1-17. doi: 10.1111/j.1533-2500.2009.00319.x. Epub 2009 Oct 5. PMID: 19807874.	Wrong publication type (review)
Facchini G, Spinnato P, Guglielmi G, Albisinni U, Bazzocchi A. A comprehensive review of pulsed radiofrequency in the treatment of pain associated with different spinal conditions. Br J Radiol. 2017 May;90(1073):20150406. doi: 10.1259/bjr.20150406. Epub 2017 Feb 10. PMID: 28186832; PMCID: PMC5605093.	No risk of bias assessment performed, and less recent compared to Vuka (2020)
Kwak SG, Lee DG, Chang MC. Effectiveness of pulsed radiofrequency treatment on cervical radicular pain: A meta-analysis. Medicine (Baltimore). 2018 Aug;97(31):e11761. doi: 10.1097/MD.0000000000011761. PMID: 30075599; PMCID: PMC6081162.	All relevant studies are included in Vuka (2020) as well, which is a more recent SR
Yang S, Chang MC. Efficacy of pulsed radiofrequency in controlling pain caused by spinal disorders: a narrative review. Ann Palliat Med. 2020 Sep;9(5):3528-3536. doi: 10.21037/apm-20-298. Epub 2020 Sep 7. PMID: 32921088.	Wrong publication type (narrative review)
Geurts JW, van Wijk RM, Stolker RJ, Groen GJ. Efficacy of radiofrequency procedures for the treatment of spinal pain: a systematic review of randomized clinical trials. Reg Anesth Pain Med. 2001 Sep-Oct;26(5):394-400. doi: 10.1053/rapm.2001.23673. PMID: 11561257.	Wrong intervention (radiofrequency)
Vanneste T, Van Lantschoot A, Van Boxem K, Van Zundert J. Pulsed radiofrequency in chronic pain. Curr Opin Anaesthesiol. 2017 Oct;30(5):577-582. doi: 10.1097/ACO.0000000000000502. PMID: 28700369.	Wrong publication type (review)
Chua NH, Vissers KC, Sluijter ME. Pulsed radiofrequency treatment in interventional pain management: mechanisms and potential indications-a review. Acta Neurochir (Wien). 2011 Apr;153(4):763-71. doi: 10.1007/s00701-010-0881-5. Epub 2010 Nov 30. PMID: 21116663; PMCID: PMC3059755.	Includes only one relevant study that is also included in Vuka (2020), which is a more recent SR
Niemistö L, Kalso E, Malmivaara A, Seitsalo S, Hurri H; Cochrane Collaboration Back Review Group. Radiofrequency denervation for neck and back pain: a systematic review within the framework of the cochrane collaboration back review group. Spine (Phila Pa 1976). 2003 Aug 15;28(16):1877-88. doi: 10.1097/01.BRS.0000084682.02898.72. PMID: 12923479.	Wrong population (patients with cervical zygapophysial joint pain, cervicobrachial pain, lumbar zygapophysial joint pain and/or discogenic low back pain)
Niemisto L, Kalso E, Malmivaara A, Seitsalo S, Hurri H. Radiofrequency denervation for neck and back pain. A systematic review of randomized controlled trials. Cochrane Database Syst Rev. 2003;(1):CD004058. doi: 10.1002/14651858.CD004058. PMID: 12535508.	Duplicate
Vallejo R, Benyamin RM, Aliaga L. Radiofrequency vs. pulse radiofrequency: The end of the controversy, Techniques in Regional Anesthesia and Pain Management. 2010; 14(3): 128-132. ISSN 1084-208doi.org/10.1053/j.trap.2010.06.003.	Wrong publication type (review)
Cohen SP, Hooten WM. Advances in the diagnosis and management of neck pain. BMJ. 2017 Aug 14;358:j3221. doi: 10.1136/bmj.j3221. PMID: 28807894.	Wrong publication type (review)
Lee SH, Choi HH, Roh EY, Chang MC. Effectiveness of Ultrasound-Guided Pulsed Radiofrequency Treatment in Patients with Refractory Chronic Cervical Radicular Pain. Pain Physician. 2020 Jun;23(3):E265-E272. PMID: 32517402.	Wrong study design (prospective outcome study)
Tella P, Stojanovic M. Novel therapies for chronic cervical radicular pain: does pulsed radiofrequency have a role? Expert Rev Neurother. 2007 May;7(5):471-2. doi: 10.1586/14737175.7.5.471. PMID: 17492898.	Wrong publication type (expert review)
Xiao L, Li J, Li D, Yan D, Yang J, Wang D, Cheng J. A posterior approach to cervical nerve root block and pulsed radiofrequency treatment for cervical radicular pain: a retrospective study. J Clin Anesth. 2015 Sep;27(6):486-91. doi: 10.1016/j.jclinane.2015.04.007. Epub 2015 Jun 4.	Wrong study design (retrospective)

PMID: 26051825.	
Snidvongs S, Mehta V. Pulsed radio frequency: a non-neurodestructive therapy in pain management. Curr Opin Support Palliat Care. 2010 Jun;4(2):107-10. doi: 10.1097/SPC.0b013e328339628a. PMID: 20440207.	Wrong publication type (review)
Hata J, Perret-Karimi D, Desilva C, Leung D. Pulsed Radiofrequency Current in the Treatment of Pain. Critical Reviews in Physical and Rehabilitation Medicine. 2011 Jan;23(1):213-240. doi: 10.1615/CritRevPhysRehabilMed.v23.i1-4.150.	Wrong publication type (review)
van Boxem K, van Eerd M, Brinkhuizen T, Patijn J, van Kleef M, van Zundert J. Radiofrequency and pulsed radiofrequency treatment of chronic pain syndromes: the available evidence. Pain Pract. 2008 Sep-Oct;8(5):385-93. doi: 10.1111/j.1533-2500.2008.00227.x. Epub 2008 Aug 19. Erratum in: Pain Pract. 2010 Mar-Apr;10(2):164. Brinkhuize, Tjinta [corrected to Brinkhuizen, Tjinta]. PMID: 18721175.	Wrong publication type (review)
Malik K, Benzon HT. Radiofrequency applications to dorsal root ganglia: a literature review. Anesthesiology. 2008 Sep;109(3):527-42. doi: 10.1097/ALN.0b013e318182c86e. PMID: 18719452.	Wrong publication type (review)
Van Zundert J, Harney D, Joosten EA, Durieux ME, Patijn J, Prins MH, Van Kleef M. The role of the dorsal root ganglion in cervical radicular pain: diagnosis, pathophysiology, and rationale for treatment. Reg Anesth Pain Med. 2006 Mar-Apr;31(2):152-67. doi: 10.1016/j.rapm.2005.11.014. PMID: 16543102.	Wrong publication type (review)
Choi GS, Ahn SH, Cho YW, Lee DK. Short-term effects of pulsed radiofrequency on chronic refractory cervical radicular pain. Ann Rehabil Med. 2011 Dec;35(6):826-32. doi: 10.5535/arm.2011.35.6.826. Epub 2011 Dec 30. PMID: 22506211; PMCID: PMC3309390.	Wrong study design (prospective follow-up study)
Vuka I, Marciuš T, Došenović S, Ferhatović Hamzić L, Vučić K, Sapunar D, Puljak L. Efficacy and Safety of Pulsed Radiofrequency as a Method of Dorsal Root Ganglia Stimulation in Patients with Neuropathic Pain: A Systematic Review. Pain Med. 2020 Dec 25;21(12):3320-3343. doi: 10.1093/pm/pnaa141. PMID: 32488240.	Includes only two relevant studies that were found in the systematic search as well and are described separately.
Lee SH, Choi HH, Chang MC. Comparison between ultrasound-guided monopolar and bipolar pulsed radiofrequency treatment for refractory chronic cervical radicular pain: A randomized trial. J Back Musculoskelet Rehabil. 2022;35(3):583-588. doi: 10.3233/BMR-201842. PMID: 34542059.	Wrong comparison (monopolar PRF versus bipolar PRF)

Literature search strategy

Zoekverantwoording
Algemene informatie

Cluster/richtlijn: NVvN Cervicaal Radiculair Syndroom	
Uitgangsvraag/modules: : UV2c Wat is de plaats van pulsed radio frequency (PRF) behandelingen bij patiënten met CRS?	
Database(s): Embase.com, Ovid/Medline	Datum: 10 februari 2023
Periode: vanaf 1998	Talen: geen restrictie
Literatuurspecialist: Alies van der Wal	
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting: Voor deze vraag is gezocht op de elementen: - CRS - pulsed radio frequency De sleutelartikelen worden gevonden met deze search	
Te gebruiken voor richtlijnen tekst: *Nederlands* In de databases Embase.com en Ovid/Medline is op 10 februari 2023 systematisch gezocht naar systematische reviews, RCTs en observationele studies over CRS en pulsed radio frequency. De literatuurzoekactie leverde 124 unieke treffers op. *Engels* On the 10th of February 2023, a systematic search was performed for systematic reviews, RCTs and observational studies about CRS and pulsed radio frequency in the databases Embase.com and Ovid/Medline. The search resulted in 124 unique hits.	

Zoekopbrengst

	EMBASE	OVID/MEDLINE	Ontdubbeld
SR	42	26	41
RCT	33	27	41
Observationele studies	37	28	42
Totaal	112	81	**124***

in Rayyan

Zoekstrategie

Embase.com

No.	Query	Results
#12	#5 AND (#8 OR #9) NOT (#10 OR #11) = observationeel	37
#11	#5 AND #7 NOT #10 = RCT	33
#10	#5 AND #6 = SR	42
#9	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR	13839269

	subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	
#8	'major clinical study'/de OR 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'comparative study'/de OR 'cohort analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti)	7490391
#7	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	3724547
#6	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	900211
#5	#4 AND [1998-2023]/py	169
#4	#3 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	175
#3	#1 AND #2	286
#2	'radiofrequency therapy'/exp OR 'pulsed radiofrequency'/exp OR 'radiofrequency'/exp OR 'nucleoplasty'/exp OR nucleoplast*:ti,ab,kw OR ((pulse* NEAR/3 ('radiofrequenc*' OR 'radio frequenc*' OR rf)):ti,ab,kw) OR prf:ti,ab,kw OR (((radiofrequenc* OR 'radio frequenc*' OR rf) NEAR/3 (decompress* OR denervat* OR neurotom* OR ablation* OR therap* OR treatment* OR procedure* OR neurolys*)):ti,ab,kw)	87987
#1	'cervicobrachial neuralgia'/exp/mj OR cervicobrachial*:ti,ab,kw OR 'cervico brachial*':ti,ab,kw OR 'cervical brachial*':ti,ab,kw OR ((radiculalgia:ti,ab,kw OR radiculitis:ti,ab,kw OR radiculitides:ti,ab,kw OR radiculopath*:ti,ab,kw OR polyradiculopath*:ti,ab,kw OR neuralgia:ti,ab,kw OR 'herniated disc*':ti,ab,kw OR hernia:ti,ab,kw OR ((radicular NEAR/3 (pain* OR neuralgia* OR symptom* OR syndrom*)):ti,ab,kw) OR (('nerve root' NEAR/3 (pain* OR inflammation* OR disorder* OR compression* OR avulsion* OR impingement)):ti,ab,kw)) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('radicular pain'/exp/mj OR 'radiculopathy'/exp/mj) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw))	11647

Ovid/Medline

#	Searches	Results
12	(5 and (8 or 9)) not (10 or 11) = observationeel	28
11	(5 and 7) not 10 = RCT	27
10	5 and 6 = SR	26
9	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled	5352618

	clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or ((exp cohort studies/ or epidemiologic studies/ or multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.))	
8	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/	4361037
7	exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,Ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.	2551939
6	meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,Kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,Kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,Kf. or (systemic* adj1 review*).ti,ab,Kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,Kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,Kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,Kf. or (("data extraction" or "data source*") and "study selection").ti,ab,Kf. or ("search strategy" and "selection criteria").ti,ab,Kf. or ("data source*" and "data synthesis").ti,ab,Kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.	647645
5	limit 4 to yr="1998 -Current"	112
4	3 not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/)	114
3	1 and 2	118
2	exp Radiofrequency Therapy/ or nucleoplast*.ti,ab,Kf. or (pulse* adj3 ('radiofrequenc*' or 'radio frequenc*' or rf)).ti,ab,Kf. or PRF.ti,ab,Kf. or ((radiofrequenc* or 'radio frequenc*' or rf) adj3 (decompress* or denervat* or neurotom* or ablation* or therap* or treatment* or procedure* or neurolys*)).ti,ab,kf.	59221
1	((exp Radiculopathy/ or radiculalgia.ti,ab,Kf. or radiculitis.ti,ab,Kf. or radiculitides.ti,ab,Kf. or radiculopath*.ti,ab,Kf. or polyradiculopath*.ti,ab,Kf. or neuralgia.ti,ab,Kf. or 'herniated disc*'.ti,ab,Kf. or hernia.ti,ab,Kf. or (radicular adj3 (pain* or neuralgia* or symptom* or syndrom*)).ti,ab,Kf. or ('nerve root' adj3 (pain* or inflammation* or disorder* or compression* or avulsion* or impingement)).ti,ab,kf.) and (exp Cervical Vertebrae/ or exp Neck/ or cervical.ti,ab,Kf. or cervico*.ti,ab,Kf. or neck.ti,ab,kf.)) or cervicobrachial*.ti,ab,Kf. or 'cervico brachial*'.ti,ab,Kf. or 'cervical brachial*'.ti,ab,kf.	7355

Module 3. Anterieure behandelingen

De volgende anterieure chirurgische behandelingen komen in deze richtlijn aan de orde:

- Chirurgische decompressie van de zenuwwortel
    - Timing van chirurgische behandeling
- ACDF met plaat (plaat versus geen plaat)
- Anterieure Cervicale Discectomie met Prothese (ACDP)
- Anterieure (micro)foraminotomie

Module 3.1. Chirurgische decompressie van de zenuwwortel

Uitgangsvraag
Wat is de plaats van chirurgische decompressie van de zenuwwortel bij patiënten met CRS?

Inleiding
Een operatie is de standaardbehandeling bij patiënten met CRS wanneer pijn en/of uitval van gevoel en/of kracht in de arm aanhouden met congruente MRI-afwijking. Vaak kent een CRS echter een voorspoedig spontaan herstel (Lyer, 2016). Over het algemeen vindt men dat alleen tot operatieve therapie moet worden overgegaan als conservatief beleid gefaald heeft. Een operatie kan gepaard gaan met complicaties en hoge kosten. Op dit moment is het onduidelijk of CRS beter te behandelen is door middel van chirurgische decompressie van de zenuwwortel of door middel van niet opereren in het algemeen. Wat levert een operatie precies op voor een patiënt en hoe staat dit in verhouding tot complicaties en kosten? Deze module gaat in op de effectiviteit van chirurgische behandeling. Omtrent de timing van chirurgische interventie verwijst de werkroep naar de submodule 'Timing'.

Search and select
A systematic review of the literature was performed to answer the following question: *What is the efficacy of surgical anterior decompression compared to conservative management in patients with cervical radiculopathy?*

P: Patients with cervical radiculopathy
I: Surgical decompression of the nerve root (anterior microforaminotomy, ACD, ACDF, ACDP)
C: Conservative treatment (e.g. physiotherapy, cervical collar, PRF, corticosteroids);
O: Patient satisfaction, arm-pain, quality of life, return to work, tingling, functioning, complications, re-operation, adjacent segment level disease

Relevant outcome measures
The guideline development group considered arm-pain, quality of life and functioning as critical outcome measures for decision making; and patient satisfaction, return to work, tingling, complications, re-operation, and adjacent segment level disease as important outcome measures for decision making.

The working group defined the outcome measures as follows:

- Pain: VAS
- Functioning: Neck Disability Index (NDI)
- Quality of life: SF-36 or 1-10 scale

A priori, the working group did not define other outcome measures but used the definitions used in the studies.

The working group defined a 10% difference for both continuous outcome measures and dichotomous outcome measures informing on relative risk (RR ≤ 0.91 and ≥ 1.10) as minimal clinically (patient) important differences.

Search and select (Methods)
The databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms from inception until 25 April 2022. The detailed search strategy is depicted under the tab Methods. The systematic literature search resulted in 582 hits. Studies were selected based on the following criteria:

- Systematic review (searched in at least two databases, and detailed search strategy, risk of bias assessment and results of individual studies available), randomized controlled trial comparing surgical decompression of the nerve root with conservative management;
- Patients aged ≥ 18 years;
- Full-text English language publication;
- Studies including ≥ 20 patients (ten in each study arm); and
- Studies according to PICO.

Initially, 29 studies were selected based on title and abstract screening. After reading the full text, 26 studies were excluded (see the table with reasons for exclusion under the tab Methods), and three studies were included.

Results

Three studies were included in the analysis of the literature. A comprehensive overview of study characteristics is depicted in Table 1. Important study characteristics and results are summarized in the evidence table. The assessment of the risk of bias is summarized in the risk of bias table.

Summary of literature

Description of studies

In the RCT by Enquist (2013), anterior cervical decompression and fusion (ACDF) was combined with a physiotherapy programme after surgery and compared with the same physiotherapy programme alone. Participants were included when they reported pain in one or both arms, had a symptom duration of 8 weeks to 5 years, had one or two symptomatic disc levels and where of working age (18-65 years). Participants with obvious or slight signs of myelopathy were excluded, as were participants with a history of neck distortion, participants in need for other types of surgery, patients with malignancies/inflammatory joint disease/psychiatric disorders, and patients with a concurrent work-disabling disease. Participants were randomized in a surgical group receiving surgery and after 3 months physiotherapy (n=31) or a non-surgical group receiving physiotherapy only (n=32). Outcomes were measured 6-, 12- and 24-months post-intervention.

In the study by Enquist (2017), the 5- and 8-years results from the RCT of Enquist (2013) were presented.

In the RCT by Persson (1997), ACDF was compared with a cervical collar and with a physiotherapy program. Potential participants reported cervico-brachial pain for more than three months and were referred to an out-patient clinic in Lund for consideration of surgical treatment. Inclusion criteria were clinical and radiological signs indicating nerve root compression without spinal cord compression. Patients with whiplash, other traumatic injuries, and serious associated somatic/psychiatric diseases were excluded from participating. Participants were randomized in a surgical group receiving surgery (n=27), a group receiving physiotherapy (n= 27) and a group wearing a cervical collar (n=27). Outcomes were measured 4- and 16-months post-intervention.

***Table 4**. Description of included studies*

Study	Intervention		Comparator		Follow-up	Outcomes
	Characteristics	**Intervention type**	**Characteristics**	**Type of control group**		
Enquist, 2013; Enquist, 2017	Mean age (SD): 49 (8) Female (%): 17 (55) Duration of pain, months (SD): - Neck symptoms: 15 (12) - Arm symptoms: 13 (10) Affected level: C5-6 (n=12(39%)), C6-7 (n=13(42%))	Surgery with physiotherapy (31) Anterior cervical decompression and fusion (one level n=27, 2 level with anterior plate n=4). Three months post-surgery the same physiotherapy program was initiated as provided in the control group.	Mean age (SD): 44 (9) Female (%): 13 (41) Duration of pain, months (SD): - Neck symptoms: 21 (19) - Arm symptoms: 17 (16) Affected level: C5-6 (n=14(44%), C6-7 (n=11(34%))	Physiotherapy (n= 32) Individualized physiotherapy program consisting of neck-specific exercises and procedures for pain relief, general exercises, and pain coping, increasing self-efficacy and stress management strategies.	6 months, 12 months, 24 months	Functioning (NDI), arm pain (VAS -100), reoperations, complications
Persson (1997)	Mean age (SD): 40 (8.5) Female (%): 11 (41) Duration of pain, months (SD): 34 (34.8) Affected level: C5-6 (n=13(48%)), C6-7(n=10(37%))	Surgery (n= 27) Anterior cervical discectomy, using a bone graft from purified cow bone for fusion (one level,n= 26). Laminectomy by a posterior approach technique (n=1)	Mean age (SD): 48 (8.1) Female (%):16 (59) Duration of pain, months (SD): 40 (32.5) Affected level: C5-6 (n=12(44%)), C6-7 (n=10(10%))	Physiotherapy (n= 27) 15 sessions of 40-45 minutes physiotherapy, for 3 months.	4 months, 16 months	Pain (VAS 0-100)
			Mean age (SD): 49 (8.5) Female (%): 10 (37) Duration of pain, months (SD): 28 (24.3) Affected level: C5-6 (n=15(56%)), C6-7 (n=10(37%))	Cervical collar (n= 27) Either a rigid or soft collar. After randomization.		

MSQ, Medication Quantitative Scale; NDI, Neck Disability Index; NRS, Numeric Rating Scale; VAS, Visual Analogue Scale

Results

1. Surgery with physiotherapy vs. physiotherapy alone; and surgery vs. physiotherapy

1.1 Arm-pain (critical)

Three studies reported on pain (Enquist, 2013; Enquist, 2017; Persson, 1997). Results are presented in three post-intervention terms: 1.1.1 Short term: until 6 months), 1.1.2. Midterm: >6 months to 12 months, 1.1.3. long term: >12 months to 8 years. In the study by Persson (1997), type of pain (neck- and/or arm-pain) was not otherwise specified. A brief overview of the main characteristics is provided in Table 2.

***Table 5**. Overview on post-intervention terms*

Study	Follow-up	Term	Scale
Enquist, 2013	6 months, 12 months, 24 months	Short term, midterm, long term	Arm pain (VAS-scale, 0-100)
Enquist, 2017	5-8 years	Long term	Arm pain (VAS-scale, 0-100)
Persson, 1997	4 months, 16 months	Short term, midterm	Pain (VAS-scale, 0-100)

NRS: Numeric rating scale; VAS: Visual Analogue Scale

1.1.1 Short term (post treatment: up to 6 months)

Two studies reported on pain up to six months (Enquist, 2013; Persson, 1997).

- *Arm pain (surgery with physiotherapy versus physiotherapy alone)*
  Enquist (2013) reported results for arm pain reduction using a VAS-scale ranging from 0-100mm. Six months after initiation of the intervention, mean reduction (within group mean change from baseline) was 21.1 (SD 38.4) in the group receiving surgery with physiotherapy and 16.0 (SD 38.6) in the group receiving only physiotherapy. This resulted in a mean difference of 5.1 (95%CI -13.9 to 24.1). Results are depicted in Figure 1.
- *Pain (surgery versus physiotherapy)*
  Persson (1997) reported results for mean current pain intensity using a VAS-scale ranging from 0-100mm. Four months after intervention, mean score was 27.0 (SD 23.0) in the group receiving surgery and 41.0 (SD 28.5) in the group receiving physiotherapy. This resulted in a mean difference of 14.00 (95%CI -0.19 to -27.81). Results are depicted in Figure 2.

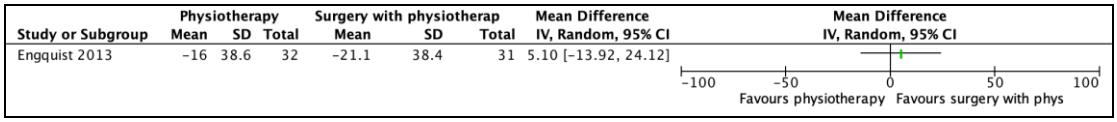

***Figure 1**. Mean reduction for armpain, surgery with physiotherapy versus physiotherapy alone (short term follow-up)*

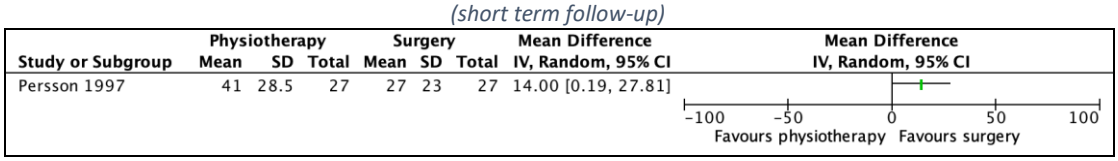

***Figure 2**. Mean differences for (arm-) pain, surgery versus physiotherapy (short term follow-up)*

1.1.2 Midterm (post-treatment >6 months to 12 months)

Two studies reported on pain after 6 months to 12 months (Enquist, 2013; Persson, 1997).

- *Arm pain (Surgery with physiotherapy versus physiotherapy alone)*
  In the study by Enquist (2013), twelve months after initiation of the intervention, mean reduction was 25.1 (SD 40.9) in the group receiving surgery with physiotherapy and 20.3 (SD 41.0) in the group receiving only physiotherapy. This resulted in a mean difference of 4.80 (95%CI -15.43 to 25.03). Results are depicted in Figure 3.
- *Pain (surgery versus physiotherapy)*
  In the study by Persson (1997), sixteen months after initiation of the intervention, mean score was 30 (SD 28.1) in the group receiving surgery and 39 (SD 25.8) in the group

receiving physiotherapy. This resulted in a mean difference of 9.00 (95%CI -5.39 to 23.39). Results are depicted in Figure 4.

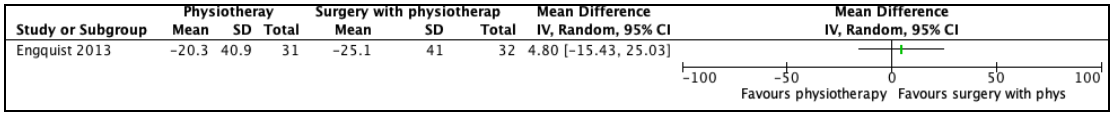

Figure 3. *Mean difference for arm-pain reduction, surgery with physiotherapy versus physiotherapy alone (mid-term follow-up)*

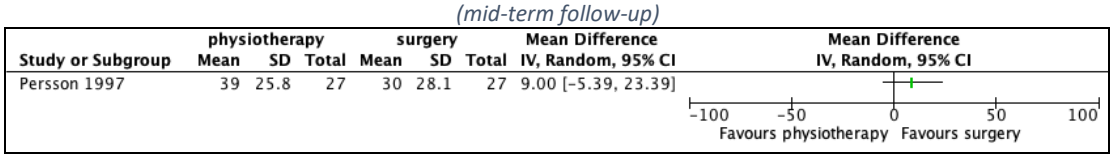

Figure 4*. Mean difference for pain, surgery versus physiotherapy (midterm follow-up)*

1.1.3 Long term (>12 months to 8 years)

Two studies reported on arm-pain after 6 months to 12 months (Enquist, 2013; Enquist, 2017). Results are depicted in Figure 5.

- *Arm pain (surgery with physiotherapy versus physiotherapy alone)*

  At 24 months after intervention (Enquist, 2013), mean reduction of arm-pain was 18.1 (SD 48.0) in the group receiving surgery with physiotherapy and 20.5 (SD 48.3) in the group receiving physiotherapy only. This resulted in a mean difference of -2.40 (95%CI -26.17 to 21.37).

  At 5-8 years after intervention (Enquist, 2017), mean reduction of arm pain was 33.0 (SD 40.9) in the group receiving surgery with physiotherapy and 19.0 (SD 33.3) in the group receiving physiotherapy only. This resulted in a mean difference of 14.00 (95%CI -4.44 to 32.44). Results are depicted in Figure 5.

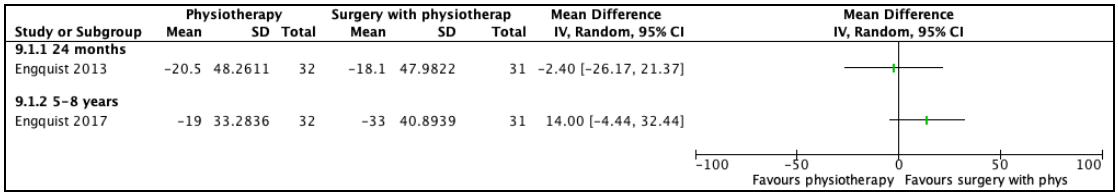

Figure 5*. Mean difference for arm-pain, surgery with physiotherapy versus physiotherapy alone (long term follow-up)*

1.2 Quality of life (critical)

One study reported on quality of life (Enquist, 2017). Quality of life was measured using both the EQ-5D (0-1) and the EQ-VAS (0-100), with higher scores indicating better quality of life.

Five to eight years after intervention, mean score increased on the EQ-5D was 0.29 (SD 0.43) in the group receiving surgery with physiotherapy and 0.14 (SD 0.34) in the group receiving physiotherapy alone. This resulted in a mean difference of -0.15 (95%CI -0.05 to 0.35). Results are depicted in Figure 6.

Five to eight years after intervention, mean score on the EQ-VAS was 29 (SD 26.8) in the group receiving surgery with physiotherapy and 30 (SD 28.9) in the group receiving physiotherapy alone. This resulted in a mean difference of 4.00 (95%CI -10.23 to 18.23). Results are depicted in Figure 7.

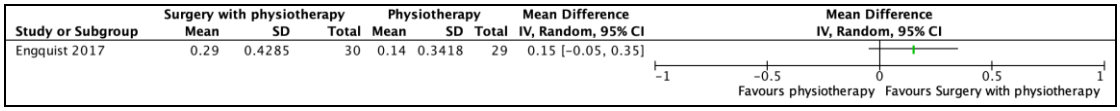

Figure 6. *Mean difference for quality of life (EQ-5D), surgery with physiotherapy versus physiotherapy alone*

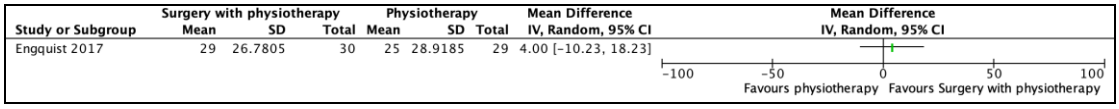

Figure 7. *Mean difference for quality of life (EQ-VAS), surgery with physiotherapy versus physiotherapy alone*

1.3 Functioning (critical)

Two studies reported on functioning (Enquist, 2013; Enquist, 2017). Functioning was measured using the Neck Disability Index (0-50), with higher scores indicating worse disability. A percentage of the reduction on the NDI was provided (0-100).

- *1.3.1 Short term (post treatment: up to 6 months)*
  One study reported on functioning up to six months (Enquist, 2013). Six months after initiation of the intervention, mean reduction was 12.1% (SD 16.9) in the group receiving surgery with physiotherapy and 7.7% (SD 16.9) in the group receiving only physiotherapy. This resulted in a mean difference of 4.40 (95%CI -3.95 to 12.75). Results are depicted in Figure 8.
- *1.3.2 Midterm (post-treatment >6 months up to 12 months)*
  One study reported on functioning after 6 months to 12 months (Enquist, 2013).
  Twelve months after initiation of the intervention, mean reduction was 13.9% (SD 20.2) in the group receiving surgery with physiotherapy and 7.1% (SD 20.2) in the group receiving only physiotherapy. This resulted in a mean difference of 6.80 (95%CI -3.18 to 16.78). Results are depicted in Figure 9.
- *1.3.3 Long term (>12 months to 8 years)*
  In the study by Enquist (2013), 24 months after intervention, mean score was 14.2 (SD 23.4) in the group receiving surgery with physiotherapy and 11.5 (SD 23.6) in the group with physiotherapy alone. This resulted in a mean difference of 2.7 (95%CI -8.91 to 14.31).
  In the study by Enquist (2017), 5-8 years after intervention, mean reduction was 21.0% (SD 19.1) in the group receiving surgery with physiotherapy and 11.0% (SD 19.4) in the group with physiotherapy alone. This resulted in a mean difference of 10.00 (95%CI 0.49 to 19.5). This difference was clinically relevant. Results are depicted in Figure 10.

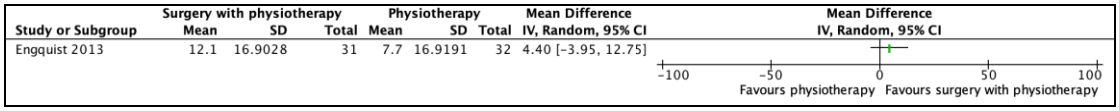

Figure 8. *Mean difference for functioning (NDI), surgery with physiotherapy versus physiotherapy alone (short term follow-up)*

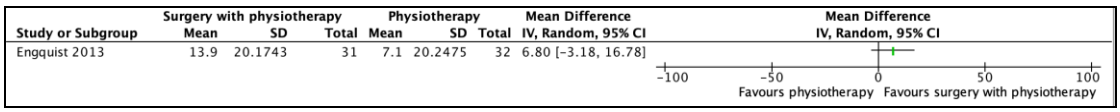

Figure 9*. Mean difference for functioning (NDI), surgery with physiotherapy versus physiotherapy alone (midterm follow-up)*

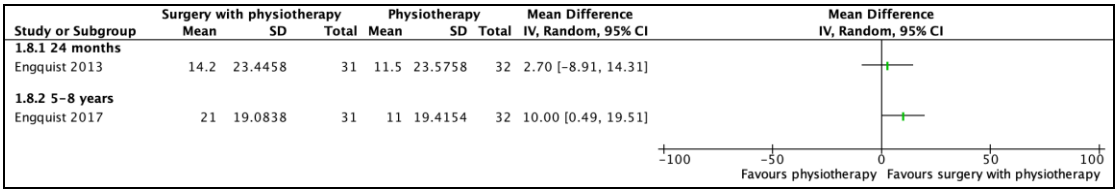

Figure 10. *Mean difference for functioning (NDI), surgery with physiotherapy versus physiotherapy alone (long term follow-up)*

1.4 Patient satisfaction (important)

In the study by Enquist (2013) and Enquist (2017), patient satisfaction was measured using the Patient's Global Assessment. Patients were asked whether after treatment, their neck/arm problems were much better, better, unchanged, worse or much worse. This score was dichotomised into better (defined by "better" or "much better") and worse. Results are depicted in Table 3 and Figure 11.

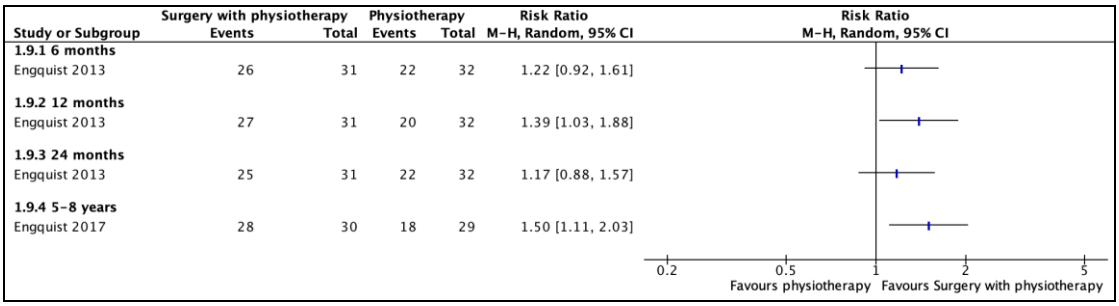

Figure 11. *Risk ratios for a better score on the Patient's Global Assessment, surgery with physiotherapy versus physiotherapy alone*

1.5 Complications (important)

One study reported on complications (Engquist, 2013). No surgery related complications (e.g. onset of neurological deficit, thromboembolism, unexpected bleeding, infection) were reported. These results could not be evaluated using the GRADE-methodology.

1.6 Re-operations (important)

Enquist 2013 reported no re-operations. After 5-8 years (Enquist, 2017), no participants from the surgery group needed another operation. In the non-surgery group, 8 participants underwent surgery.

1.7 Return to work, tingling, re-operation and adjacent segment level disease (important)

None of the RCTs assessed the effect of surgery on these outcomes in patients with cervical radiculopathy.

1. Level of evidence of the literature

1.1 Arm-pain (critical)

- *Short term (post treatment: up to 6 months)*
  The level of evidence regarding the outcome measure pain (short term) started as high because it was based on RCTs and was downgraded by three levels to very low because lack of blinding in all studies (-1, risk of bias), and crossing of both thresholds of clinical decision-making (Enquist, 2013) (-2, imprecision).
- *Midterm (post-treatment >6 months to 12 months)*
  The level of evidence regarding the outcome measure pain (midterm) started as high because it was based on RCTs and was downgraded by three levels to very low because lack of blinding in all studies (-1, risk of bias), and crossing of both thresholds of clinical decision-making (Enquist, 2013) (-2, imprecision).
- *Long term (>12 months to 8 years)*
  The level of evidence regarding the outcome measure pain (long term) started as high because it was based on RCTs and was downgraded by three levels to very low because lack of blinding in all studies (-1, risk of bias), and crossing of both thresholds of clinical decision-making (Enquist, 2013) (-2, imprecision).

1.2 Quality of life (critical)

The level of evidence regarding the outcome measure quality of life started as high because it was based on RCTs and was downgraded by three levels to very low because lack of blinding in all studies (-1, risk of bias), and crossing of both thresholds of clinical decision-making (-2, imprecision).

1.3 Functioning (critical)

- *1.3.1 Short term (post treatment: up to 6 months)*
  The level of evidence regarding the outcome measure functioning (short term) started as high because it was based on RCTs and was downgraded by two levels to low because lack of blinding (Enquist, 2013) (-1, risk of bias), and crossing of one threshold of clinical decision-making (-1, imprecision).
- *1.3.2 Midterm (post-treatment >6 months to 12 months)*
  The level of evidence regarding the outcome measure functioning (midterm) started as high because it was based on RCTs and was downgraded by two levels to low because lack of blinding (Enquist, 2013) (-1, risk of bias), and crossing of one threshold of clinical decision-making (-1, imprecision).
- *1.3.3 Long term (>12 months to 8 years)*
  The level of evidence regarding the outcome measure functioning (long term) started as high because it was based on RCTs and was downgraded by two levels to low because lack of blinding in all studies (-1, risk of bias), and crossing of one threshold of clinical decision-making (Enquist, 2013) (-1, imprecision).

1.4 Patient satisfaction (important)

- *1.4.1 Short term (post treatment: up to 6 months)*
  The level of evidence regarding the outcome measure patient satisfaction (short term) started as high because it was based on RCTs and was downgraded by two levels to low because lack of blinding in all studies (-1, risk of bias), and crossing of one threshold of clinical decision-making (Enquist, 2013) (-1, imprecision).
- *1.4.2 Midterm (post-treatment >6 months to 12 months)*
  The level of evidence regarding the outcome measure patient satisfaction (midterm) started as high because it was based on RCTs and was downgraded by two levels to low

because lack of blinding in all studies (-1, risk of bias), and crossing of one threshold of clinical decision-making (Enquist, 2013) (-1, imprecision).

- *1.4.3 Long term (>12 months to 8 years)*
  The level of evidence regarding the outcome measure patient satisfaction (long term) started as high because it was based on RCTs and was downgraded by three levels to very low because lack of blinding in all studies (-1, risk of bias), and crossing of both thresholds of clinical decision-making (Enquist, 2013) (-2, imprecision).

1.5 Complications (important)
The level of evidence of the outcome measure complications could not be GRADED due to a lack of data.

1.6 Re-operations (important)
The level of evidence regarding the outcome measure complications started as high because it was based on RCTs and was downgraded by three levels to very low because lack of blinding in all studies (-1, risk of bias), and very few events (Enquist, 2013) (-2, imprecision).

1.7 Return to work, tingling, re-operation and adjacent segment level disease (important)
The level of evidence regarding these outcomes was not graded because of lack of data.

1. Conclusions

1.1. Pain (short-, mid- and long term) (critical)

Very low GRADE	The evidence is very uncertain about the effect of surgery with or without physiotherapy on pain (any term) compared with physiotherapy alone in patients with cervical radiculopathy. *Sources: Enquist 2013; Enquist, 2017; Persson, 1997*

1.2 Quality of life (critical)

Very low GRADE	The evidence is very uncertain about the effect of surgery with physiotherapy on quality of life compared with physiotherapy alone in patients with cervical radiculopathy. *Sources: Enquist 2017*

1.3 Functioning (short-, mid- and long term) (critical)

Low GRADE	Surgery with physiotherapy may increase functioning (any term) when compared with physiotherapy alone in patients with cervical radiculopathy. *Sources: Enquist, 2013; Enquist, 2017*

1.4 Patient satisfaction (short-, mid- and long term) (important)

Low GRADE	Surgery with physiotherapy may increase functioning (any term) when compared with physiotherapy alone in patients with cervical radiculopathy. *Sources: Enquist, 2013; Enquist, 2017*

1.5 Complications (important)

Low GRADE	The evidence is very uncertain about the effect of surgery with physiotherapy on complications compared with physiotherapy alone in patients with cervical radiculopathy. *Sources: Enquist, 2013; Enquist, 2017*

1.6 Re-operation; 1.7 Return to work, tingling, and adjacent segment disease

- GRADE	No evidence was found regarding the effect of surgery on return to work, tingling, re-operation or adjacent segment disease, compared with conservative management in patients with cervical radiculopathy. *Sources: -*

5

2. Surgery vs. cervical collar

2.1 Arm-pain (critical)

One study reported on current pain (Persson, 1997) using a VAS-scale ranging from 0-100mm. Type of pain (neck- and/or arm-pain) was not otherwise specified by the authors.

- *2.1.1 Short term (post treatment: up to 6 months)*
  Four months after intervention, mean score was 27.0 (SD 23.0) in the group receiving surgery and 48.0 (SD 23.2) in the group wearing a cervical collar. This resulted in a mean difference of -21.00 (95%CI -33.34 to -8.68). This difference was clinically relevant. Results are depicted in Figure 12.
- *2.1.2. Long term (>12 months to 8 years)*
  Sixteen months after intervention, mean score was 30.0 (SD 28.1) in the group receiving surgery and 35.0 (SD 23.6) in the group wearing a cervical collar. This resulted in a mean difference of -5.00 (95%CI -18.8 to 8.84). This difference was not clinically relevant. Results are depicted in Figure 13.

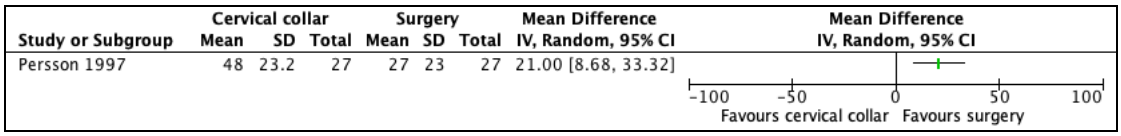

Figure 12. *Mean difference for pain, surgery versus cervical color (short term follow-up)*

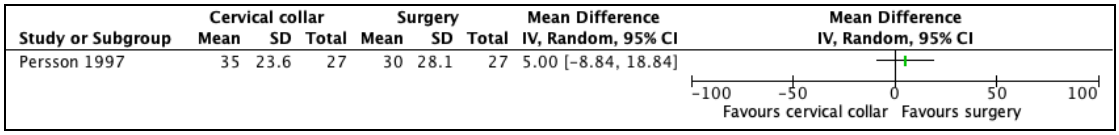

Figure 13*. Mean difference for pain, surgery versus cervical collar (midterm follow-up)*

Quality of life, functioning, patient satisfaction, complications, return to work, tingling, re-operation, and adjacent segment disease

The level of evidence regarding these outcomes was not graded because of lack of data.

2. Level of evidence of the literature

2.1 Pain (critical)

- *Short term (post treatment: up to 6 months)*
  The level of evidence regarding the outcome measure pain (short term) started as high because it was based on RCTs and was downgraded by two levels to low because lack of blinding in all studies (-1, risk of bias), and crossing of both thresholds of clinical decision-making (Persson, 1997) (-1, imprecision).
- *Midterm (post-treatment >6 months to 12 months)*
  The level of evidence regarding the outcome measure pain (midterm) started as high because it was based on RCTs and was downgraded by two levels to low because lack of blinding in all studies (-1, risk of bias), and crossing of both thresholds of clinical decision-making (Persson, 1997) (-1, imprecision).

2. Conclusions

2.1 Pain (short-, mid- and long term) (critical)

Low GRADE	Surgery may decrease pain on the short term, but may result in little to no difference in pain after one year, when compared with a cervical collar in patients with cervical radiculopathy. *Sources: Persson, 1997*

Quality of life, functioning, patient satisfaction, complications, return to work, tingling, re-operation, and adjacent segment disease

- GRADE	No evidence was found regarding the effect of surgery on return to work, tingling, re-operation or adjacent segment disease, compared with a cervical collar in patients with cervical radiculopathy. *Sources: -*

Overwegingen – van bewijs naar aanbeveling

<u>Voor- en nadelen van de interventie en de kwaliteit van het bewijs</u>

Het doel van deze uitgangsvraag was om te achterhalen wat de waarde van chirurgische decompressie van de zenuwwortel was, in vergelijking met een conservatieve behandeling bij patiënten met CRS. In totaal zijn er drie publicaties van twee uitgevoerde RCTs gevonden die deze interventie vergeleken met conservatieve behandeling. De bewijskracht voor de kritieke uitkomstmaten (pijn, kwaliteit van leven en functioneren) was laag tot zeer laag. Dit betekent dat andere studies kunnen leiden tot nieuwe inzichten. De betrouwbaarheidsintervallen rondom de gevonden effecten waren breed (leidend tot onnauwkeurigheid) en geen van de studies maakte gebruik van blindering van de patiënten, artsen of onderzoekers (methodologische beperking). Daarom kunnen er op basis van de literatuur geen harde conclusies geformuleerd worden. De opzet van een gerandomiseerde studie zal ook in de toekomst lastig kunnen blijken. Patiënten met ernstige pijnklachten zullen niet willen randomiseren en a priori opteren voor chirurgie, wat de haalbaarheid beperkt.

Mogelijke voordelen chirurgie

De gevonden studies zijn dus niet optimaal opgezet en hier ligt een duidelijk kennishiaat. Daarbij dient ook opgemerkt te worden dat geïncludeerde patiënten vaak niet representatief zijn voor de klinische praktijk die zowel fysiek (bijvoorbeeld patiënten met obesitas) als mentaal (bijvoorbeeld patiënten met depressie) zwaarder belast is. Ook is het de vraag of de uitkomstmaten gebruikt in de studies het effect van operatie goed weergeven (Jack, 2022).

Om het effect van operatie te beoordelen wordt daarom ook de klinische ervaring van de werkgroep en prospectieve cohortstudies (Sampath, 1999; Butterman, 2018; Hermansen, 2011) meegenomen. In lijn met de gerandomiseerde studies is het te verwachten effect van een operatie dat op de korte termijn (eerste maanden) zowel de arm- als nekklachten afnemen. Of er effecten zijn -gunstig of ongunstig- op de lange termijn is onzeker. De patiënttevredenheid na operatie is hoog (66-95%) (Wichmann 2021, Butterman 2018) en is duidelijk hoger als de klachten relatief kort (<3 maanden) bestaan. Het lijkt daarbij niet uit te maken of er sprake is van een hernia van de discus of een degeneratieve foraminale stenose (Butterman, 2018).

De discrepantie tussen de uitstekende resultaten van cohortstudies en de onzekere resultaten uit de gerandomiseerde studies wordt waarschijnlijk mede verklaard door het gunstige spontane beloop, analoog aan het lumbosacrale radiculaire syndroom. De rationale

rondom de keuze wel of niet opereren komt dan neer op optimale timing, wat beschouwd dient te worden als expert opinion (zie submodule 'Timing').

Mogelijke nadelen chirurgie

Een direct nadeel van een operatie blijkt niet uit de gevonden studies ten opzichte van een conservatief beleid. Operatie gaat gepaard met een risico van ongeveer 19% op complicaties (Fountas, 2007). De meest voorkomende complicaties zijn: slikklachten (10-31%), heesheid door letsel ipsilaterale nervus recurrens (3-29%), wondinfectie (<1-5%), hematoom (<1-2%) en duralek tijdens operatie (0.5-4%) (Fountas, 2007; Wichmann, 2021). Het risico op complicaties is hetzelfde ongeacht de techniek of benadering (anterior/posterior) (Fang, 2020).

Een te verwachten complicatie is een parese van de armspieren gerelateerd aan de aangedane zenuwwortel. Toch wordt dit maar in 1 studie bij 1% gemeld als naar alle complicaties wordt gekeken (Wichmann, 2021). Vermeldenswaardig is nog een tijdelijke uitval van C5 spieren, welke enkele dagen na de operatie vaker wordt gezien na chirurgie, waarbij een incidentie van 1.5-6% na een anterieure benadering wordt genoemd (Takase, 2020). De etiologie hiervan is onduidelijk, mogelijk speelt mee dat de C5 wortel het kortst is en daardoor gevoelig voor schade door rek. Redelijk herstel treedt op bij de meerderheid. (Houten, 2020)

Op de langere termijn is pseudoartrose een risico met een incidentie van 2.6% als alle soorten ingrepen worden meegenomen. Dit risico heeft een incidentie van 3.7% bij 1-niveau ACD (Schryver, 2015). Definities verschillen echter, waardoor het klinisch belang onduidelijk blijft. Hetzelfde geldt voor *adjacent level disease*, dat bij 2-4% per jaar wordt gezien, maar veel minder vaak leidt tot een nieuwe operatie. Aangezien de incidentie hoger is na een 2-niveau fusie in vergelijking met een 1-niveau fusie, is het aan te bevelen de operatie te beperken tot het symptomatische niveau (Epstein, 2022)

Roken geeft niet alleen een hogere kans op complicaties, maar ook op post-operatieve nekpijn (Zheng, 2022). Als de ingreep electief is, is het aan te bevelen de patiënt eerst te laten stoppen met roken alvorens te opereren. De termijn tussen datum stop roken en datum van opereren is onderwerp van discussie; een minimum van 2 weken lijkt al effect te hebben op peri-operatieve complicaties.

Een verhoogde BMI>30 kg/m^2 geeft een verhoogde kans op complicaties, vooral wondinfectie en veneuze trombose. (Jackson, 2016; Sebastian, 2016) Als de ingreep electief is, is het te overwegen patiënt eerst te laten afvallen. Er zijn aanwijzingen dat het risico op complicaties dan weer daalt (Passias, 2018).

<u>Waarden en voorkeuren van patiënten (en evt. hun verzorgers)</u>

De beslissing tot het al dan niet ondergaan van een operatie dient in samenspraak met de patiënt te worden genomen (shared decision making), waarbij de patiënt een goed inzicht dient te hebben in het beloop van de symptomen en de risico's van de ingreep. Behalve de wens van de patiënt dient ook de premorbide toestand en co-morbiditeiten van patiënt te worden meegenomen in het advies van de arts. Ook de ernst van de pijn en het belang van een snelle terugkeer op de arbeidsmarkt, spelen in dit besluitvormingsproces een rol. Bij geringe pijnklachten heeft het voortzetten van de conservatieve behandeling de voorkeur.

<u>Kosten (middelenbeslag)</u>

In Nederland worden jaarlijks gemiddeld 2000 patiënten met CRS geopereerd, wat resulteert in directe kosten van ongeveer €30 miljoen per jaar (van Geest, 2014). Hoewel de directe kosten voor conservatieve zorg lager zijn, kan deze groep mogelijk hogere indirecte kosten hebben als gevolg van een langere periode van verminderde arbeidsproductiviteit (van Geest, 2014). De MOVE-it trial start in 2024 om een economische evaluatie in Nederland te

geven van chirurgie vergeleken met multimodale fysiotherapie. Er is elders gesuggereerd dat een ACDF-operatie kosteneffectief is zolang een cervicaal epiduraal blok niet bij 50% of meer een operatie voorkomt (Rhin, 2019).

Aanvaardbaarheid, haalbaarheid en implementatie

Gezien er geen studies zijn gedaan naar de aanvaardbaarheid en haalbaarheid van chirurgie vergeleken met conservatieve behandelingen voor patiënten met een CRS, is vervolgonderzoek hiernaar aangewezen.

De werkgroep is van mening dat er onenigheid in de klinische praktijk zou kunnen bestaan over de timing om tot een chirurgische behandeling over te gaan in geval van falen van de conservatieve behandeling. Hiervoor wordt verwezen naar submodule 'Timing'. Overigens zal er door het verwijspatroon in de Nederlandse setting zelden een onnodig vroege verwijzing naar een neurochirurg of orthopeed worden gedaan, waardoor het natuurlijk beloop niet kan worden geobserveerd.

Voorts is de werkgroep van mening dat er geen belemmerende factoren zijn op het gebied van implementatie van de chirurgische interventie. De chirurgische behandeling van patiënten met CRS is verzekerde zorg. Voorts is de chirurgische behandeling voldoende ingebed in de moderne neurochirurgische en orthopedische praktijk.

Bij patiënten met risicofactoren adviseert de werkgroep om voorzorgsmaatregelen te nemen voor zover mogelijk. Adviseer rokers om dit minimaal twee weken voor de operatie te staken en adviseer patiënten met overgewicht om gewichtsreductie na te streven. Overigens is het resultaat van de operatie niet direct afhankelijk van het gewicht, maar wel het optreden van mogelijke complicaties. Patiënten met onderliggende psychopathologie, zoals een depressie, kennen een minder effect van chirurgische behandeling en dienen hierover te worden geconsulteerd.

Aanbevelingen

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventies

Op basis van de beschikbare literatuur kan de werkgroep geen sterke aanbevelingen formuleren ten aanzien van de effectiviteit van de chirurgische behandeling van een CRS vergeleken met conservatieve behandelmodaliteiten. Een chirurgische behandeling in het algemeen lijkt te resulteren in een sneller herstel van de pijnklachten in vergelijking met conservatieve behandeling. Dit effect wordt echter op de langere termijn niet bevestigd. Het is de mening van de werkgroep een chirurgische behandeling te overwegen bij patiënten met een CRS waarbij een conservatieve behandeling niet leidt tot herstel van de klachten. Ten aanzien van de timing wordt verwezen naar submodule 'Timing'.

Start eerst met actieve conservatieve behandeling (denk bijvoorbeeld aan medicatie, fysiotherapie). Zet chirurgische behandeling niet als eerste keus in.

Behandel het cervicaal radiculair syndroom chirurgisch met congruente MRI-afwijking en wanneer conservatieve behandeling onvoldoende effect heeft, de patiënt dit weloverwogen wenst in samenspraak met de behandelend arts, afwegende de premorbide status en de mogelijke complicaties.

Overweeg in een aantal situaties om vroegtijdig chirurgisch in te grijpen:

- Bij onhoudbare en niet te beïnvloeden pijn, en/of
- Bij progressieve motorische uitval.

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Bijlagen bij module Chirurgisch versus conservatief

Implementatieplan

Aanbeveling	Tijdspad voor implementatie: < 1 jaar, 1 tot 3 jaar of > 3 jaar	Verwacht effect op kosten	Randvoorwaarden voor implementatie (binnen aangegeven tijdspad)	Mogelijke barrières voor implementatie[1]	Te ondernemen acties voor implementatie[2]	Verantwoordelijken voor acties[3]	Overige opmerkingen
Alle aanbevelingen	< 1 jaar	Beperkt	Bekendheid met de richtlijn	Geen	• Voldoende kennis bij / scholing voor zorgverleners. • Vervolg onderzoek • Verspreiden van richtlijn.	• Zorgprofessionals van instellingen. • Beroepsverenigingen.	Niet van toepassing.

[1] Barrières kunnen zich bevinden op het niveau van de professional, op het niveau van de organisatie (het ziekenhuis) of op het niveau van het systeem (buiten het ziekenhuis). Denk bijvoorbeeld aan onenigheid in het land met betrekking tot de aanbeveling, onvoldoende motivatie of kennis bij de specialist, onvoldoende faciliteiten of personeel, nodige concentratie van zorg, kosten, slechte samenwerking tussen disciplines, nodige taakherschikking, etc.

[2] Denk aan acties die noodzakelijk zijn voor implementatie, maar ook acties die mogelijk zijn om de implementatie te bevorderen. Denk bijvoorbeeld aan controleren aanbeveling tijdens kwaliteitsvisitatie, publicatie van de richtlijn, ontwikkelen van implementatietools, informeren van ziekenhuisbestuurders, regelen van goede vergoeding voor een bepaald type behandeling, maken van samenwerkingsafspraken.

[3] Wie de verantwoordelijkheden draagt voor implementatie van de aanbevelingen, zal tevens afhankelijk zijn van het niveau waarop zich barrières bevinden. Barrières op het niveau van de professional zullen vaak opgelost moeten worden door de beroepsvereniging. Barrières op het niveau van de organisatie zullen vaak onder verantwoordelijkheid van de ziekenhuisbestuurders vallen. Bij het oplossen van barrières op het niveau van het systeem zijn ook andere partijen, zoals de NZA en zorgverzekeraars, van bel

Risk of bias table for intervention studies

Study reference	Was the allocation sequence adequately generated?	Was the allocation adequately concealed?	Blinding: Was knowledge of the allocated interventions adequately prevented? Were patients blinded? Were healthcare providers blinded? Were data collectors blinded? Were outcome assessors blinded? Were data analysts blinded?	Was loss to follow-up (missing outcome data) infrequent?	Are reports of the study free of selective outcome reporting?	Was the study apparently free of other problems that could put it at a risk of bias?	Overall risk of bias If applicable/necessary, per outcome measure LOW Some concerns HIGH
Enquist, 2013	Reason: Central randomization	Reason: Sealed envelopes were used	Reason: Study did not state blinding of patients, outcome assessors, healthcare providers, data analysts or collectors.	Reason: Drop-outs after randomization (4 in surgery and 1 in physiotherapy).	Reason: No trial protocol available. EQ-5D was not stated in methods, however measured in publication of Enquist (2017).	Reason: no other problems noted	**HIGH (all measures)**
Enquist, 2017	Reason: Central randomization	Reason: Sealed envelopes were used	Reason: Study did not state blinding of patients, outcome assessors, healthcare providers, data analysts or collectors.	Reason: Drop-outs after randomization (4 in surgery and 1 in physiotherapy).	Reason: No trial protocol available. EQ-5D was not stated in methods of Enquist (2013), however measured in publication of Enquist (2017).	Reason: no other problems noted	**HIGH (all measures)**
Persson, 1997	Reason: Randomization, not further stated	Reason: Sealed envelopes were used	Reason: Study did not state blinding of patients, outcome assessors, healthcare providers, data analysts or collectors.	Reason: Drop-out was infrequent, at follow-up, one participant from the cervical collar group and one from the surgery group dropped out.	Reason: No trial protocol available, aforementioned measurements were reported.	Reason: no other problems noted	**HIGH (all measures)**

Table of excluded studies

Taso 2020	protocol (wrong publication type)
Bhagawati 2015	no comparison between conservative and surgical (wrong study design)
Bono 2011	guideline, 2011 mostly consensus based (wrong publication type)
Carragee 2008	systematic search but less recent than used reviews
Ellenberg 1994	non-systematic review (wrong study design)
Joaquim 2016	narrative review of case series and observational research (wrong study design)
van Geest 2014	study protocol (wrong publication type)
Fouyas 2002	2001 version of Nicolaidis cochrane (outdated)
Fouyas 2007	2006 version of Nicolaidis cochrane (outdated)
Wang 2005	Atrikel niet leverbaar, search tot 2004 dus niet recenter dan andere reviews
Gebremariam 2012	Only 1 matching RCT included (outdated)
Matz 2009	no comparison between conservative and surgical (wrong study design)
Bhagawati 2015	Refers to Matz2009 and Nikolaidis2010 for radiculopathy (outdated)
Eichen 2014	no comparison between conservative and surgical (wrong study design)
Enquist 2015	Prospective factors for effect in Enquist (2013) (wrong outcome)
Fehlings 2009	Overview article (wrong study design)
McCornick 2017	Two types of epidural steroid injections are compared (wrong intervention)
Carragee 2008	Overview article (wrong study design)
Zang 2015	Delphi article for Chinese clinical consensus (wrong publication type)
Persson 1997b	SIP and MACL compared with nonrandomized reference group (wrong outcome)
Persson 1998	Shoulder mobility, neck mobility, muscle tenderness and correlation (wrong outcome)
Persson 2001	Disability rating index only before treatment, coping correlations with pain and HADS and MACL for total group (wrong outcome)
Luyao 2022	most recent systematic review, data-extraction, analysis and reporting unsufficient
Manchikanti 2014	interlaminar versus transforaminal epidural injections (wrong intervention)
Lenzi 2017	No measures of dispersion reported, no blinding (very low study quality)
Peolsson 2013	No comparative measures were reported (wrong outcome)
de Rooij 2020	percutaneous nucleoplasty versus anterior discectomy, no conservative treatment (wrong control)
Nicolaidis 2010	Systematic review not containing Halim (2017) and Enquist (2013, 2017)
Broekema 2020	Systematic review not containing Halim (2017) and Enquist (2017)
Halim 2017	percutaneous nucleoplast as controlgroup (wrong control)

Literature search strategy

Zoekverantwoording

Algemene informatie

Richtlijn: Cervicaal Radiculair Syndroom	
Uitgangsvraag: Wat is de plaats van chirurgische decompressie van de zenuwwortel bij patiënten met CRS?	
Database(s): Ovid/Medline, Embase.com	Datum: 25-02-2022
Periode: geen restrictie	Talen: Engels, Nederlands
Literatuurspecialist: Miriam van der Maten	
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting: → Voor deze vraag is gezocht op de elementen: • CRS • Chirurgische ingrepen bij CRS inclusief genoemde technieken/ingrepen → De sleutelartikelen worden gevonden met de zoekopdracht	
Te gebruiken voor richtlijnen tekst: In de databases Embase.com en Ovid/Medline is op 25 april 2022 met relevante zoektermen gezocht naar systematische reviews en RCTs over de plaats van chirurgische decompressie van de zenuwwortel bij patiënten met CRS. De literatuurzoekactie leverde 582 unieke treffers op.	

5

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SRs	206	226	269
RCT	242	256	313
Totaal	448	482	**582**

Zoekstrategie

Embase.com

No.	**Query**	**Results**
#14	#11 OR #12	448
#12	#7 AND #9 NOT #11 **= RCT**	242
#11	#7 AND #8 **= SR**	206
#9	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	1839814
#8	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	733409
#7	#4 AND #5 AND ([english]/lim OR [dutch]/lim) NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	3318
#5	'surgery'/exp/mj OR 'surgery'/lnk OR surgical:ti,kw OR surger*:ti,kw OR operation*:ti,kw OR operative:ti,kw OR 'decompression surgery'/exp OR decompress*:ti,ab,kw OR ((anterior NEAR/2 cervical NEAR/2 (foraminotomy OR microforaminotomy)):ti,ab,kw) OR 'anterior cervical discectomy'/exp OR 'anterior cervical discectomy and fusion'/exp OR cad:ti,ab,kw OR cadf:ti,ab,kw OR cadp:ti,ab,kw OR acdf:ti,ab,kw OR ((anterior NEAR/2 cervical NEAR/2 (dis*ectom* OR 'disc fusion')):ti,ab,kw) OR 'foraminotomy'/exp	4662407

#4	'cervicobrachial neuralgia'/exp/mj OR cervicobrachialgia:ti,ab,kw OR ((radiculalgia:ti,ab,kw OR radiculitis:ti,ab,kw OR radiculitides:ti,ab,kw OR radiculopath*:ti,ab,kw OR polyradiculopath*:ti,ab,kw OR neuralgia:ti,ab,kw OR 'herniated disc*':ti,ab,kw OR hernia:ti,ab,kw OR ((radicular NEAR/3 (pain* OR neuralgia* OR symptom*)):ti,ab,kw) OR (('nerve root' NEAR/3 (pain* OR inflammation* OR disorder* OR compression* OR avulsion* OR impingement)):ti,ab,kw)) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('radicular pain'/exp/mj OR 'radiculopathy'/exp/mj) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw))	10643

Ovid/Medline

#	Searches	Results
12	9 or 10	482
10	(5 and 7) not 9 **= RCT**	256
9	5 and 6 **= SR**	226
7	(exp randomized controlled trial/ or randomized controlled trials as topic/ or random*.ti,ab. or rct?.ti,ab. or ((pragmatic or practical) adj "clinical trial*").ti,ab,kf. or ((non-inferiority or noninferiority or superiority or equivalence) adj3 trial*).ti,ab,kf.) not (animals/ not humans/)	1369026
6	(meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.) not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	560304
5	limit 4 to (english language or dutch)	3648
4	1 and 2	4107
2	exp Surgical Procedures, Operative/ or exp Specialties, Surgical/ or su.fs. or (surgical or surger* or operation* or operative).ti,ab,kf. or exp Decompression, Surgical/ or decompress*.ti,ab,kf. or (anterior adj2 cervical adj2 (foraminotomy or Microforaminotomy)).ti,ab,kf. or exp Diskectomy/ or CAD.ti,ab,kf. or CADF.ti,ab,kf. or CADP.ti,ab,kf. or ACDF.ti,ab,kf. or (anterior adj2 cervical adj2 (dis*ectom* or 'disc fusion')).ti,ab,kf.	5210832
1	((exp Radiculopathy/ or radiculalgia.ti,ab,kf. or radiculitis.ti,ab,kf. or radiculitides.ti,ab,kf. or radiculopath*.ti,ab,kf. or polyradiculopath*.ti,ab,kf. or neuralgia.ti,ab,kf. or 'herniated disc*'.ti,ab,kf. or hernia.ti,ab,kf. or (radicular adj3 (pain* or neuralgia* or symptom*)).ti,ab,kf. or ('nerve root' adj3 (pain* or inflammation* or disorder* or compression* or avulsion* or impingement)).ti,ab,kf.) and (exp Cervical Vertebrae/ or exp Neck/ or cervical.ti,ab,kf. or cervico*.ti,ab,kf. or neck.ti,ab,kf.)) or cervicobrachialgia.ti,ab,kf.	6515

Submodule 3.1.1 Timing chirurgische behandeling

Uitgangsvraag

Wat is het optimale moment na aanvang van klachten voor chirurgische interventie?

Inleiding

Omdat het grootste deel (ca. 90%) van de cervicale radiculaire syndromen een gunstig natuurlijk beloop kent (Lyer, 2016; Alentado, 2014) moet voldoende tijd worden genomen om het natuurlijk beloop een kans te geven alvorens chirurgische behandeling wordt overwogen. Het is echter onduidelijk hoe lang de periode moet zijn waarin het spontaan herstel wordt afgewacht. Ook moet wellicht niet te lang worden afgewacht, omdat er aanwijzingen zijn dat de kans op herstel na chirurgische behandeling afneemt, wanneer de klachten langer dan zes maanden bestaan.

Gezien de praktijkvariatie en het gebrek aan bewijs, evalueert de werkgroep in deze module de optimale timing om een chirurgische interventie te initiëren.

Samenvatting literatuur

Er is geen search uitgevoerd, omdat het niet de verwachting was dat er onderzoek beschikbaar is die deze uitgangsvraag beantwoord. De uitgangsvraag is daarom beantwoord met behulp van 1) expert opinion en expertise van de werkgroep, 2) leerartikelen, 3) consensus artikelen, en 4) bestaande afspraken met betrekking tot de timing van chirurgische interventies.

Overwegingen – van bewijs naar aanbeveling

Het doel van deze uitgangsvraag was te achterhalen op welk moment na aanvang van klachten, chirurgische interventie ingezet kan worden. Om deze vraag te beantwoorden is er geen systematische search uitgevoerd zoals eerder al benoemd omdat gedegen onderzoek binnen dit onderwerp voor CRS op dit gebied ontbreekt.

Er is een narratieve review naar timing van chirurgische therapie bij CRS bij de werkgroep bekend (Alentado, 2014), evenals een Delphi-studie naar de timing van conservatieve interventies bij patiënten met CRS (Thoomes, 2022).

<u>Voor- en nadelen van de interventie en de kwaliteit van het bewijs</u>

Een mogelijk voordeel van een vroege operatie (<2 maanden) is een snellere reductie van de cervicoradiculaire pijnklachten (Nikolaidis, 2011; Persson, 1997; Alentado, 2014). Er zijn geen goede studies op basis waarvan een optimale duur van een conservatieve behandeling kan worden gesteld, alvorens tot een chirurgische behandeling over te gaan. Alentado (2014) stelt dat het optimale time-window binnen 2maanden na start van de symptomen is. Uit een Delphi-studie (Thoomes, 2022) komt echter naar voren dat conservatieve behandelopties kunnen worden voorgesteld voor patiënten op verschillende tijdspunten vanaf het begin van de klachten. Ook in het chronisch stadium (>3 maanden) zijn er conservatieve behandelopties. Deze kunnen bijdragen aan het verdere spontane herstel.

Een mogelijk nadeel van een vroege operatie is dat patiënten de kans wordt ontnomen om een spontaan herstel te bereiken, waarvan bekend is dat dit in de meerderheid van de gevallen zo is (Lyer, 2016). Bovendien wordt met een chirurgische ingreep een risico genomen op mogelijke complicaties (Fountas, 2007). Gezien de pijnklachten op de lange termijn niet verschillen tussen een operatie of conservatief beleid, dienen deze risico's goed afgewogen te worden.

Mogelijke subgroepen bij wie een vroege operatie mogelijk gerechtvaardigd is, zouden patiënten met een progressieve motorische uitval of een (partiele) dwarslaesie kunnen zijn.

Waarden en voorkeuren van patiënten (en evt. hun verzorgers)

Patiënten lijken over het algemeen een voorkeur te hebben voor een spoedige chirurgische behandeling om cervicoradiculaire pijnklachten te behandelen. Het is inderdaad zo dat patiënten die worden geopereerd in een vroeg stadium, op de korte termijn een betere pijnreductie en verbetering van kracht en sensibiliteit te kennen (Nikolaidis, 2010). Dit effect is echter na 1 jaar en 3 jaar follow-up niet meer zichtbaar. Dit wordt bevestigd door Persson (1997). Ook het psychologisch aspect en het effect op kwaliteit van leven van langdurige pijn dient in overweging te worden genomen.

Kosten (middelenbeslag)

Er zijn geen kosteneffectiviteit studies bekend bij de werkgroep. Rihn (2019) heeft gesuggereerd, op basis van een UK cohort simulatie, dat een ACDF-operatie kosteneffectief is zolang een cervicaal epiduraal blok niet bij 50% of meer een operatie voorkomt (Rihn, 2019). Behoudens de kosten van de zorg in het algemeen, zou kunnen worden gesteld dat een vroege operatie ervoor zorgt dat indirecte kosten (zoals bijvoorbeeld terugkeer op de arbeidsmarkt) kunnen worden verminderd. Helaas garandeert een vroege operatie niet per definitie een snelle re-integratie in het arbeidsproces. Er is een zekere hersteltijd met eventuele fysiotherapeutische ondersteuning te verwachten. Deze kostenweging zal niet eenvoudig zijn om te bepalen, hier ligt een kennislacune.

Aanvaardbaarheid, haalbaarheid en implementatie

De vraag over de timing van een operatieve behandeling van een cervicoradiculair syndroom in de Nederlandse praktijk is enigszins arbitrair, gezien de gemiddelde patiënt na evaluatie door huisarts en neuroloog bij verwijzing naar een chirurgisch specialist reeds langere tijd klachten kent. De verwachting is dat de meeste patiënten een klachtenduur van meer dan 2 maanden kennen, waarbij meerdere conservatieve behandelopties zijn uitgeprobeerd en niet effectief zijn gebleken. Voorts blijkt uit een recente survey onder Nederlandse neurochirurgen dat de meerderheid (69%) een minimale klachtenduur van 2 maanden accepteert alvorens tot operatie over te gaan (de Rooij, 2017).
Een systematische review komt eveneens tot het oordeel dat er geen aanbeveling voor de timing van chirurgie is te geven (Matz, 2009). Overigens blijkt uit de prospectieve studie van Persson (1997) dat de resultaten van chirurgie en conservatieve behandeling elkaar na een jaar niet veel ontlopen (Persson, 1997).

Aanbevelingen

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventies

Op basis van de bestaande literatuur kan de werkgroep geen sterke aanbevelingen doen ten aanzien van de timing van een chirurgische interventie voor patiënten met een radiculair syndroom. Op basis van de aanbevelingen van de voorgaande richtlijn en de weinig beschikbare literatuur is het de mening van de werkgroep dat een chirurgische behandeling kan worden overwogen bij patiënten met tenminste twee maanden klachten van een CRS die niet verbeteren met conservatieve behandeling. Een uitzondering hierop vormen patiënten met progressieve motore uitval of zelfs een dwarslaesie.

Overweeg een operatieve behandeling bij patiënten met tenminste twee maanden CRS met onhoudbare pijn die niet verbetert met conservatieve behandeling. Indien sprake is van progressieve motore uitval of het ontstaan van een (partiële) dwarslaesie, overweeg om eerder te opereren.

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Bijlagen bij module 'Timing chirurgische interventie'

Implementatieplan

Aanbeveling	Tijdspad voor implementatie: < 1 jaar, 1 tot 3 jaar of > 3 jaar	Verwacht effect op kosten	Randvoorwaarden voor implementatie (binnen aangegeven tijdspad)	Mogelijke barrières voor implementatie[1]	Te ondernemen acties voor implementatie[2]	Verantwoordelijken voor acties[3]	Overige opmerkingen
Alle	< 1 jaar	Geen	Bekendheid met de (vorige) richtlijn	Geen	• Geen	• Zorgprofessionals • Beroepsverenigingen	Geen

[1] Barrières kunnen zich bevinden op het niveau van de professional, op het niveau van de organisatie (het ziekenhuis) of op het niveau van het systeem (buiten het ziekenhuis). Denk bijvoorbeeld aan onenigheid in het land met betrekking tot de aanbeveling, onvoldoende motivatie of kennis bij de specialist, onvoldoende faciliteiten of personeel, nodige concentratie van zorg, kosten, slechte samenwerking tussen disciplines, nodige taakherschikking, etc.

[2] Denk aan acties die noodzakelijk zijn voor implementatie, maar ook acties die mogelijk zijn om de implementatie te bevorderen. Denk bijvoorbeeld aan controleren aanbeveling tijdens kwaliteitsvisitatie, publicatie van de richtlijn, ontwikkelen van implementatietools, informeren van ziekenhuisbestuurders, regelen van goede vergoeding voor een bepaald type behandeling, maken van samenwerkingsafspraken.

[3] Wie de verantwoordelijkheden draagt voor implementatie van de aanbevelingen, zal tevens afhankelijk zijn van het niveau waarop zich barrières bevinden. Barrières op het niveau van de professional zullen vaak opgelost moeten worden door de beroepsvereniging. Barrières op het niveau van de organisatie zullen vaak onder verantwoordelijkheid van de ziekenhuisbestuurders vallen. Bij het oplossen van barrières op het niveau van het systeem zijn ook andere partijen, zoals de NZA en zorgverzekeraars, van belang.

Module 3.2 ACDF: met of zónder plaat

Uitgangsvraag

Wat is de waarde van een plaat in de Anterieure Cervicale Discectomie en Fusie (ACDF) met cage?

Inleiding

Momenteel bestaat er praktijkvariatie in het gebruik van een plaat na een anterieure discectomie met cage als vervanging voor de cervicale tussenwervelschijf (Anterieure Cervicale Discectomie en Fusie, ACDF). De keuze om wel of geen plaat te gebruiken, verschilt onder andere op basis van opleiding (e.g. locatie, opleider)), samenwerking neurochirurgie en orthopedie en praktijkervaring. Het is echter onduidelijk of de plaat daadwerkelijk bijdraagt aan het bevorderen van de stabiliteit en fusie van de wervelkolom en of dit leidt tot een hogere kans op complicaties. In deze module wordt de waarde van de plaat bij een ACDF bij patiënten met een cervicaal radiculair syndroom geëvalueerd. We maken hierbij onderscheid tussen een ACDF op 1 niveau en een multilevel ingreep.

Search and select

A systematic review of the literature was performed to answer the following question: *What is the effectiveness and safety of using a cage with plating compared with a stand-alone cage for patients with radiculopathy?*

P: Patients with radiculopathy (regardless acute or chronic, developmental degenerative or non-degenerative)
I: Cage with plate (osteosynthesis)
C: Cage without plate
O: Pain (critical), patient satisfaction (critical), complications (critical), return to work (important), medication use (important), quality of life (important), functioning (important), neck stability (important)

<u>Relevant outcome measures</u>

The guideline development group considered pain, patient satisfaction, complications as a *critical* outcome measure for decision making; and return to work, medication use, quality of life, functioning, neck stability as an *important* outcome measure for decision making.

A priori, the working group did not define the outcome measures listed above but used the definitions used in the studies.

The working group defined a 10% difference for continuous outcome measures (weighted mean difference), 10% for dichotomous outcome measures informing on relative risk ($0.91 \leq RR \geq 1.1$), and standardized mean difference (≤ -0.5 SMD ≥ 0.5) as minimal clinically (patient) important differences.

<u>Search and select (Methods)</u>

The databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms from 2000 until 17 August 2022. The detailed search strategy is depicted under the tab Methods. The systematic literature search resulted in 198 hits. Studies were selected based on the following criteria:

- systematic review and/or meta-analysis, with detailed search strategy, risk of bias assessment, and results of individual studies available; or randomized controlled trial (RCT);
- patients aged ≥ 18 years;

- studies including ≥20 patients (10 in each study arm);
- cage without screws;
- studies according to the PICO. Cage with plate (osteosynthesis) as an intervention, and described cage without plate as a comparison; and
- full-text English or Dutch language publication.

Initially, 31 studies were selected based on title and abstract screening. After reading the full text, 30 studies were excluded (see the table with reasons for exclusion under the tab Methods), and one study was included.

Results

One study was included in the analysis of the literature, which was a systematic review. Important study characteristics and results are summarized in the evidence table. The assessment of the risk of bias is summarized in the risk of bias table.

Summary of literature

Description of studies

Boer (2021) performed a systematic review to determine clinical and radiological outcomes following discectomy and anterior cervical fusion for the treatment of cervical degenerative disorder (CDD) performed with stand-alone cages and anterior cervical plates. Various databases (MEDLINE, LILACS, Cochrane Systematic Reviews) were searched up to September 2018. No language or date restrictions were applied. Inclusion criteria were:

- randomized and quasi-randomized clinical trials that employed stand-alone cages in the treatment of CDD;
- adult patients aged ≥ 18 years of both sexes with degenerative diseases of the cervical column such as discopathy, arthritis, herniated disc, and cervical stenosis; and
- one of the following outcomes: visual analogue scale (VAS) score, Japanese Orthopaedic Association (JOA) score, cervical incapacity (neck disability index [NDI]) score, bone consolidation, operative time, blood loss, cervical lordosis, segmental kyphosis, presence of dysphagia, loosening of plate, and treatment costs.

Studies with patients that presented a nondegenerative indication for ACDF (anterior cervical discectomy and fusion) were excluded. Six randomized clinical trials were included, with in total 309 patients (Dai 2008, Kim 2013, Lee 2016, Nabhan 2007, Nemoto 2015, Panchal 2017). The Cochrane Risk of Bias Tool was used to assess the individual study quality.

Results

1. Pain (critical)

Boer (2021) reported neck pain and arm pain with the visual analogue scale (VAS) and cervical incapacity with the neck disability index (NDI).

1.1 Neck pain

Five studies reported neck pain. The pooled mean difference (before versus after) in the VAS score for the neck between the cage without plate group and the cage with plate group was -0.09 (95%CI -0.46 to 0.27), favouring the cage and plate group. This difference was not clinically relevant (figure 1).

1.2 Arm pain

Arm pain was reported in five studies. The pooled mean difference (before versus after) in the VAS score for the arm between the cage without plate group and the cage with plate group was 0.30 (95%CI -0.29 to 0.88), favouring the cage without plate group. This difference was not clinically relevant (figure 2).

1.3 Neck Disability Index (NDI)

Three studies reported NDI scores. The pooled mean difference (before versus after) in the NDI score between the cage without plate group and the cage with plate group was -0.70 (95%CI -1.88 to 0.47), favouring the cage with plate group. This difference was not clinically relevant (figure 3).

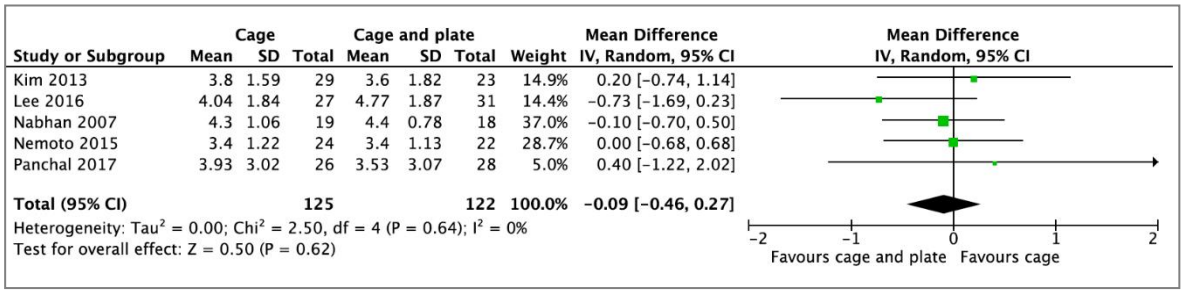

Figure 1. Forest plot and pooled mean difference in VAS score for the neck.

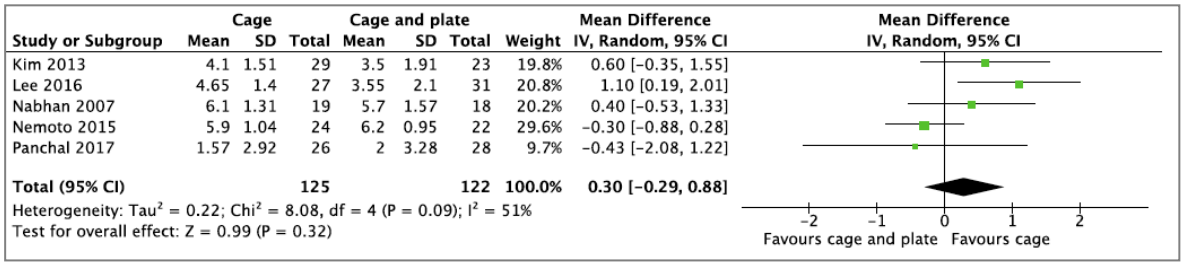

Figure 2. Forest plot and pooled mean difference in VAS score for the arm.

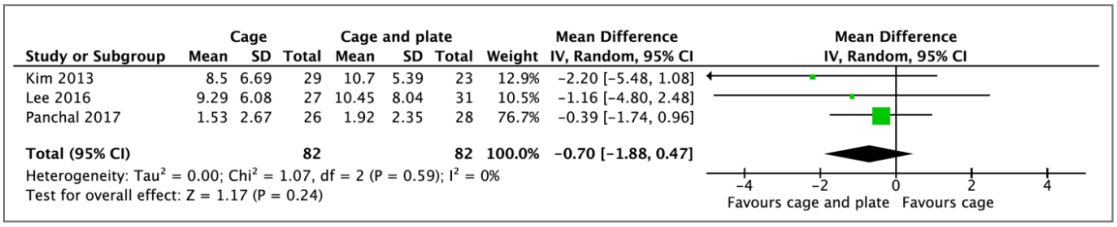

Figure 3. Forest plot and pooled mean difference in neck disability index (NDI) score.

2. Patient satisfaction (critical); 3. Complications (critical); 4. Return to work (important); 5. Medication use (important); 6. Quality of life (important); 7. Functioning (important); 8. Neck stability (important)

Not reported.

Level of evidence of the literature

The level of evidence regarding the outcome measure **pain** started as high because it was based on a systematic review of RCTs and was downgraded by three levels to *very low* because of concerns regarding selection bias and blinding (-1, risk of bias), conflicting results (-1, inconsistency) and the 95% confidence interval crossed the line of no (clinically relevant) effect (-1, imprecision).

The level of evidence regarding the outcome measures **patient satisfaction, complications, return to work, medication use, quality of life, functioning and neck stability** were not assessed.

Conclusions

1. Pain (critical)

Very low GRADE	The evidence is very uncertain about the effect of a cage with plate on pain when compared to a cage without plate in patients with radiculopathy. *Source: Boer, 2021*

2. Patient satisfaction (critical); 3. Complications (critical); 4. Return to work (important); 5. Medication use (important); 6. Quality of life (important); 7. Functioning (important); 8. Neck stability (important)

No GRADE	No evidence was found regarding the effect of a cage with plate on patient satisfaction, complications, return to work, medication use, quality of life, functioning, and neck stability when compared with a cage without plate in patients with radiculopathy. *Sources: -*

Overwegingen – van bewijs naar aanbeveling

<u>Voor- en nadelen van de interventie en de kwaliteit van het bewijs</u>

Het doel van deze uitgangsvraag was om te achterhalen wat de toegevoegde waarde van een plaat is in de anterieure benadering mét cage in de operatieve behandeling van patiënten met cervicaal radiculair syndroom. Er is één systematische review gevonden die een cage mét en zónder plaat vergelijkt (Boer, 2021). De bewijskracht voor de kritieke uitkomstmaat pijn was zeer laag vanwege methodologische beperkingen, niet eenduidige resultaten en kleine studiepopulaties. Dit betekent dat andere studies kunnen leiden tot nieuwe inzichten. Daarom kunnen er op basis van de literatuur geen harde conclusies geformuleerd worden.

Voor de kritieke uitkomstmaten ‘patiënttevredenheid’ en ‘complicaties’ en de belangrijke uitkomstmaten ‘werkhervatting’, ‘medicatiegebruik’, ‘kwaliteit van leven’, ‘functioneren’ en ‘stabiliteit van de nek’ werd geen literatuur gevonden.

Hoewel er genoeg literatuur beschikbaar is waarbij anterieure cervicale decompressie en fusie met plaat (ACDFP) en zonder plaat (ACDF) worden vergeleken, ontbreekt literatuur bij mensen met specifiek een cervicaal radiculair syndroom.

Gekeken naar alleen de verschillende operatieve technieken, zijn er verschillende studies interessant. Cheung (2018) heeft in een systematische review gekeken naar het verschil tussen een ACDF en ACDFP in een single level procedure. Auteurs keken naar complicaties, operatieduur, mate van fusie en subsidence, cervicale alignement en PROMS. Wat hierbij opvalt is dat dysfagie bij ADCFP vijf keer zo hoog ligt in vergelijking met ACDF. Tevens is de kans op degeneratie van het aangrenzende segment (adjacent level disease) 2 tot 3 keer lager in vergelijking met ACPF (Cheung, 2018). Een mogelijke verklaring hiervoor is de positie van de anterieure plaat ten opzichte van de aanliggende discus, welke vrij dichtbij is. Kijkend naar de fusiekans, operatieduur, opnameduur, heesheid postoperatief en PROMS (e.g. Odom’s criteria, VAS nek, VAS arm, JOA, NDI) worden geen verschillen tussen ACDF en ACDFP gezien.

Savio (2022) heeft in een meta-analyse het gebruik van een plaat bij ACDF bekeken bij cervical degenerative discus disease. Bij het gebruik van een stand alone cage werd een kortere operatieduur van circa 20 minuten, een kleinere kans op dysfagie (4% vs 18%) en een kleinere kans op adjacent level disease gezien dan bij het gebruik van een aanvullende

plaat osteosynthese. Het bloedverlies was zonder plaat 10ml minder dan indien er wel een plaat werd geplaatst dit is klinisch niet relevant.

Waarden en voorkeuren van patiënten (en evt. hun verzorgers)

Het doel van de operatie is het verlichten van de pijn in de arm, die immers reden was voor het uitvoeren van een anterieure discectomie bij een cervicaal radiculair syndroom. Het is wenselijk dat de pijn in de nek zo minimaal mogelijk is en dat de nek zo maximaal mogelijk functioneel is. Qua ervaren pijn, hersteltijd en/of complicaties laat de literatuur geen klinisch relevante verschillen zien. Voor patiënten is dan ook een goede en volledige toelichting van de operatie essentieel.

Kosten (middelenbeslag)

Kijkend naar de kosten, heeft de ACDF zonder plaat de voorkeur. De extra plaat met schroeven resulteren in extra kosten. We zien echter geen hogere complicatiekans, geen langere opnameduur en geen grotere kans op een re-operatie in de literatuur als een plaat achterwege wordt gelaten. De werkgroep verwacht dat er naast de directe kosten van de operatie dus geen grote kostenverschillen zullen zijn. Een toekomstige kosten-effectiviteitstudie op dit gebied is gewenst.

Aanvaardbaarheid, haalbaarheid en implementatie

De kans op subsidence, waarbij de cage in het corpus zakt, is zonder plaat hoger in vergelijking met plaat bij een ACDF. Karikari (2014) evalueerde middels een systematische review de mate van subsidence met en zonder plaat bij een ACDF. Auteurs concluderen dat als er geen plaat gebruikt wordt in een ACDF, er een grotere kans is op subsidence van de cage, maar dat dit geen effect heeft op de mate van fusie en klinische uitkomstmaten (Karikari, 2014). Ook Savio (2022) rapporteerde een hogere kans op subsidence van de cage indien er geen plaat werd gebruikt, maar ook een minder goede correctie van de mechanische balans in de cervicale wervelkolom. Auteurs adviseren om geen plaat te gebruiken bij een monolevel ACDF. Voor een multilevel probleem is een plaat wel te overwegen voor een beter herstel van de cervicale lordose (Savio, 2022). Dit is in overeenkomst met Matz (2009).

Een alternatief zou kunnen zijn, is een locking cage met schroeven die de cage aan de belendende corpora bevestigt. Hier is matig onderzoek naar gedaan, met name industry-driven zonder goede vergelijkende studies (Chen, 2016; Dong, 2015; Duan, 2016; Gabr, 2019; Guo, 2021; He, 2018; Lu, 2019; Lu, 2020; Nambiar, 2017; Shao, 2015; Shen, 2016; Sun, 2018; Tong, 2017; Xiao, 2017; Yang, 2019; Zhang, 2019; Zhang, 2022; Zhao, 2020; Zhou, 2020). Dit type cage is niet meegenomen in de zoekstrategie.

Aanbevelingen

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventies

De voordelen van een plaat bij een multilevel ACDF zijn zeer minimaal. Fs maar dit heeft geen bewezen invloed op de klinische uitkomsten zover dit op de beperkte aanwezige literatuur kan worden geconcludeerd. Er zijn nadelen van een plaat beschreven in de literatuur: een hogere kans op adjacent level disease, meer dysfagie, hogere kosten, langere operatieduur. Ook deze complicaties leiden niet tot minder functionaliteit van de nek of meer pijn bij de patiënt, volgens de beperkte literatuur die over die onderwerp voor handen is. De kans op deze plaat-gerelateerde complicaties zijn klein, waardoor de werkgroep van mening is dat een aanvullend plaat veilig kan worden gebruikt.

Overweeg het toepassen van een stand-alone cage (zonder plaat) bij een mono-level Anterieure Cervicale Discectomie en Fusie (ACDF) bij patiënten met CRS.

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Lu Y, Fang Y, Shen X, Lu D, Zhou L, Gan M, Zhu X. Does zero-profile anchored cage accompanied by a higher postoperative subsidence compared with cage-plate construct? A meta-analysis. J Orthop Surg Res. 2020 May 24;15(1):189. Doi: 10.1186/s13018-020-01711-9. PMID: 32448320; PMCID: PMC7247200.

Matz PG, Ryken TC, Groff MW, Vresilovic EJ, Anderson PA, Heary RF, Holly LT, Kaiser MG, Mummaneni PV, Choudhri TF, Resnick DK; Joint Section on Disorders of the Spine and Peripheral Nerves of the American Association of Neurological Surgeons and Congress of Neurological Surgeons. Techniques for anterior cervical decompression for radiculopathy. J Neurosurg Spine. 2009 Aug;11(2):183-97. Doi: 10.3171/2009.2.SPINE08721. PMID: 19769498.

Nambiar M, Phan K, Cunningham JE, Yang Y, Turner PL, Mobbs R. Locking stand-alone cages versus anterior plate constructs in single-level fusion for degenerative cervical disease: a systematic review and meta-analysis. Eur Spine J. 2017 Sep;26(9):2258-2266. Doi: 10.1007/s00586-017-5015-9. Epub 2017 Mar 10. PMID: 28283840.

Savio SD, Deslivia MF, Arimbawa IBG, Suyasa IK, Wiguna IGLNAA, Ridia KGM. Thorough Comparative Analysis of Stand-Alone Cage and Anterior Cervical Plate for Anterior Cervical Discectomy and Fusion in the Treatment of Cervical Degenerative Disease: A Systematic Review and Meta-analysis. Asian Spine J. 2022 Oct;16(5):812-830. Doi: 10.31616/asj.2021.0123. Epub 2022 Mar 11. PMID: 35263831; PMCID: PMC9633235.

Shao H, Chen J, Ru B, Yan F, Zhang J, Xu S, Huang Y. Zero-profile implant versus conventional cage-plate implant in anterior cervical discectomy and fusion for the treatment of degenerative cervical spondylosis: a meta-analysis. J Orthop Surg Res. 2015 Sep 17;10:148. Doi: 10.1186/s13018-015-0290-9. PMID: 26381236; PMCID: PMC4574194.

Shen Q, Ding H, Zhu ZH, Zhu L, Wei XK, He XF. Anterior cervical discectomy and fusion versus anterior cervical corpectomy and fusion for treating two-level contiguous cervical spondylotic myelopathy. Chinese Journal of Tissue Engineering Research. 2016 Nov 25;20(48):7175.

Sun Z, Liu Z, Hu W, Yang Y, Xiao X, Wang X. Zero-Profile Versus Cage and Plate in Anterior Cervical Discectomy and Fusion with a Minimum 2 Years of Follow-Up: A Meta-Analysis. World Neurosurg. 2018 Dec;120:e551-e561. Doi: 10.1016/j.wneu.2018.08.128. Epub 2018 Aug 29. PMID: 30172062.

Tong MJ, Xiang GH, He ZL, Chen DH, Tang Q, Xu HZ, Tian NF. Zero-Profile Spacer Versus Cage-Plate Construct in Anterior Cervical Diskectomy and Fusion for Multilevel Cervical Spondylotic Myelopathy: Systematic Review and Meta-Analysis. World Neurosurg. 2017 Aug;104:545-553. Doi: 10.1016/j.wneu.2017.05.045. Epub 2017 May 17. PMID: 28526640.

Xiao S, Liang Z, Wei W, Ning J. Zero-profile anchored cage reduces risk of postoperative dysphagia compared with cage with plate fixation after anterior cervical discectomy and fusion. Eur Spine J. 2017 Apr;26(4):975-984. Doi: 10.1007/s00586-016-4914-5. Epub 2016 Dec 21. PMID: 28004243.

Xu J, He Y, Li Y, Lv GH, Dai YL, Jiang B, Zheng Z, Wang B. Incidence of Subsidence of Seven Intervertebral Devices in Anterior Cervical Discectomy and Fusion: A Network Meta-Analysis. World Neurosurg. 2020 Sep;141:479-489.e4. doi: 10.1016/j.wneu.2020.03.130. Epub 2020 Apr 3. PMID: 32251812.

Yang Z, Zhao Y, Luo J. Incidence of dysphagia of zero-profile spacer versus cage-plate after anterior cervical discectomy and fusion: A meta-analysis. Medicine (Baltimore). 2019 Jun;98(25):e15767. Doi: 10.1097/MD.0000000000015767. PMID: 31232918; PMCID: PMC6636941.

Zhang D, Liu B, Zhu J, Li C, Wei F, Yuan Y, Zhu D. Comparison of Clinical and Radiologic Outcomes Between Self-Locking Stand-Alone Cage and Cage with Anterior Plate for Multilevel Anterior Cervical Discectomy and Fusion: A Meta-Analysis. World Neurosurg. 2019 May;125:e117-e131. Doi: 10.1016/j.wneu.2018.12.218. Epub 2019 Jan 21. PMID: 30677575.

Zhang T, Guo N, Gao G, Liu H, Li Y, Gao F, Zhang Q, Tao X, Yang W, Wang Y. Comparison of outcomes between Zero-p implant and anterior cervical plate interbody fusion systems for anterior cervical decompression and fusion: a systematic review and meta-analysis of randomized controlled trials. J Orthop Surg Res. 2022 Jan 25;17(1):47. Doi: 10.1186/s13018-022-02940-w. PMID: 35078496; PMCID: PMC8787904.

Zhao Y, Yang S, Huo Y, Li Z, Yang D, Ding W. Locking stand-alone cage versus anterior plate construct in anterior cervical discectomy and fusion: a systematic review and meta-analysis based on randomized controlled trials. Eur Spine J. 2020 Nov;29(11):2734-2744. Doi: 10.1007/s00586-020-06561-x. Epub 2020 Aug 8. PMID: 32770359.

Zhou J, Li J, Lin H, Li X, Dong J, Zhou X. Could self-locking stand-alone cage reduce adjacent-level ossification development after aneterior cervical discectomy and fusion? J Clin Neurosci. 2020 Aug;78:60-66. Doi: 10.1016/j.jocn.2020.06.014. Epub 2020 Jul 2. PMID: 32624365.

Bijlagen bij module ‘ACDF: met of zónder plaat’

Implementatieplan

Aanbeveling	Tijdspad voor implementatie: < 1 jaar, 1 tot 3 jaar of > 3 jaar	Verwacht effect op kosten	Randvoorwaarden voor implementatie (binnen aangegeven tijdspad)	Mogelijke barrières voor implementatie[1]	Te ondernemen acties voor implementatie[2]	Verantwoordelijken voor acties[3]	Overige opmerkingen
Alle aanbevelingen	< 1 jaar	Beperkt	Bekendheid met de richtlijn.	Onvoldoende motivatie bij de zorgverleners.	Verspreiden en publicatie van richtlijn. Optimaliseren kennis bij zorgverleners	Beroepsverenigingen. Betrokken zorgverleners.	-

[1] Barrières kunnen zich bevinden op het niveau van de professional, op het niveau van de organisatie (het ziekenhuis) of op het niveau van het systeem (buiten het ziekenhuis). Denk bijvoorbeeld aan onenigheid in het land met betrekking tot de aanbeveling, onvoldoende motivatie of kennis bij de specialist, onvoldoende faciliteiten of personeel, nodige concentratie van zorg, kosten, slechte samenwerking tussen disciplines, nodige taakherschikking, etc.

[2] Denk aan acties die noodzakelijk zijn voor implementatie, maar ook acties die mogelijk zijn om de implementatie te bevorderen. Denk bijvoorbeeld aan controleren aanbeveling tijdens kwaliteitsvisitatie, publicatie van de richtlijn, ontwikkelen van implementatietools, informeren van ziekenhuisbestuurders, regelen van goede vergoeding voor een bepaald type behandeling, maken van samenwerkingsafspraken.

[3] Wie de verantwoordelijkheden draagt voor implementatie van de aanbevelingen, zal tevens afhankelijk zijn van het niveau waarop zich barrières bevinden. Barrières op het niveau van de professional zullen vaak opgelost moeten worden door de beroepsvereniging. Barrières op het niveau van de organisatie zullen vaak onder verantwoordelijkheid van de ziekenhuisbestuurders vallen. Bij het oplossen van barrières op het niveau van het systeem zijn ook andere partijen, zoals de NZA en zorgverzekeraars, van belang.

Evidence table

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Boer, 2021 [individual study characteristics deduced from [Boer, 2021]] PS., study characteristics and results are extracted from the SR (unless stated otherwise)	SR and meta-analysis of RCTs *Literature search up to September 2018* **A**: Panchal, 2017 **B**: Dai, 2008 **C**: Kim, 2013 **D**: Lee, 2016 **E**: Nabhan, 2007 **F**: Nemoto, 2015 <u>Study design</u>: RCT <u>Setting and Country</u>: **A**: USA **B**: China **C**: South Korea **D**: South Korea **E**: Germany **F**: Japan <u>Source of funding and conflicts of interest:</u> The author(s) declared no potential conflicts of interest with respect to the research,	<u>Inclusion criteria SR:</u> - Randomized and quasi-randomized clinical trials that employed stand-alone cages in the treatment of cervical degenerative disorder (CDD) - Adult patients aged 18 years or older, of both sexes, with degenerative diseases of the cervical column - Reported one of the following outcomes: visual analogue scale (VAS) score, Japanese Orthopaedic Association (JOA) score, cervical incapacity (neck disability index [NDI]) score, bone consolidation, operative time, blood loss, cervical lordosis, segmental kyphosis, presence of dysphagia, loosening of plate, and treatment costs <u>Exclusion criteria SR:</u> Studies with patients that presented a nondegenerative indication for anterior cervical discectomy and fusion (ACDF) *6 studies included* <u>Population:</u> **A**: Degenerative disc disease at only 1 level from C3 to C7. **B**: Progressive upper extremity radicular symptoms and/or	<u>Describe intervention</u>: Stand-alone cage Cage material: **A**: PEEK **B**: PEEK + Beta-TCP **C**: PEEK* **D**: PEEK* **E**: PEEK **F**: PEEK PEEK; polyetheretherketone Beta-TCP; b-tricalcium phosphate *cage + autograft	Describe control<u>:</u> Cage and cervical plate	<u>Endpoint of follow-up</u>: Not reported. <u>For how many participants were no complete outcome data available?</u> Not reported.	<u>Outcome measure 1: visual analogue scale (VAS) neck</u> Mean difference [95% CI]: **A**: 0.40 [-1.22 to 2.02] **B**: -0.20 **C:** 0.20 [-0.74 to 1.14] **D:** -0.73 [-1.69 to 0.23] **E:** -0.10 [-0.70 to 0.50] **F:** 0.00 [-0.68 to 0.68] Pooled effect (random effects model): -0.09 [95% CI -0.46 to 0.27] favoring cage and plate Heterogeneity (I^2): 83.39% <u>Outcome measure 2: visual analogue scale (VAS) arm</u> Mean difference [95% CI]: **A**: -0.43 [-2.08 to 1.22] **B**: -0.20 **C:** 0.60 [-0.35 to 1.55] **D:** 1.10 [0.19 to 2.01] **E:** 0.40 [-0.53 to 1.33] **F:** -0.30 [-0.8 8 to 0.28] Pooled effect (random effects model): 0.30 [95% CI -0.29 to 0.88] favoring cage Heterogeneity (I^2): 97.47% <u>Outcome measure 3: neck</u>	<u>Brief description of author's conclusion</u> The use of stand-alone cage is equivalent to the use of plate in ACDF. The results do not show significant differences in the clinical outcomes (VAS and NDI scores). <u>Personal remarks on study quality, conclusions, and other issues (potentially) relevant to the research question</u> - No limitations were mentioned - No conflict of interest mentioned for individual studies <u>Level of evidence: GRADE</u> RS = random sequence generation AC = allocation concealment BP = blinding participants and personnel BO = blinding outcome assessment IO = incomplete outcome SR = selective reporting OB = other Bias low = low risk of bias high = high risk of bias

	authorship, and/or publication of this article. This study received financial support from the Sociedade Brasileira de Coluna.	myelopathy resulting from cervical degenerative disc disease underwent one- to two-level discectomy at contiguous levels from C3–4 to C6–7 for soft disc herniation or spondylosis. **C**: Patients with radiculopathy or myelopathy due to disc herniation, osteophyte formation, or hypertrophied posterior longitudinal ligament (single-level ACDF). **D**: Radiculopathy or myelopathy due to cervical disc herniation, spinal stenosis, or hypertrophy of the posterior longitudinal ligaments (single-level ACDF). **E**: Symptomatic degenerative disc disease with radiculopathy and / or progressive myelopathy and not responding to conservative treatment (one-level ACDF). **F**: Single-level cervical radiculopathy presenting with chronic neck pain and irradiating upper extremity symptoms (single-level ACDF). <u>Important patient characteristics at baseline</u>: Not reported Unclear if groups were comparable at baseline				<u>disability index (NDI)</u> Mean difference [95% CI]: **A**: -0.39 (-1.74 to 0.96) **C:** -2.20 (-5.48 to 1.08) **D:** -1.16 (-4.80 to 2.48) Pooled effect (random effects model): -0.70 [95% CI -1.88 to 0.47] favoring plate Heterogeneity (I^2): 98.45%	unclear risk of bias **A:** RS = low; AC = low; BP = high; BO = unclear; IO = low; SR = high; OB = high **B:** RS = low; AC = high; BP = low; BO = low; IO = low; SR = low; OB = low **C:** RS = low; AC = high; BP = low; BO = unclear; IO = low; SR = unclear; OB = low **D:** RS = low; AC = high; BP = low; BO = unclear; IO = low; SR = low; OB = low **E:** RS = low; AC = low; BP = unclear; BO = unclear; IO = low; SR = low; OB = unclear **F:** RS = low; AC = low; BP = unclear; BO = unclear; IO = low; SR = high; OB = high <u>No sensitivity analyses</u> <u>Heterogeneity</u> Heterogeneity was assessed with Cochran's Q test and I^2

Table of quality assessment for systematic reviews of RCTs and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study	Appropriate and clearly focused question?[1]	Comprehensive and systematic literature search?[2]	Description of included and excluded studies?[3]	Description of relevant characteristics of included studies?[4]	Appropriate adjustment for potential confounders in observational studies?[5]	Assessment of scientific quality of included studies?[6]	Enough similarities between studies to make combining them reasonable?[7]	Potential risk of publication bias taken into account?[8]	Potential conflicts of interest reported?[9]
Boer, 2021	No. Research question not clearly defined.	Yes. Search period and strategy described. Medline was searched.	Yes. Reason for exclusion of individual studies was described.	No. Only brief description of characteristics.	Not applicable. Only RCTs were included.	Yes. Risk of bias was assessed for the individual studies and presented in a risk of bias table.	No. High heterogeneity (high I^2).	No. Not reported that publication bias could not be assessed because there were less than 10 studies included.	No. Conflicts of interest were reported for the systematic review but not for the individual studies.

Table of excluded studies

Reference	Reason for exclusion
Botelho RV, Dos Santos Buscariolli Y, de Barros Vasconcelos Fernandes Serra MV, Bellini MN, Bernardo WM. The choice of the best surgery after single level anterior cervical spine discectomy: a systematic review. Open Orthop J. 2012;6:121-8. doi: 10.2174/1874325001206010121. Epub 2012 Mar 8. PMID: 22523524; PMCID: PMC3314868.	Wrong intervention: discectomy alone as intervention
Chen Y, Chen H, Wu X, Wang X, Lin W, Yuan W. Comparative analysis of clinical outcomes between zero-profile implant and cages with plate fixation in treating multilevel cervical spondilotic myelopathy: A three-year follow-up. Clin Neurol Neurosurg. 2016 May;144:72-6. doi: 10.1016/j.clineuro.2016.03.010. Epub 2016 Mar 15. PMID: 26999528.	Wrong intervention: cage with screws
Cheung ZB, Gidumal S, White S, Shin J, Phan K, Osman N, Bronheim R, Vargas L, Kim JS, Cho SK. Comparison of Anterior Cervical Discectomy and Fusion With a Stand-Alone Interbody Cage Versus a Conventional Cage-Plate Technique: A Systematic Review and Meta-Analysis. Global Spine J. 2019 Jun;9(4):446-455. doi: 10.1177/2192568218774576. Epub 2018 May 17. PMID: 31218204; PMCID: PMC6562216.	Better systematic review available: no RCTs included
Dong J, Lu M, Lu T, Liang B, Xu J, Zhou J, Lv H, Qin J, Cai X, Huang S, Li H, Wang D, He X. Meta-Analysis Comparing Zero-Profile Spacer and Anterior Plate in Anterior Cervical Fusion. PLoS One. 2015 Jun 11;10(6):e0130223. doi: 10.1371/journal.pone.0130223. PMID: 26067917; PMCID: PMC4466022.	Wrong intervention: cage with screws
Duan Y, Yang Y, Wang Y, Liu H, Hong Y, Gong Q, Song Y. Comparison of anterior cervical discectomy and fusion with the zero-profile device versus plate and cage in treating cervical degenerative disc disease: A meta-analysis. J Clin Neurosci. 2016 Nov;33:11-18. doi: 10.1016/j.jocn.2016.01.046. Epub 2016 Jul 18. PMID: 27443497.	Wrong intervention: cage with screws
Fraser JF, Härtl R. Anterior approaches to fusion of the cervical spine: a metaanalysis of fusion rates. J Neurosurg Spine. 2007 Apr;6(4):298-303. doi: 10.3171/spi.2007.6.4.2. PMID: 17436916.	Wrong comparison: no plates
Gabr MA, Touko E, Yadav AP, Karikari I, Goodwin CR, Groff MW, Ramirez L, Abd-El-Barr MM. Improved Dysphagia Outcomes in Anchored Spacers Versus Plate-Screw Systems in Anterior Cervical Discectomy and Fusion: A Systematic Review. Global Spine J. 2020 Dec;10(8):1057-1065. doi: 10.1177/2192568219895266. Epub 2019 Dec 26. PMID: 32875838; PMCID: PMC7645096.	Wrong intervention: cage with screws
Gao QY, Wei FL, Zhu KL, Zhou CP, Zhang H, Cui WX, Li T, Qian JX, Hao DJ. Clinical Efficacy and Safety of Surgical Treatments in Patients With Pure Cervical Radiculopathy. Front Public Health. 2022 Jul 14;10:892042. doi: 10.3389/fpubh.2022.892042. PMID: 35910906; PMCID: PMC9330161.	Better systematic review available: only four RCTs with less than 30 patients per arm (two included in systematic review of Boer 2021)
Guo Z, Wu X, Yang S, Liu C, Zhu Y, Shen N, Guo Z, Su W, Wang Y, Chen B, Xiang H. Anterior Cervical Discectomy and Fusion Using Zero-P System for Treatment of Cervical Spondylosis: A Meta-Analysis. Pain Res Manag. 2021 Dec 16;2021:3960553. doi: 10.1155/2021/3960553. PMID: 34956433; PMCID: PMC8702348.	Wrong intervention: cage with screws
He S, Feng H, Lan Z, Lai J, Sun Z, Wang Y, Wang J, Ren Z, Huang F, Xu F. A Randomized Trial Comparing Clinical Outcomes Between Zero-Profile and Traditional Multilevel Anterior Cervical Discectomy and Fusion Surgery for Cervical Myelopathy. Spine (Phila Pa 1976). 2018 Mar 1;43(5):E259-E266. doi: 10.1097/BRS.0000000000002323. PMID: 29432408.	Wrong intervention: cage with screws
Jacobs W, Willems PC, van Limbeek J, Bartels R, Pavlov P, Anderson PG, Oner C. Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease. Cochrane Database Syst Rev. 2011 Jan 19;(1):CD004958. doi: 10.1002/14651858.CD004958.pub2. PMID: 21249667.	Better systematic review available: only two RCTs with less than 30 patients per arm (included in systematic review of Boer 2021)
Karikari IO, Jain D, Owens TR, Gottfried O, Hodges TR, Nimjee SM, Bagley CA. Impact of subsidence on clinical outcomes and radiographic fusion rates in anterior cervical discectomy and fusion: a systematic review. J Spinal Disord Tech. 2014 Feb;27(1):1-10. doi: 10.1097/BSD.0b013e31825bd26d. PMID: 24441059.	Better systematic review available: no suitable studies and no direct comparison between cage with plate and cage without plate

Katsuura Y, York PJ, Goto R, Yang J, Vaishnav AS, McAnany S, Albert T, Iyer S, Gang CH, Qureshi SA. Sagittal Reconstruction and Clinical Outcome Using Traditional ACDF, Versus Stand-alone ACDF Versus TDR: A Systematic Review and Quantitative Analysis. Spine (Phila Pa 1976). 2019 Oct 1;44(19):E1151-E1158. doi: 10.1097/BRS.0000000000003077. PMID: 31261280.	Better systematic review available: unclear which studies are included
Lu VM, Mobbs RJ, Fang B, Phan K. Clinical outcomes of locking stand-alone cage versus anterior plate construct in two-level anterior cervical discectomy and fusion: a systematic review and meta-analysis. Eur Spine J. 2019 Jan;28(1):199-208. doi: 10.1007/s00586-018-5811-x. Epub 2018 Nov 2. PMID: 30390163.	Wrong intervention: cage with screws
Lu Y, Fang Y, Shen X, Lu D, Zhou L, Gan M, Zhu X. Does zero-profile anchored cage accompanied by a higher postoperative subsidence compared with cage-plate construct? A meta-analysis. J Orthop Surg Res. 2020 May 24;15(1):189. doi: 10.1186/s13018-020-01711-9. PMID: 32448320; PMCID: PMC7247200.	Wrong intervention: cage with screws
Matz PG, Ryken TC, Groff MW, Vresilovic EJ, Anderson PA, Heary RF, Holly LT, Kaiser MG, Mummaneni PV, Choudhri TF, Resnick DK; Joint Section on Disorders of the Spine and Peripheral Nerves of the American Association of Neurological Surgeons and Congress of Neurological Surgeons. Techniques for anterior cervical decompression for radiculopathy. J Neurosurg Spine. 2009 Aug;11(2):183-97. doi: 10.3171/2009.2.SPINE08721. PMID: 19769498.	Better systematic review available: no suitable studies and no raw data presented
Nambiar M, Phan K, Cunningham JE, Yang Y, Turner PL, Mobbs R. Locking stand-alone cages versus anterior plate constructs in single-level fusion for degenerative cervical disease: a systematic review and meta-analysis. Eur Spine J. 2017 Sep;26(9):2258-2266. doi: 10.1007/s00586-017-5015-9. Epub 2017 Mar 10. PMID: 28283840.	Wrong intervention: cage with screws
Oliver JD, Goncalves S, Kerezoudis P, Alvi MA, Freedman BA, Nassr A, Bydon M. Comparison of Outcomes for Anterior Cervical Discectomy and Fusion With and Without Anterior Plate Fixation: A Systematic Review and Meta-Analysis. Spine (Phila Pa 1976). 2018 Apr 1;43(7):E413-E422. doi: 10.1097/BRS.0000000000002441. PMID: 29016435.	Better systematic review available: only three RCTs with less than 30 patients per arm (included in systematic review of Boer 2021)
Savio SD, Deslivia MF, Arimbawa IBG, Suyasa IK, Wiguna IGLNAA, Ridia KGM. Thorough Comparative Analysis of Stand-Alone Cage and Anterior Cervical Plate for Anterior Cervical Discectomy and Fusion in the Treatment of Cervical Degenerative Disease: A Systematic Review and Meta-analysis. Asian Spine J. 2022 Oct;16(5):812-830. doi: 10.31616/asj.2021.0123. Epub 2022 Mar 11. PMID: 35263831; PMCID: PMC9633235.	Better systematic review available: no RCTs included
Shao H, Chen J, Ru B, Yan F, Zhang J, Xu S, Huang Y. Zero-profile implant versus conventional cage-plate implant in anterior cervical discectomy and fusion for the treatment of degenerative cervical spondylosis: a meta-analysis. J Orthop Surg Res. 2015 Sep 17;10:148. doi: 10.1186/s13018-015-0290-9. PMID: 26381236; PMCID: PMC4574194.	Wrong intervention: cage with screws
Shen Q, Ding H, Zhu ZH, Zhu L, Wei XK, He XF. Anterior cervical discectomy and fusion versus anterior cervical corpectomy and fusion for treating two-level contiguous cervical spondylotic myelopathy. Chinese Journal of Tissue Engineering Research. 2016 Nov 25;20(48):7175.	Wrong intervention: cage with screws
Sun Z, Liu Z, Hu W, Yang Y, Xiao X, Wang X. Zero-Profile Versus Cage and Plate in Anterior Cervical Discectomy and Fusion with a Minimum 2 Years of Follow-Up: A Meta-Analysis. World Neurosurg. 2018 Dec;120:e551-e561. doi: 10.1016/j.wneu.2018.08.128. Epub 2018 Aug 29. PMID: 30172062.	Wrong intervention: cage with screws
Tong MJ, Xiang GH, He ZL, Chen DH, Tang Q, Xu HZ, Tian NF. Zero-Profile Spacer Versus Cage-Plate Construct in Anterior Cervical Diskectomy and Fusion for Multilevel Cervical Spondylotic Myelopathy: Systematic Review and Meta-Analysis. World Neurosurg. 2017 Aug;104:545-553. doi: 10.1016/j.wneu.2017.05.045. Epub 2017 May 17. PMID: 28526640.	Wrong intervention: cage with screws
Xiao S, Liang Z, Wei W, Ning J. Zero-profile anchored cage reduces risk of postoperative dysphagia compared with cage with plate fixation after anterior cervical discectomy and fusion. Eur Spine J. 2017 Apr;26(4):975-984. doi: 10.1007/s00586-016-4914-5. Epub 2016 Dec 21. PMID: 28004243.	Wrong intervention: cage with screws
Xu J, He Y, Li Y, Lv GH, Dai YL, Jiang B, Zheng Z, Wang B. Incidence of Subsidence of Seven Intervertebral Devices in Anterior Cervical Discectomy and Fusion: A	Better systematic review available: no RCTs included

Network Meta-Analysis. World Neurosurg. 2020 Sep;141:479-489.e4. doi: 10.1016/j.wneu.2020.03.130. Epub 2020 Apr 3. PMID: 32251812.	
Yang Z, Zhao Y, Luo J. Incidence of dysphagia of zero-profile spacer versus cage-plate after anterior cervical discectomy and fusion: A meta-analysis. Medicine (Baltimore). 2019 Jun;98(25):e15767. doi: 10.1097/MD.0000000000015767. PMID: 31232918; PMCID: PMC6636941.	Wrong intervention: cage with screws
Zhang D, Liu B, Zhu J, Li C, Wei F, Yuan Y, Zhu D. Comparison of Clinical and Radiologic Outcomes Between Self-Locking Stand-Alone Cage and Cage with Anterior Plate for Multilevel Anterior Cervical Discectomy and Fusion: A Meta-Analysis. World Neurosurg. 2019 May;125:e117-e131. doi: 10.1016/j.wneu.2018.12.218. Epub 2019 Jan 21. PMID: 30677575.	Wrong intervention: cage with screws
Zhang T, Guo N, Gao G, Liu H, Li Y, Gao F, Zhang Q, Tao X, Yang W, Wang Y. Comparison of outcomes between Zero-p implant and anterior cervical plate interbody fusion systems for anterior cervical decompression and fusion: a systematic review and meta-analysis of randomized controlled trials. J Orthop Surg Res. 2022 Jan 25;17(1):47. doi: 10.1186/s13018-022-02940-w. PMID: 35078496; PMCID: PMC8787904.	Wrong intervention: cage with screws
Zhao Y, Yang S, Huo Y, Li Z, Yang D, Ding W. Locking stand-alone cage versus anterior plate construct in anterior cervical discectomy and fusion: a systematic review and meta-analysis based on randomized controlled trials. Eur Spine J. 2020 Nov;29(11):2734-2744. doi: 10.1007/s00586-020-06561-x. Epub 2020 Aug 8. PMID: 32770359.	Wrong intervention: cage with screws
Zhou J, Li J, Lin H, Li X, Dong J, Zhou X. Could self-locking stand-alone cage reduce adjacent-level ossification development after aneterior cervical discectomy and fusion? J Clin Neurosci. 2020 Aug;78:60-66. doi: 10.1016/j.jocn.2020.06.014. Epub 2020 Jul 2. PMID: 32624365.	Wrong intervention: cage with screws

Literature search strategy

Zoekverantwoording

Algemene informatie

Cluster/richtlijn: Cervicaal radiculair syndroom	
Uitgangsvraag/modules: Wat is de waarde van een plaat in de anterieure benadering met cage?	
Database(s): Ovid/Medline, Embase.com	Datum: 17-08-2022
Periode: 2000 - heden	Talen: Engels, Nederlands
Literatuurspecialist: Miriam van der Maten	
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting: Voor deze vraag is gezocht op de elementen: - Patiënten met CRS - Plaat gebruik In eerste instantie is er alleen naar SR + RCT gezocht. Mocht dit niet toereikend zijn, kan er naar vergelijkend onderzoek worden gekeken. De twee sleutelartikelen worden gevonden met de search	
Te gebruiken voor richtlijnen tekst: *Nederlands* In de databases Embase.com en Ovid/Medline is op 17 augustus met relevante zoektermen gezocht naar systematische reviews en RCT over is de waarde van een plaat in de anterieure benadering met plaat bij patiënten met CRS. De literatuurzoekactie leverde 198 unieke treffers op. *Engels* On the 17th of August 2022 relevant search terms were used to search for systematic reviews and RCT about the effectiveness and safety of using a cage with plating compared with a stand-alone cage for patients with radiculopathy in the databases Embase.com and Ovid/Medline. The search resulted in 198 unique hits.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SRs	53	59	67
RCT	115	106	131
Totaal	168	165	**198**

Zoekstrategie

Embase.com

No.	**Query**	**Results**
#8	#6 OR #7	168
#7	#3 AND #5 NOT #6 **= RCT**	115
#6	#3 AND #4 **= SR**	53
#5	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	1945704
#4	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR	733409

	(('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	
#3	#1 AND #2 AND ([english]/lim OR [dutch]/lim) AND [2000-2022]/py NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	915
#2	'bone plate'/mj OR 'bone implant'/mj OR 'cervical plate'/exp OR plate*:ti,ab,kw OR plating:ti,ab,kw OR 'osteosynthesis'/exp/mj	677375
#1	'cervicobrachial neuralgia'/exp/mj OR cervicobrachialgia:ti,ab,kw OR ((radiculalgia:ti,ab,kw OR radiculitis:ti,ab,kw OR radiculitides:ti,ab,kw OR radiculopath*:ti,ab,kw OR polyradiculopath*:ti,ab,kw OR neuralgia:ti,ab,kw OR 'herniated disc*':ti,ab,kw OR hernia:ti,ab,kw OR ((radicular NEAR/3 (pain* OR neuralgia* OR symptom*)):ti,ab,kw) OR (('nerve root' NEAR/3 (pain* OR inflammation* OR disorder* OR compression* OR avulsion* OR impingement)):ti,ab,kw)) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('radicular pain'/exp/mj OR 'radiculopathy'/exp/mj) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR ((anterior NEAR/2 cervical NEAR/2 (foraminotomy OR microforaminotomy)):ti,ab,kw) OR 'anterior cervical discectomy'/exp OR 'anterior cervical discectomy and fusion'/exp OR cadf:ti,ab,kw OR cadp:ti,ab,kw OR acdf:ti,ab,kw OR ((anterior NEAR/2 cervical NEAR/2 (dis*ectom* OR 'disc fusion' OR microdiscectom*)):ti,ab,kw) OR 'foraminotomy'/exp OR 'degenerative cervical disc':ti,ab,kw	16069

Ovid/Medline

#	Searches	Results
10	8 or 9	165
9	(5 and 7) not 8 **= RCT**	106
8	5 and 6 **= SR**	59
7	exp randomized controlled trial/ or randomized controlled trials as topic/ or random*.ti,ab. or rct?.ti,ab. or ((pragmatic or practical) adj "clinical trial*").ti,ab,kf. or ((non-inferiority or noninferiority or superiority or equivalence) adj3 trial*).ti,ab,kf.	1538278
6	meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.	612107
5	limit 4 to ((english language or dutch) and yr="2000 -Current")	980
4	3 not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	1114
3	1 and 2	1168
2	exp Bone Plates/ or Plate*.ti,ab,kf. or plating.ti,ab,kf.	498199
1	((exp Radiculopathy/ or radiculalgia.ti,ab,kf. or radiculitis.ti,ab,kf. or radiculitides.ti,ab,kf. or radiculopath*.ti,ab,kf. or polyradiculopath*.ti,ab,kf. or neuralgia.ti,ab,kf. or 'herniated disc*'.ti,ab,kf. or hernia.ti,ab,kf. or (radicular adj3 (pain* or neuralgia* or symptom*)).ti,ab,kf. or ('nerve root' adj3 (pain* or inflammation* or disorder* or compression* or avulsion* or impingement)).ti,ab,kf.) and (exp Cervical Vertebrae/ or exp Neck/ or cervical.ti,ab,kf. or cervico*.ti,ab,kf. or neck.ti,ab,kf.)) or cervicobrachialgia.ti,ab,kf. or 'degenerative cervical disc'.ti,ab,kf. or (anterior adj2 cervical adj2 (foraminotomy or Microforaminotomy or microdiscectom*)).ti,ab,kf. or exp Diskectomy/ or CADF.ti,ab,kf. or CADP.ti,ab,kf. or ACDF.ti,ab,kf. or (anterior adj2 cervical adj2 (dis*ectom* or 'disc fusion')).ti,ab,kf.	14584

Module 3.3. Anterieure Cervicale Discectomie met Prothese (ACDP)

Uitgangsvraag

Wat is de plaats van ACDP (Anterieure Cervicale Discectomie met Prothese) in vergelijking met ACDF (Anterieure Cervicale Discectomie en Fusie) als chirurgische behandeling bij patiënten met CRS?

Introductie

De vaakst uitgevoerde chirurgische behandeling van degeneratieve cervicale problematiek is de anterieure discectomie met of zonder cage plaatsing, ook wel Anterieure Cervicale Discectomie en Fusie (ACDF) genoemd (Broekema, 2020; Saifi, 2018; Weiss, 2020). Deze chirurgische behandeling heeft als doel een benige fusie te bereiken tussen twee wervels. Hierdoor verdwijnt de beweeglijkheid uit het segment. Dit leidt tot een toename van biomechanische belasting van de nog beweeglijke segmenten boven en onder het geopereerde niveau, wat in theorie tot versnelde degeneratie van deze niveaus (adjacent segment disease, ASD) kan leiden. Om ASD te voorkomen zijn cervicale discus protheses geïntroduceerd die de beweeglijkheid van het geopereerde niveau trachten te behouden. Deze anterieure discectomie met prothese (ACDP) wordt in het buitenland, in tegenstelling tot de Nederlandse praktijk, veelvuldig aangeboden aan patiënten in plaats van een ACDF. De Nederlandse terughoudendheid is gelieerd aan meerdere factoren. Ten eerste, het ontstaan van ASD wordt vaak als een radiologische diagnose beschouwd, waarbij onduidelijk is of deze entiteit leidt tot een hogere incidentie van symptomatologie. Ten tweede, eerdere studies toonden geen betere klinische uitkomst op korte termijn aan (Goedmakers, 2019). Het is onduidelijk of het gebrek aan klinisch relevante meerwaarde op korte termijn ook stand houdt op lange termijn, gezien het optreden van ASD mogelijk pas na meerdere jaren klinisch relevant wordt. In deze module wordt de meerwaarde van de ACDP in vergelijking met ACDF als chirurgische behandeling bij patiënten met CRS geëvalueerd.

Search and select

An international group of experts performed a systematic review concerning clinical outcomes (Goedmakers, 2019). The systematic review provided a detailed search strategy with search date (August 2017), searched six databases, provided clear in- and exclusion criteria, a clear description of the included studies, performed a risk of bias assessment per study, and graded the level of evidence per outcome measure. Additionally, Yang (2018) performed a systematic review concerning radiological outcomes using the same search strategy. For the outcomes heterotopic ossification (HO) and adjacent segment disease (ASD) we used the results of Yang (2018), which were radiologically confirmed. Because of these publications, the working group decided to update the search of the systematic review.

A systematic review of the literature (published after August 2017) was performed to answer the following question: *What is the effectiveness of prosthesis after anterior cervical discectomy (ACDP) in comparison to anterior cervical discectomy with fusion - with or without a cage (ACDF) in patients with CRS?*

P: Patients with cervical radiculopathy with anterior discectomy with or without disc placement
I: Anterior cervical discectomy with prosthesis (ACDP)
C: Anterior cervical discectomy with fusion - with or without cage (ACDF)
O: Neck pain (VAS), disability (NDI), reoperation rate, heterotopic ossification (HO), adjacent segment disease (ASD)

Relevant outcome measures

The guideline development group considered neck pain and disability as *critical* outcome measures for decision making, and reoperation rate, heterotopic ossification and ASD as *important* outcome measures for decision making.

The working group did not define the other outcome measures above but used the definitions used in the studies.

The working group defined a 10% difference for continuous outcome measures (weighted mean difference), 10% for dichotomous outcome measures informing on relative risk (0.91 ≥ RR ≥ 1.1), and standardized mean difference (≤-0.5 SMD ≥0.5) as minimal clinically (patient) important differences.

Search and select (Methods)

The databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms from 2 August 2016 until 13 April 2023. The detailed search strategy is depicted under the tab Methods. The systematic literature search resulted in 190 hits. Studies were selected based on the following criteria:

- Systematic reviews (searched in at least two databases, and detailed search strategy, risk of bias assessment and results of individual studies available) or randomized controlled trials;
- Studies performed in adults (≥ 18 years);
- Studies with ≥20 participants (10 participants per arm);
- Full-text English or Dutch language publication; and
- Studies according to the PICO.

Initially, 24 studies were selected based on title and abstract screening. After reading the full text, 19 studies were excluded (see the table with reasons for exclusion under the tab Methods), and five studies (Coric, 2018; Donk, 2017; Goedmakers, 2023; Johansen, 2021; Kontakis, 2022) were included additional to Goedmakers (2019).

Results

Six studies were included in the analysis of the literature. Important study characteristics and results are summarized in the evidence tables. The assessment of the risk of bias is summarized in the risk of bias tables.

Summary of literature

Description of studies

Goedmakers (2019) conducted a systematic review to compare the outcome of fusion versus prosthesis in patients that primarily suffer from radiculopathy. Authors searched PubMed, EMBASE, Web of Science, COCHRANE, CENTRAL and CINAHL databases on 2 August 2016, and repeated the literature search in August 2017. An adjusted version of the checklist for cohort studies of the Dutch Cochrane Center was used for quality assessment. Goedmakers (2019) included eight radiculopathy studies: Coric (2013), Hou (2016), Janssen (2015), Nabhan (2007), Park (2008), Sala (2015), Sundseth (2017), and Zhang (2014). These studies were all included in our literature analysis as well. A total of 777 participants were included, with sample sizes ranging from 41 to 209. The cervical disc arthroplasty (ACDA) group consisted of 388 patients (mean age: 45 years, 46% male) and the anterior cervical discectomy and fusion (ACDF) group consisted of 389 patients (mean age: 45 years, 49%

male). Follow-up varied from one to seven years. One study (Sundseth, 2017) was judged at low risk of bias, whereas the other seven studies were judged at intermediate risk of bias.

Coric (2018) published five year outcome data of a prospective randomized multicenter study (Coric, 2011), which was designed to evaluate the safety and efficacy of total disc replacement compared with ACDF in the treatment of spondylosis with radiculopathy. A total of 269 patients with symptomatic, single-level, cervical disc disease from C3 to C7 with radiculopathy were included. Patients were randomly assigned to either the ACDA or ACDF group. Outcomes reported were neck pain, disability, reoperation rate, heterotopic ossification, and ASD.

Donk (2017) conducted an RCT with nine years follow-up investigating the efficacy of anterior cervical discectomy (ACD), ACDF with cage, or ACDA treatment in patients with radiculopathy. A total of 142 patients with monoradicular signs and/or symptoms in the arm due to a herniated cervical disc were included. Patients were randomly assigned to one of the following three surgical options: fusion by cage stand-alone (ACDF), arthroplasty (ACDA) or no implant at all (ACD). In order to answer the clinical question of this module, only results from ACDA and ACDF groups were extracted. Outcomes reported were neck pain, disability, and reoperation rate.

Goedmakers (2023) reported five year outcome data of a trial (Vleggeert-Lankamp, 2019) to evaluate long-term outcomes in patients with cervical radiculopathy undergoing ACDA, ACDF or ACD treatment. A total of 109 patients with cervical radiculopathy caused by a single-level cervical disc herniation were included. Patients were randomized to one of the following treatments: ACDA, ACDF with intervertebral cage, or ACD without cage. To answer the clinical question of this module, only results from ACDA and ACDF groups were extracted. Outcomes reported were neck pain, disability, reoperation rate, and ASD.

Johansen (2021) reported five year follow-up data of a randomized clinical trial (Sundseth, 2017) to evaluate clinical outcomes at five years for arthroplasty versus fusion in patients who underwent surgical treatment for cervical radiculopathy. A total of 136 patients with C6 or C7 radiculopathy were included. Patients were randomized to one of the following two surgical treatments: arthroplasty or fusion using a stand-alone cage. Outcomes reported were neck pain, disability, reoperation rate, and ASD.

Kontakis (2022) reported ten-year outcomes of a randomized trial (Skeppholm, 2015) to investigate whether artificial disc replacement (ADR) surgery results in better long-term clinical outcomes compared to fusion surgery in patients with degenerative cervical radiculopathy. In total, 153 patients with symptoms of radiating arm pain for at least three months and correlative findings on MRI at one or two cervical levels were included. Patients were randomized to either ACDA or ACDF treatment. Outcomes reported were neck pain, disability, reoperation rate, and ASD.

Table 1 shows the study characteristics of the included studies.

Table 1: Description of included studies

Study	Design	Intervention		Comparison		Outcomes of interest reported	Follow-up
		Characteristics	**Type**	**Characteristics**	**Type**		
Goedmakers, 2019							
-Coric, 2013	RCT	n = 41 Mean age: 49.5 Men (%): 39	ACDA Bryan, KineFlexIC	n = 32 Mean age: 49.3 Men (%): 44	ACDF PEEK cage without plate	Neck pain (VAS), Disability (NDI), Reoperation rate, ASD	5 years
-Hou, 2016	RCT	n = 51 Mean age (SD): 46.3 (7.8) Men (%): 58.8	ACDA Mobi-C	n = 48 Mean age (SD): 48.5 (8.3) Men (%): 58.3	ACDF Autograft alone	Neck pain (VAS), Disability (NDI), Reoperation rate, ASD	5 years
-Janssen, 2015	RCT	n = 103 Mean age (SD): 42.1 (8.42) Men (%): 45	ACDA ProDisc-C	n = 106 Mean age (SD): 43.5 (7.15) Men (%): 46	ACDF Plate fixation	Neck pain (VAS), Disability (NDI), Reoperation rate, ASD	7 years
-Nabhan, 2007	RCT	n = 21[a] Mean age: 44[b] Men (%): 56.1[b]	ACDA ProDisc-C	n = 20[a] Mean age: 44[b] Men (%): 56.1[b]	ACDF Plate fixation	Neck pain (VAS), Reoperation rate, ASD	3 years
-Park, 2008	Retrospective	n = 21 Mean age: 45 Men (%): 52.4	ACDA Mobi-C	n = 32 Mean age: 47 Men (%): 62.5	ACDF PEEK cage without plate	Neck pain (VAS), Disability (NDI), ASD	1 year
-Sala, 2015	Prospective cohort study	n = 28 Mean age: 41 Men (%): 25	ACDA Prestige ST, Bryan or ProDisc-C	n = 27 Mean age: 41 Men (%): 33.3	ACDF PEEK cage without plate	Neck pain (VAS), ASD	2 years
-Sundseth, 2017	RCT	n = 68 Mean age: 44.7 Men (%): 47.1	ACDA Discover	n = 68 Mean age: 43.4 Men (%): 45.6	ACDF PEEK cage without plate	Neck pain (VAS), Disability (NDI), Reoperation rate, ASD	2 years *NORCAT trial*
-Zhang, 2014	RCT	n = 55 Mean age: 44.8 Men (%): 45.5	ACDA Mobi-C	n = 56 Mean age: 46.7 Men (%): 46.4	ACDF Securing with a plate	Neck pain (VAS), Disability (NDI), Reoperation rate, ASD	4 years
Coric, 2018	RCT	n = 136 Mean age (SD): 43.7 (7.76) Men (%): 37.5 <u>Affected level</u>: C3-4: 7 (5.1%) C4-5: 9 (6.6%) C5-6: 83 (61.0%) C6-7: 37 (27.2%)	ACDA KineFlexIC	n = 133 Mean age (SD): 43.9 (7.39) Men (%): 44.4 <u>Affected level</u>: C3-4: 3 (2.3%) C4-5: 6 (4.5%) C5-6: 83 (62.4%) C6-7: 41 (30.8%)	ACDF Structural allograft and an anterior plate	Neck pain (VAS), Disability (NDI), Reoperation rate, Heterotopic ossification, ASD	5 years
Donk, 2017	RCT	n = 50 Mean age (SD): 44.1 (6.4) Men (%): 48	ACDA Bryan	n = 47 Mean age (SD): 43.1 (7.5) Men (%): 53	ACDF Cage stand-alone filled with	Neck pain (VAS), Disability (NDI), Reoperation rate	9 years

		<u>Affected level</u>: C4-5: 0 C5-6: 21 (42%) C6-7: 29 (58%)		<u>Affected level</u>: C4-5: 2 (4.3%) C5-6: 19 (40.4%) C6-7: 26 (55.3%)	autologous bone		
Goedmakers, 2023	RCT	n = 35 Mean age (SD): 46.5 (8.7) Men (%): 49 Mean pain duration (SD): 44.2 (64.3) weeks <u>Affected level</u>: C5-6: 19 (54.3%) C6-7: 16 (45.7%) C7-T1: 0	ACDA ActivC	n = 36 Mean age (SD): 47.5 (8.0) Men (%): 39 Mean pain duration (SD): 55.4 (90.4) weeks <u>Affected level</u>: C5-6: 19 (52.8%) C6-7: 16 (44.4%) C7-T1: 1 (2.8%)	ACDF PEEK cage without plate	Neck pain (VAS), Disability (NDI), Reoperation rate, ASD	5 years
Johansen, 2021	RCT	n = 68 Mean age (SD): 44.7 (7.2) Men (%): 47.1 <u>Affected level</u>: C5-6: 38 (55.9%) <u>Duration of neck pain</u> No neck pain: 3 (4.5%) <3 mo: 4 (6.1%) 3 mo – 1 y: 27 (40.9%) 1-2 y: 11 (16.7%) >2 y: 21 (31.8%)	ACDA Discover	n = 68 Mean age (SD): 43.4 (6.8) Men (%): 45.6 <u>Affected level</u>: C5-6: 36 (52.9%) <u>Duration of neck pain</u> No neck pain: 2 (3.0%) <3 mo: 3 (4.5%) 3 mo – 1 y: 28 (41.8%) 1-2 y: 19 (28.4%) >2 y: 15 (22.4%)	ACDF Stand-alone cage	Neck pain (VAS), Disability (NDI), Reoperation rate, ASD	5 years *NORCAT trial*
Kontakis, 2022	RCT	n = 83 Mean age (SD): 46.9 (6.8) Men (%): 50.6	ACDA Discover	n = 70 Mean age (SD): 47.0 (6.9) Men (%): 47.1	ACDF Autologous graft and plate	Neck pain (VAS), Disability (NDI), Reoperation rate, ASD	10 years

Abbreviations: ACDA = anterior cervical disc arthroplasty; ACDF = anterior cervical discectomy and fusion; ASD = adjacent segment disease; NRS = numeric rating scale; RCT = randomized controlled trial; SD = standard deviation; VAS = visual analogue scale. [a] 41 patients in total, division between groups not clear. [b] Mean value for all participants.

Results

1. Neck pain (critical)

All studies included in Goedmakers (2019) reported on neck pain, assessed by using either visual analogue scale (VAS) or numeric rating scale (NRS) (see *Table 1*). Goedmakers (2019) presented study results at two years of follow-up, except for one study (Hou, 2016) because for this study only three-year follow-up data was available. In addition, Coric (2018), Goedmakers (2023), Johansen (2021), and Kontakis (2022) reported on VAS neck pain, and Johansen (2021) reported on NRS neck pain (*Table 1*). Data could not be pooled due to the heterogeneity in reporting of the data (median/mean) and missing dispersion measures (SE/SD). Results on neck pain are displayed in *Table 2*.

Table 2: Results on neck pain at baseline and follow-up.

Reference	Neck pain					
	Baseline		Follow-up			MD (95%CI) between groups at follow-up
	ACDA	ACDF	Period	ACDA	ACDF	
Coric, 2013	8[a]	8[a]	2 years	1.5[a]	1[a]	Not estimable
Hou, 2016	7.1[b]	7.6[b]	3 years	0.4[b]	0.5[b]	Not estimable
Janssen, 2015	7.3 ± 1.95[c]	6.6 ± 2.17[c]	2 years	2.8[c]	2.3[c]	Not estimable
Nabhan, 2007	6.0 ± 1.2	6.2 ± 0.9	2 years	1.8 ± 0.5	2.7 ± 0.4	-0.90 (-1.18 to -0.62)
Park, 2008	4.85	6.11	2 years	1.9	2	Not estimable
Sala, 2015	10	10	2 years	2	3	Not estimable
Sundseth, 2017	7.0[d]	7.0[d]	2 years	3.0[d]	3.0[d]	Not estimable
Zhang, 2014	6.7	6.6	2 years	1.8[b]	1.7[b]	Not estimable
Coric, 2018	7.71[c]	7.57[c]	5 years	2.08[c]	2.42[c]	Not estimable
Donk, 2017	4.76 ± 2.96[c]	3.95 ± 2.60[c]	5 years	2.30[b,c]	1.50[b,c]	Not estimable
Goedmakers, 2023	5.0 ± 2.7[c]	5.3 ± 2.6[c]	5 years	1.7 ± 2.5[c]	1.9 ± 2.4[c]	-0.20 (-1.46 to 1.06)
Johansen, 2021	7[a,d]	7[a,d]	5 years	2[a,d]	2[a,d]	Not estimable
Kontakis, 2022	5.7 (5.11 to 6.29)[c,e]	5.81 (5.24 to 6.39)[c,e]	10 years	3.18 (2.55 to 3.81)[c,e]	2.88 (2.20 to 3.57)[c,e]	0.30 (-0.61 to 1.21)

Values are mean (± SD) VAS scores unless stated otherwise. Abbreviations: ACDA = anterior cervical disc arthroplasty; ACDF = anterior cervical discectomy and fusion; MD = mean difference. [a] Authors reported median scores; [b] The value is estimated from the figure in articles; [c] VAS score was based on the 100- or 20-point VAS and modified (divided by 10 or 2) to fit this comparison; [d] Article reported NRS values for neck pain instead of VAS; [e] Authors reported mean (95%CI)

2. Disability (critical)

Six studies included in Goedmakers (2019) reported on disability by using NDI (*Table 1*). Goedmakers (2019) presented study results at two years of follow-up, except for one study (Hou, 2016) because for this study only three year follow-up data was available. In addition, Coric (2018), Donk (2017), Goedmakers (2023), Johansen (2021), and Kontakis (2022) reported on NDI scores. Data could not be pooled due to missing dispersion measures (SE/SD). Results on disability are presented in *Table 3*.

Table 3: Results on disability at baseline and follow-up.

Reference	Baseline		Follow-up			MD (95%CI) between groups at follow-up
	ACDA	ACDF	Period	ACDA	ACDF	
Coric, 2013	62.4	61.3	2 years	18.7	23.9	Not estimable
Hou, 2016	37[a]	37.5[a]	3 years	19[a]	18[a]	Not estimable
Janssen, 2015	53.9 ± 15.1	52.3 ± 14.5	2 years	21.88	22.53	Not estimable
Park, 2008	45.8[b]	46.9[b]	2 years	20.1[b]	16.7[b]	Not estimable
Sundseth, 2017	45.7	51.2	2 years	25.0	21.2	Not estimable
Zhang, 2014	37.4	37.8	2 years	19.0	19.3	Not estimable
Coric, 2018	62.8	61.8	5 years	18.5	23.0	Not estimable
Donk, 2017	37.6 ± 15.0[b]	37.6 ± 14.8[b]	9 years	13.4[a,b]	14.4[a,b]	Not estimable
Goedmakers,2023	55.5 ± 14.0	51.2 ± 10.7	5 years	15 ± 14	13 ± 15	2.00 (-5.41 to 9.41)
Johansen, 2021	45.9 (43.3 to 48.4)[c]	51.3 (48.1 to 54.4)[c]	5 years	22.2 (18.0 to 26.3)[c]	21.3 (17.0 to 25.6)[c]	0.90 (-4.93 to 6.73)
Kontakis, 2022	64.1 (60.4 to 67.7)[c]	61.4 (57.8 to 65.0)[c]	10 years	25.3 (20.6 to 30.0)[c]	22.4 (16.8 to 28.0)	2.90 (-4.29 to 10.09)

Values are mean (± SD) NDI scores unless stated otherwise. Abbreviations: ACDA = anterior cervical disc arthroplasty; ACDF = anterior cervical discectomy and fusion; MD = mean difference. [a] The value is estimated from the figure in articles; [b] NDI score was based on the 50-point NDI scale and modified (multiplied by 2) to fit this comparison; [c] Authors reported mean (95%CI)

3. Reoperation rate (important)

Six studies included in Goedmakers (2019), and Coric (2018), Donk (2017), Goedmakers (2023), Johansen (2021), and Kontakis (2022) reported on reoperation rate. The pooled data show reoperations in 11% (76/706) of patients in the ACDA group and in 12% (84/688) of patients in the ACDF group. *Figure 1* shows an overall risk ratio of 0.93 (95%CI 0.54 to 1.60), favoring ACDA. This difference is not clinically relevant.

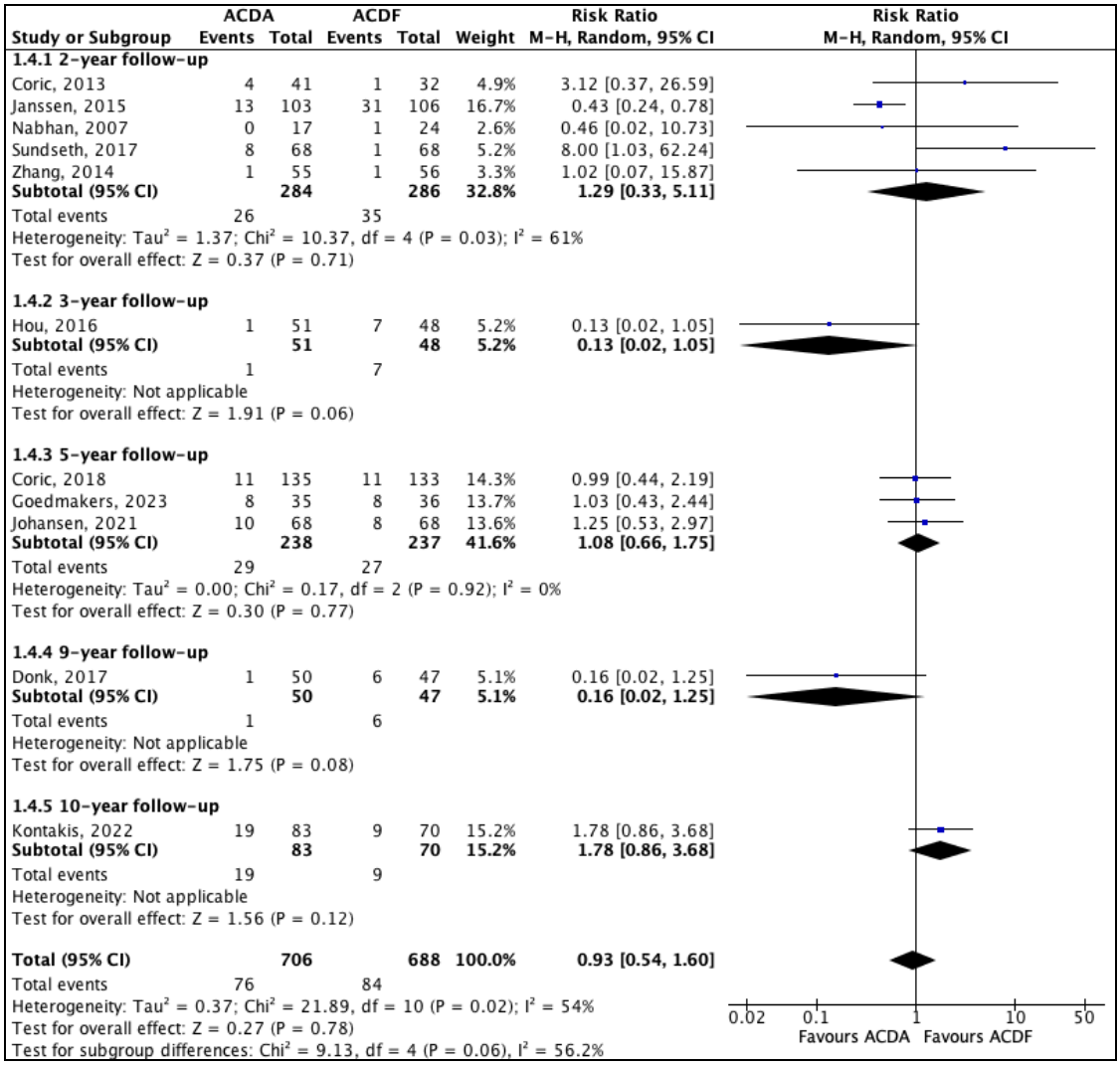

Figure 1: The effect of ACDA on reoperation rate with subgroups for follow-up.

Z: p-value of the pooled effect; df: degrees of freedom; I2: statistic heterogeneity; CI: confidence interval.

4. Adjacent Segment Disease (important)

No studies reported on radiologically evaluated Adjacent Segment Disease (ASD) based on Yang (2018). Four studies included in Goedmakers (2019) reported on the incidence of clinically evaluated ASD (Jansen, 2015; Hou, 2016; Nabhan, 2007; Zhang, 2014). Additionally, Coric (2018), Goedmakers (2023), Johansen (2021), and Kontakis (2022) reported on ASD. Results of Coric (2018) and Kontakis (2022) could not be pooled due to the heterogeneity in reporting about ASD.

Coric (2018) reported on superior and inferior level ASD after five years of follow-up, assessed by a scale ranging from 0 to 3 indicating none, mild, moderate, or severe ASD. Results are displayed in *Table 4.*

Table 4: Results on ASD after five years of follow-up.

ASD		ACDA (n=136)	ACDF (n=133)
Superior level	*No*	34.3%	6.8%
	Mild	18.6%	23.7%
	Moderate	30.0%	37.3%
	Severe	17.1%	32.2%
Inferior level	*No*	15.1%	13.2%
	Mild	30.2%	15.8%
	Moderate	30.2%	42.1%
	Severe	24.5%	28.9%

Values are percentage of patients in each ASD group. Abbreviations: ACDA = anterior cervical disc arthroplasty; ACDF = anterior cervical discectomy and fusion; ASD = adjacent segment disease.

Kontakis (2022) reported on ASD, defined as clinical adjacent-segment pathology (CASP) and radiographic adjacent-segment pathology (RASP). Authors reported CASP in 8 out of 83 (9.6%) patients in the ACDA group and in 7 out of 70 (10%) patients in the ACDF group. Risk ratio was 0.96 (95%CI 0.37 to 2.53) in favor of ACDA treatment, which was not considered clinically relevant. Also, RASP progressed from grade 2.6 at baseline to grade 3.8 after 10 years in the ACDA group compared with 2.7 to 3.6 in the ACDF group.

The pooled data show ASD in 1.8% (6/329) of patients in the ACDA group and in 4.4% (15/318) of patients in the ACDF group. *Figure 2* shows an overall risk ratio of 0.52 (95%CI 0.21 to 1.31), favoring ACDA. This difference is clinically relevant.

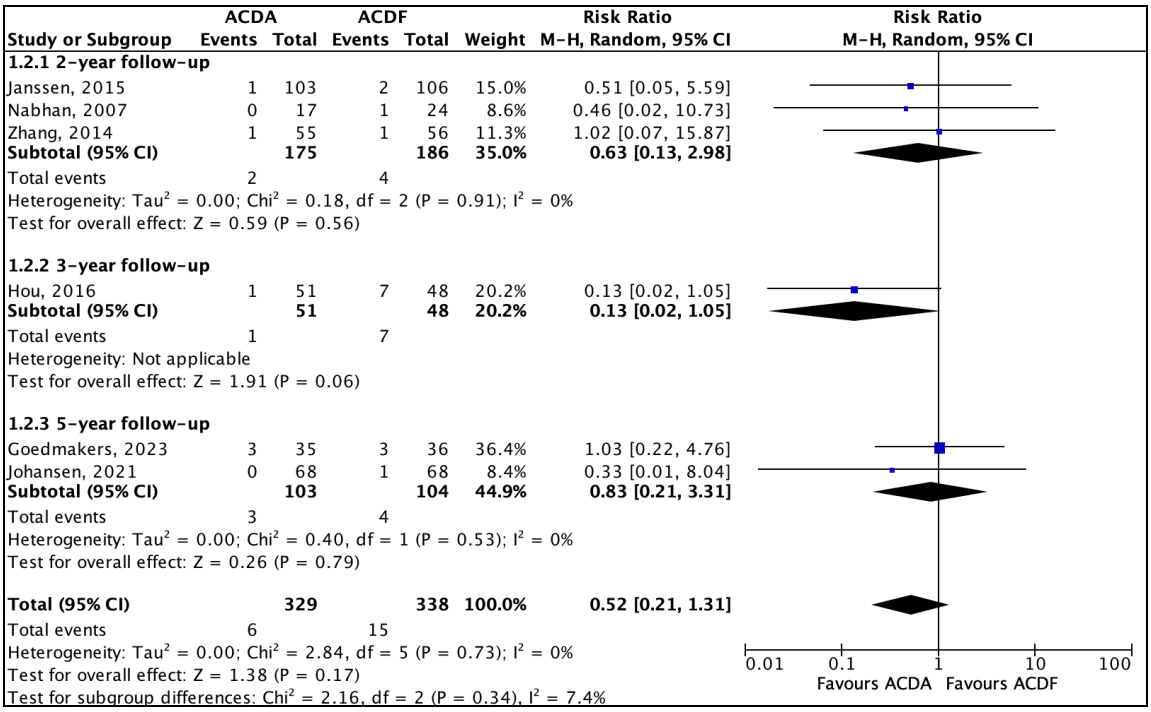

Figure 2: The effect of ACDA on ASD incidence with subgroups for follow-up.

Z: p-value of the pooled effect; df: degrees of freedom; I2: statistic heterogeneity; CI: confidence interval.

5. Heterotopic ossification (important)

Goedmakers (2019) did not report on HO. Four studies reported on radiologically evaluated heterotopic ossification (HO) in the ACDA group based on Yang (2018). Hou (2016) and Park (2008) reported no participants with HO in the intervention group, whereas Zhang (2014) reported a HO incidence of 32.7% (18/55 participants) in the intervention group. Coric

(2013), Janssen (2015), Nabhan (2007), and Sala (2015) did not report on radiologically evaluated HO.

One study (Coric, 2018) reported on HO, defined as different stages of ossification (adapted from the McAfee scale). Preoperatively, 26.4% of patients had no HO, 44.2% of patients had mild HO, 14.7% of patients had moderate HO, and 14.7% had severe HO. At 5-year follow-up, 37.7% of patients had no HO, 27.5% of patients had mild HO, 8.7% of patients had moderate HO, 23.2% of patients had severe HO, and 2.9% of patients had bridging HO.

Level of evidence of the literature

1. Neck pain

The level of evidence regarding neck pain was downgraded by two levels to *low* because of study limitations (risk of bias: -1) and the lack of reporting (means and) dispersion measures (imprecision: -1).

2. Disability

The level of evidence regarding disability was downgraded by two levels to *low* because of study limitations (risk of bias: -1) and the lack of reporting (means and) dispersion measures (imprecision: -1).

3. Reoperation rate

The level of evidence regarding reoperation rate was downgraded by three levels to *very low* because of study limitations (risk of bias: -1), conflicting results (inconsistency: -1) and because the confidence interval is crossing both borders of clinical relevance (imprecision: -1).

4. ASD

The level of evidence regarding ASD was downgraded by three levels to *very low* because of study limitations (risk of bias: -1) and because the confidence interval is crossing both borders of clinical relevance (imprecision: -2).

5. Heterotopic ossification

The level of evidence regarding heterotopic ossification was downgraded by three levels to *very low* because of study limitations (risk of bias: -1) and the low number of included patients and the lack of reporting dispersion measures (imprecision: -2).

Conclusions

1. Neck pain (crucial)

Low GRADE	ACDA may result in little to no difference in neck pain when compared to ACDF in patients with cervical radiculopathy. *Source: Goedmakers, 2019*; Coric, 2018; Goedmakers, 2023; Johansen, 2021; Kontakis, 2022.* **Including: Coric, 2013; Hou, 2016; Janssen, 2015; Nabhan, 2007; Park, 2008; Sala, 2015; Sundseth, 2017; Zhang, 2014.*

2. Disability (crucial)

Low GRADE	ACDA may result in little to no difference in disability when compared to ACDF in patients with cervical radiculopathy. *Source: Goedmakers, 2019*; Coric, 2018; Donk, 2017; Goedmakers, 2023; Johansen, 2021; Kontakis, 2022.* **Including: Coric, 2013; Hou, 2016; Janssen, 2015; Park, 2008; Sundseth, 2017; Zhang, 2014.*

3. Reoperation rate (important)

Very low GRADE	The evidence is very uncertain about the effect of ACDA on reoperation rate when compared with ACDF in patients with cervical radiculopathy. *Source: Goedmakers, 2019*; Coric, 2018; Donk, 2017; Goedmakers, 2023; Johansen, 2021; Kontakis, 2022.* **Including: Coric, 2013; Hou, 2016; Janssen, 2015; Nabhan, 2007; Sundseth, 2017; Zhang, 2014.*

4. ASD (important)

Very low GRADE	The evidence is very uncertain about the effect of ACDA on ASD when compared with ACDF in patients with cervical radiculopathy. *Source: Goedmakers, 2019*; Coric, 2018; Goedmakers, 2023; Johansen, 2021; Kontakis, 2022.* **Including: Hou, 2016; Janssen, 2015; Nabhan, 2007; Zhang, 2014.*

5. Heterotopic ossification (important)

Very low GRADE	The evidence is very uncertain about the effect of ACDA on heterotopic ossification when compared with ACDF in patients with cervical radiculopathy. *Source: Coric, 2018.*

Overwegingen – van bewijs naar aanbeveling

Voor- en nadelen van de interventie en de kwaliteit van het bewijs

Het doel van deze uitgangsvraag was om te achterhalen wat de effectiviteit is van ACDP in vergelijking met ACDF bij patiënten met CRS. In totaal is er één systematische review (met acht RCTs) en zijn er vijf RCTs gevonden die ACDP vergeleken met ACDF. De studies hadden methodologische beperkingen en spreidingsmaten werden nauwelijks gerapporteerd waardoor de klinische relevantie niet kon worden beoordeeld. De bewijskracht voor de kritieke uitkomstmaten (nek pijn en functioneren) was *laag*. Dit betekent dat andere studies kunnen leiden tot nieuwe inzichten. Daarom kunnen er op basis van de literatuur geen harde conclusies worden geformuleerd.

Bij zowel ACDF als ACDP wordt de totale discus vervangen voor een prothese. Bij ACDF wordt een fusie van twee segmenten nagestreefd, terwijl er bij ACDP een prothese wordt geplaatst, die de normale beweeglijkheid van een niet degeneratief segment nabootst. Dit heeft als theoretisch voordeel dat de normale biomechanica van de nek behouden zou blijven en daarmee versnelde degeneratie van boven en onderliggende segmenten voorkomen zou kunnen worden. In de literatuur komt dit voordeel echter niet naar voren. Meerdere RCT's laten zowel op korte, als lange termijn geen voordeel zien van de discusprothese boven de cage-plaatsing en fusie (Donk, 2017; Goedmakers, 2019; Vleggeert-Lankamp, 2019). Dit geldt voor alle meegenomen uitkomstmaten, namelijk nek pijn, disability, re-operaties en adjacent segment disease (ASD).

Van ASD wordt juist een verschil verwacht ten gunste van de discusprothese. Dat dit verschil in de literatuur niet wordt gevonden, kan komen door een verschijnsel wat heterotope ossificatie wordt genoemd, waardoor bot ter plaatse van de discusprothese de mobiliteit van de discusprothese wegneemt en het voordeel verloren gaat. Heterotope ossificatie wordt in de literatuur gevonden bij ongeveer driekwart van de patiënten (Coric, 2018; Goedmakers, 2019; Yang, 2018). Mogelijkerwijs speelt de manier van implantatie hierbij een rol. Het wegnemen van osteofyten kan leiden tot aviveren van bot en daarmee fusie en heterotope ossificatie in de hand werken. Er zijn geen studies die deze theorie ondersteunen. Daarnaast blijft de vraag bestaan of ASD een daadwerkelijk bestaande entiteit is, of eerder een radiologische diagnose of zelfs een normale ontwikkeling van de degeneratie. In deze gevallen zou het voorkomen van ASD klinisch zinloos zijn. Helaas zijn de studiepopulaties in de gevonden RCT's te klein om hier uitspraken over te kunnen doen. Of discusprotheses voordelen hebben bij subgroepen patiënten, bijvoorbeeld jongere patiënten, komt eveneens niet uit de literatuur naar voren.

Waarden en voorkeuren van patiënten (en evt. hun verzorgers)

Het is wenselijk dat de pijn in de nek zo minimaal mogelijk is en dat de nek zo maximaal mogelijk functioneel is. Qua ervaren pijn, hersteltijd en/of complicaties laat de literatuur geen klinisch relevante verschillen zien. Voor patiënten is dan ook een goede en volledige toelichting van de operatie essentieel.

Kosten (middelenbeslag)

Over de kosteneffectiviteit van ACDF in vergelijking met ACDP bestaat in de literatuur discussie (Schuermans, 2022). De initiële chirurgische kosten zijn hoger bij ACDP dan bij ACDF, door verschil in kosten van het gebruikte implantaat. In theorie zou het gebruik van een discusprothese op lange termijn kosteneffectief kunnen worden, als het gebruik van de discusprothese adjacent segment disease (ASD) voorkomt en daarmee leidt tot minder re-operaties. Tevens zou de discusprothese voordeliger zijn als het zou leiden tot een betere kwaliteit van leven. De literatuur over de kosteneffectiviteit van ACDF in vergelijking met ACDP is schaars en heterogeen.

Schuermans (2022) stelt dat er geen verschil in QALY´s bestaat tussen de ACDF en ACDP, maar dat de geïncludeerde studies erg heterogeen zijn en hierdoor geen conclusies kunnen worden getrokken over de kosteneffectiviteit, zeker op lange termijn. De auteurs pleitten voor nieuwe kosteneffectiviteitsstudies.

Heijdra Suasnabar (2023) stelt in een studie naar kosteneffectiviteit van ACDP in vergelijking met ACDF, dat ACDF resulteerde in een betere kosteneffectiviteit van ACDF, gezien de lagere initiële kosten van operatie en gelijke uitkomsten bij 2-jaar follow up duur. Gezien deze studie zich baseerde op de data van de NECK- trial (Vleggeert-Lankamp, 2019) en de 5-jaars follow-up van deze trial geen andere uitkomsten lieten zien (Goedmakers, 2019), zowel ten aanzien van klinische/radiologische uitkomsten als ten aanzien van het aantal re-operaties, verwacht de werkgroep geen ander beeld van de kosteneffectiviteit op deze 5-jaars cijfers zouden worden gebaseerd.

Zes studies rapporteerde re-operatiecijfers (Coric, 2018; Donk, 2017; Goedmakers, 2019; Goedmakers, 2023; Johansen, 2021; Kontakis, 2022). Gepoolde data tonen geen voordeel van ACDP boven ACDF op het gebied van re-operaties. Ook de RCT´s met langere follow-up tonen geen voordeel van ACDP ten opzichte van ACDF, iets wat wel nodig zou zijn om de discusprothese kosteneffectief te maken (Donk, 2017; Kontakis, 2022). Kontakis (2022) is de enige RCT die 10-jaars resultaten heeft gepubliceerd. In deze studie ondergingen 19 patiënten in de ACDP groep en 9 in de ACDF groep een re-operatie. De meeste re-operaties gebeurde binnen 5 jaar na de initiële operatie in de ACDP groep, wegens loslating en subsidence van het implantaat. Dit kan de data mogelijk onterecht negatief kleuren op het gebied van re-operaties bij ACDP patiënten. Echter ondergingen in totaal 8 patiënten in de ACDP groep en 7 patiënten in de fusie groep een operatie vanwege ASD in deze studie, waardoor ook hier geen voordeel van de ACDP boven de ACDF wordt gezien. Donk (2017) liet met een gemiddelde follow up van 9 jaar, re-operatie zien wegens ASD bij 5 patiënten van de ACDF groep en in geen een patiënt in de ACDA groep, dit verschil was niet statistisch significant.

In de literatuur wordt dus geen klinisch voordeel van ACDP boven ACDF gezien dat kan compenseren voor de hogere kosten van ACDP in vergelijking met de ACDF.

<u>Aanvaardbaarheid, haalbaarheid en implementatie</u>

De werkgroep verwacht een brede acceptatie van deze aanbeveling omdat de aanbeveling aansluit bij de huidige klinische praktijk in Nederland.

Aanbevelingen

<u>Rationale van de aanbeveling: weging van argumenten voor en tegen de interventies</u>

Gezien de huidige literatuur bestaat er geen klinisch voordeel van het plaatsen van een kostbare discusprothese (ACDP), dus adviseert de werkgroep geen discusprothese te implanteren bij patiënten met CRS. De anterieure cervicale discectomie en fusie (ACDF) heeft de voorkeur indien tot een anterieure discectomie besloten wordt in deze patiëntengroep.

Implanteer geen discusprothese (ACDP) bij patiënten met CRS, indien een chirurgische behandeling geïndiceerd is.

Literatuur

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Bijlagen bij module 'ACDP versus ACDF'

Implementatieplan

Aanbeveling	Tijdspad voor implementatie: < 1 jaar, 1 tot 3 jaar of > 3 jaar	Verwacht effect op kosten	Randvoorwaarden voor implementatie (binnen aangegeven tijdspad)	Mogelijke barrières voor implementatie[1]	Te ondernemen acties voor implementatie[2]	Verantwoordelijken voor acties[3]	Overige opmerkingen
Alle aanbevelingen	<1 jaar	Beperkt	*Bekendheid met de richtlijn. *Bekendheid met chirurgische techniek.	Geen	*Verspreiden en publicatie van de richtlijn. *Optimaliseren kennis en vaardigheden bij zorgverleners.	*Beroepsverenigingen. *Betrokken zorgverleners.	n.v.t.

[1] Barrières kunnen zich bevinden op het niveau van de professional, op het niveau van de organisatie (het ziekenhuis) of op het niveau van het systeem (buiten het ziekenhuis). Denk bijvoorbeeld aan onenigheid in het land met betrekking tot de aanbeveling, onvoldoende motivatie of kennis bij de specialist, onvoldoende faciliteiten of personeel, nodige concentratie van zorg, kosten, slechte samenwerking tussen disciplines, nodige taakherschikking, etc.

[2] Denk aan acties die noodzakelijk zijn voor implementatie, maar ook acties die mogelijk zijn om de implementatie te bevorderen. Denk bijvoorbeeld aan controleren aanbeveling tijdens kwaliteitsvisitatie, publicatie van de richtlijn, ontwikkelen van implementatietools, informeren van ziekenhuisbestuurders, regelen van goede vergoeding voor een bepaald type behandeling, maken van samenwerkingsafspraken.

[3] Wie de verantwoordelijkheden draagt voor implementatie van de aanbevelingen, zal tevens afhankelijk zijn van het niveau waarop zich barrières bevinden. Barrières op het niveau van de professional zullen vaak opgelost moeten worden door de beroepsvereniging. Barrières op het niveau van de organisatie zullen vaak onder verantwoordelijkheid van de ziekenhuisbestuurders vallen. Bij het oplossen van barrières op het niveau van het systeem zijn ook andere partijen, zoals de NZA en zorgverzekeraars, van belang.

Evidence table

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Goedmakers 2019 PS., study characteristics and results are extracted from the SR (unless stated otherwise)	SR and meta-analysis of RCTs and cohorts *Literature search up to August 2017* **A**: Coric, 2013 **B**: Hou, 2016 **C**: Janssen, 2015 **D**: Nabhan, 2007 **E**: Park, 2008 **F**: Sala, 2015 **G**: Sundseth, 2017 **H:** Zhang, 2014 Study design: **A**: RCT **B**: RCT **C**: RCT **D**: RCT **E**: Retrospective **F**: Prospective cohort **G**: RCT **H**: RCT Setting and Country: Not reported. Source of funding and conflicts of interest:	Inclusion criteria SR: - The study compares ACDF to ACDA in one-level anterior discectomy. - The study includes at least twenty patients in each treatment arm. - The study provides follow-up data for at least 2 years. - The study measures primary or secondary outcome in either the NDI or VAS neck pain. - The study only includes patients suffering from radiculopathy, excluding patients suffering from myelopathy. - The article is not a meeting abstract. Exclusion criteria SR: Not specifically reported. *8 studies included* Important patient characteristics at baseline: N, mean age ± SD **A**: *ACDA*: 41, 49,5 *ACDF*: 32, 49,3 **B**: *ACDA*: 51, 46,3 ± 7,8 *ACDF*: 48, 48,5 ± 8,3 **C**: *ACDA*: 103, 42,1 ± 8,4 *ACDF*: 106, 43,5 ± 7,1 **D:** *ACDA*: 21*, 44[a]	Describe intervention: **A**: ACDA; Bryan, KineFlexIC prosthetic device **B**: ACDA; Mobi-C prosthetic device **C**: ACDA; ProDisc-C prosthetic device **D**: ACDA; ProDisc-C prosthetic device **E**: ACDA; Mobi-C prosthetic device **F**: ACDA; Prestige ST, Bryan or ProDisc-C prosthetic device **G**: ACDA; Discover prosthetic device **H**: ACDA; Mobi-C prosthetic device	Describe control: **A**: ACDF with plate fixation **B**: ACDF methods using autograft **C**: ACDF with plate fixation **D**: ACDF with plate fixation **E**: PEEK cage without plate fixation **F**: PEEK cage without plate fixation **G**: PEEK cage without plate fixation **H**: ACDF with plate fixation	Endpoint of follow-up: **A**: 5 years **B**: 5 years **C**: 7 years **D**: 3 years **E**: 1 year **F**: 2 years **G**: 2 years **H**: 4 years For how many participants were no complete outcome data available? The only thing that is reported is that outcome reporting on the level of reoperation is rather incomplete.	Disability Defined as neck disability index (NDI) (0-100) **A**: *ACDA*: 18,7 *ACDF*: 23,9 **B**: *ACDA*: 19[a,c] *ACDF*: 18[a,c] **C**: *ACDA*: 21,88 *ACDF*: 22,53 **D**: *ACDA*: NA *ACDF*: NA **E**: *ACDA*: 20,1[e] *ACDF*: 16,7[e] **F**: *ACDA*: NA *ACDF*: NA **G**: *ACDA*: 25,0 *ACDF*: 21,2 **H**: *ACDA*: 19,0 *ACDF*: 19,3 Neck pain Defined as visual analogue scale (VAS) (0-10) neck pain **A**: *ACDA*: 1,5[d] *ACDF*: 1[d] **B**: *ACDA*: 0,4[a,c] *ACDF*: 0,5[a,c] **C**: *ACDA*: 2,8[b] *ACDF*: 2,3[b] **D**: *ACDA*: 1,8 ± 0,5 *ACDF*: 2,7 ± 0,4 **E**: *ACDA*: 1,9 *ACDF*: 2 **F**: *ACDA*: 2 *ACDF*: 3 **G**: *ACDA*: 3,0[f] *ACDF*: 3,0[f]	Risk of bias (high, some concerns or low): Tool used by authors: Adjusted version of the checklist for cohort studies of the Dutch Cochrane Center **A**: Some concerns **B**: Some concerns **C**: Some concerns **D**: Some concerns **E**: High risk of bias **F**: Some concerns **G**: Low risk of bias **H**: High risk of bias Author's conclusion: The results of ACDF and ACDA do not differ in the treatment of cervical radiculopathy. Limitations: - The majority of included studies used a combined success score to define which treatment arm performed better. This included an evaluation conducted by the investigator for muscle strength, sensory assessments and reflex assessments, which are prone to bias (not mentioned if these investigators were

	The majority of studies received industry sponsoring and authors reported extensive disclosures.	*ACDF*: 20*, 44[a] **E**: *ACDA*: 21, 45 *ACDF*: 32, 47 **F**: *ACDA*: 28, 41 *ACDF*: 27, 41 **G**: *ACDA*: 68, 44,7 *ACDF*: 68, 43,4 **H**: *ACDA*: 55, 44,8 *ACDF*: 56, 46,7 <u>*Sex (%Male)*</u>*:* **A**: *ACDA*: 39% *ACDF*: 44% **B**: *ACDA*: 58,8% *ACDF*: 58,3% **C**: *ACDA*: 45% *ACDF*: 46% **D:** *ACDA*: 56,1%[a] *ACDF*: 56,1%[a] **E**: *ACDA*: 52,4% *ACDF*: 62,5% **F**: *ACDA*: 25% *ACDF*: 33,3% **G**: *ACDA*: 47,1% *ACDF*: 45,6% **H**: *ACDA*: 45,5% *ACDF*: 46,4% * 41 patients in total, division between groups is not clear [a] Mean value for all participants <u>Groups comparable at baseline</u>? Yes				**H**: *ACDA*: 1,8[a] *ACDF*: 1,7[a] NA: information not available [a] The value is estimated from the figure in articles. [b] VAS score was based on the 100- or 20-point VAS and modified (divided by 10 or 2) to ft this comparison. [c] Three-year follow-up results, as the two-year follow-up was not available. [d] Authors reported the median VAS scores. [e] NDI score was based on the 50-point NDI scale and modified (multiplied by 2) to fit this comparison. [f] Article reported NRS values for neck pain instead of VAS. <u>Reoperation rate</u> Defined as the number of reoperations **A**: *ACDA*: 4/41 *ACDF*: 1/32 **B**: *ACDA*: 1/51 *ACDF*: 7/48 **C**: *ACDA*: 13/103 *ACDF*: 31/106 **D**: *ACDA*: 0/17 *ACDF*: 1/24 **E**: *ACDA*: NA *ACDF*: NA **F**: *ACDA*: NA *ACDF*: NA **G**: *ACDA*: 8/68 *ACDF*: 1/68 **H**: *ACDA*: 1/55* *ACDF*: 1/56* * Concerning the same patient	blinded). <u>Level of evidence</u>: *Disability*: Low (risk of bias, inconsistency, no dispersion measures reported in majority of studies) *Neck pain*: Moderate (risk of bias, no dispersion measures reported in majority of studies) *Reoperation rate*: Not reported. *Complications*: Not reported. No heterogeneity tests were performed because the data were not pooled.

						Complications Defined as ASD incidence **A**: *ACDA*: NA *ACDF*: NA **B**: *ACDA*: 1/51 *ACDF*: 7/48 **C**: *ACDA*: 1/103 *ACDF*: 2/106 **D**: *ACDA*: 0/17 *ACDF*: 1/24 **E**: *ACDA*: NA *ACDF*: NA **F**: *ACDA*: NA *ACDF*: NA **G**: *ACDA*: NA *ACDF*: NA **H**: *ACDA*: 1/55* *ACDF*:1/56* * Concerning the same patient	
Coric, 2018	Type of study: RCT Setting and country: Multicenter study in the USA Funding and conflicts of interest: SpinalMotion Inc. Conflicts of interests are declared.	Inclusion criteria: - Failure of at least 6 months of nonoperative care or progressive symptoms, signs of nerve root compression, and a score of at least 40 on the NDI Exclusion criteria: - Severe facet degeneration - Bridging osteophytes - Prior cervical fusion - Severe myelopathy N total at baseline: Intervention: 136 Control: 133 Important prognostic factors[2]: *Age ± SD:* *I:* 43.7 (7.76) *C:* 43.9 (7.39)	Describe intervention: ACDA KineFlexIC prosthetic device	Describe control: ACDF Structural allograft and an anterior plate	Length of follow-up: 5 years Loss-to-follow-up: Intervention: 31.6% Reasons not reported Control: 37.6% Reasons not reported Incomplete outcome data: Not reported, except loss to follow-up as reported above.	Outcome measures and effect size **Neck pain (VAS)** I: 2.08 C: 2.42 **Disability (NDI)** I: 18.5 C: 23.0 **Reoperation rate** I: 11/135 C: 11/133 **Heterotopic ossification** No: 37.7% Mild: 27.5% Moderate: 8.7% Severe: 23.2% Bridging: 2.9%	Author's conclusion: This study confirms ACDA as a viable alternative to ACDF for the treatment of single-level radiculopathy.

		Sex (%male): *I:* 37.5% *C:* 44.4% Groups comparable at baseline? Yes					
Donk, 2017	Type of study: RCT Setting and country: Canisius Wilhelmina Hospital, Department of Neurosurgery, Nijmegen, the Netherlands Funding and conflicts of interest: No funding No competing interests exist.	Inclusion criteria: - Adults between 18-55 years - Monoradicular signs and/or symptoms in the arm due to a herniated cervical intervertebral disc and/or an osteophyte at MRI. Exclusion criteria: - History of any cervical spine surgery. N total at baseline: Intervention: 50 Control: 47 Important prognostic factors[2]: *Age ± SD:* *I:* 44.1 (6.4) *C:* 43.1 (7.5) *Sex (%male):* *I:* 48% *C:* 53% Groups comparable at baseline? Yes	Describe intervention: ACDA Bryan prosthetic device	Describe control: ACDF Cage stand-alone filled with autologous bone	Length of follow-up: 9 years Loss-to-follow-up: Intervention: 1/50 Reason: decreased due to cause unrelated to trial Control: 1/47 Reason: contact was lost Incomplete outcome data: Not reported, except loss to follow-up as reported above.	Outcome measures and effect size **Neck pain (VAS)** I: 2.30 C: 1.50 **Disability (NDI)** I: 13.4 C: 14.4 **Reoperation rate** I: 1/50 C: 6/47	Author's conclusion: No difference between the surgical modalities for treating single-level degenerative disc disease could be detected.
Goedmakers, 2023	Type of study: RCT Setting and country: Multicenter	Inclusion criteria: - Patients aged 18-65 years - Radicular signs and symptoms in one or both arms for at least 8 weeks - Conservative therapy failed	Describe intervention: ACDA ActivC prosthetic device	Describe control: ACDF PEEK cage without plate	Length of follow-up: 5 years Loss-to-follow-up: 20 Reason: one patient died, no other reasons	Outcome measures and effect size **Neck pain (VAS)** I: 1.7 (2.5) C: 1.9 (2.4) **Disability (NDI)**	Author's conclusion: Implanting a disc prosthesis cannot prevent adjacent level disease.

	study in the Netherlands Funding and conflicts of interest: Grant Braun Medical; Grant CSRS-Europe. One or more of the authors declare financial or professional relationships on ICMJE-TSJ disclosure forms.	- MRI confirmed single level cervical disc herniation, with or without accompanying osteophyte, at one level. Exclusion criteria: - Previous cervical surgery - Absence of motion - Increased anteroposterior translation - Very narrow intervertebral space - Severe segmental kyphosis - Neck pain only or symptoms and signs of myelopathy. N total at baseline: Intervention: 35 Control: 36 Important prognostic factors[2]: *Age ± SD:* *I:* 46.5 (8.7) *C:* 47.5 (8.0) *Sex (%male):* *I:* 49% *C:* 39% Groups comparable at baseline? Yes			mentioned. Incomplete outcome data: 2 (additional surgery on the cervical spine) Reason: 1 patient changed phone numbers and could not be contacted.	I: 15 (14) C: 13 (15) **Reoperation rate** I: 8/35 C: 8/36 **ASD** I: 3/35 C: 3/36	
Johansen, 2021	Type of study: RCT Setting and country: 5 neurosurgical departments in Norway Funding and	Inclusion criteria: - Age between 25 and 60 years - Clinical C6 or C7 radiculopathy with corresponding radiological findings - NDI ≥30% - No response to non-operative treatment	Describe intervention: ACDA Discover prosthetic device	Describe control: ACDF Stand-alone cage	Length of follow-up: 5 years Loss-to-follow-up: Intervention: 7/68 Reasons: not reported Control: 11/68 Reasons: not reported	Outcome measures and effect size **Neck pain (VAS)** I: 2 C: 2 **Disability (NDI)** I: 22.2 (18.0 to 26.3) C: 21.3 (17.0 to 25.6) **Reoperation rate**	Author's conclusion: This study found similar efficacy and reoperation rates after arthroplasty versus fusion. Both treatment options are equally good for treating cervical radiculopathy.

	conflicts of interest: Unconditional grant from DePuy Synthes Spine. No conflicts of interest reported.	- No clinical improvement during six weeks prior to surgery Exclusion criteria: - Significant spondylosis involving more than one level - Adjacent level ankylosis - Intramedullary changes on MRI - Myelopathy N total at baseline: Intervention: 68 Control: 68 Important prognostic factors[2]: *Age ± SD:* *I:* 44.7 (7.2) *C:* 43.4 (6.8) *Sex (%male):* *I:* 47.1% *C:* 45.6% Groups comparable at baseline? Yes			Incomplete outcome data: Intervention: 2 Reasons: attended follow-up without returning questionnaire (n=1), did not attend follow-up (n=1). Control: 2 Reasons: attended follow-up without returning questionnaire (n=2).	I: 10/68 C: 8/68 **ASD** I: 0/68 C: 1/68	
Kontakis, 2022	Type of study: RCT Setting and country: Multicenter trial at three Swedish study centers. Funding and conflicts of interest: DePuy Synthes provided an	Inclusion criteria: - Age between 25-60 years - Symptoms of radiating arm pain for ≥3 months - Correlative findings on MRI at 1 or 2 cervical levels - Eligibility for both treatments - Ability to read and understand Swedish. Exclusion criteria: - Previous cervical spine surgery	Describe intervention: ACDA Discover prosthetic device	Describe control: ACDF Autologous graft and plate	Length of follow-up: 10 years Loss-to-follow-up: 10 participants Reasons not reported Incomplete outcome data: Not reported, except loss to follow-up as above.	Outcome measures and effect size **Neck pain (VAS)** I: 3.18 (2.55 to 3.81) C: 2.88 (2.20 to 3.57) **Disability (NDI)** I: 25.3 (20.6 to 30.0) C: 22.4 (16.8 to 28.0) **Reoperation rate** I: 19/83 C: 9/70 **ASD**	Author's conclusion: Patient-reported outcome measures were similar for both treatment groups but there were more reoperations in the arthroplasty group due to implant loosening.

	unrestricted grant. No conflicts of interest reported.	- >2 cervical levels requiring treatment - Severe facet arthropathy symptoms or marked radiological signs of myelopathy - Drug abuse - Dementia or expected poor compliance - Cervical malformation or marked instability - History of severe cervical trauma - Pregnancy - Rheumatoid arthritis, - Malignancy - Active infection or other systemic disease - Known allergy to an implant material or NSAIDs. <u>N total at baseline</u>: Intervention: 83 Control: 70 <u>Important prognostic factors[2]</u>: *Age ± SD:* *I:* 46.9 (6.8) *C:* 47.0 (6.9) *Sex (%male):* *I:* 50.6% *C:* 47.1% Groups comparable at baseline? Yes				*CASP* I: 8/83 C: 7/70 *RASP* I: 3.8 C: 3.6	

Risk of bias table

Study reference	Was the allocation sequence adequately generated?	Was the allocation adequately concealed?	Blinding: Was knowledge of the allocated interventions adequately prevented? Were patients/healthcare providers/ data collectors/outcome assessors/data analysts blinded?	Was loss to follow-up (missing outcome data) infrequent?	Are reports of the study free of selective outcome reporting?	Was the study apparently free of other problems that could put it at a risk of bias?	Overall risk of bias If applicable/ necessary, per outcome measure
Coric, 2018	Probably yes Reason: Randomization using a 1:1 ratio	No information	Probably no Reason: Single-blinded (only participants)	Probably no Reason: Percentage of patients lost to follow-up increased by the 5-year follow-up. Follow-up rates are similar to those of another study with a follow-up period of 5 years.	Definitely yes Reason: Registered at ClinicalTrials.gov (NCT00374413). Primary and secondary outcomes are reported as pre-specified in the register.	Definitely yes Reason: No other problems noted.	SOME CONCERNS
Donk, 2017	Probably yes Reason: Randomization using a 1:1:1 ratio	Definitely yes Reason: Closed envelopes were used, which were delivered by an independent co-worker.	Definitely no Reason: Double-blind trial, but participants were not blinded.	Probably yes Reason: Two patients were lost to follow-up. Missing data were not imputed.	Definitely yes Reason: Trial is registered (ISRCTN41681847). Primary and secondary outcomes are reported as pre-specified in the register, except for short-term outcomes at 3 months and 1 year.	Probably no Reason: - Trial was ended before reaching the calculated sample size. - Protocol deviation by adapting the maximum age.	HIGH
Goedmakers, 2023	Definitely yes Reason: Randomization in a 1:1:1 ratio using variable block sizes. Allocation was stratified by center.	Definitely yes Reason: Prepared, opaque, coded and sealed envelopes were used. After induction of anaesthesia, the envelope was opened. Patients and research nurses were blinded to the allocated treatment.	Definitely yes Reason: Double-blind trial, patients, nurses and researchers remained blinded for two years. After follow-up of two years, patients were unblinded.	Definitely yes Reason: Numbers of participants lost to follow-up are equal between the different treatment groups. Groups were compared based on an ITT analysis.	Probably yes Reason: Trial is registered (NTR1289), but not available.	Definitely yes Reason: No other problems noted.	LOW
Johansen, 2021	Definitely yes Reason: Web-based randomization	Definitely yes Reason: Central allocation	Probably yes Reason: Single-blinded trial, patients were blinded until 2- or 5-year follow-up, surgical team was blinded until nerve root	Probably yes Reason: Numbers of participants lost to follow-up are equal between the different treatment groups.	Definitely yes Reason: Trial is registered at ClinicalTrials.gov (NCT00735176). Primary and secondary outcomes are	Probably yes Reason: The surgeon's opinion may have influenced the decision whether to reoperate	LOW

			decompression was completed.	No imputation methods used.	reported as pre-specified in the register.	because no well- or predefined criteria were composed beforehand.	
Kontakis, 2022	Probably no Reason: Randomization, not further stated	No information	Probably yes Reason: Both the participant and surgeon were blinded until decompression was completed and the instruments to perform surgery were prepared.	Definitely no Reason: Participants were lost to follow-up at 10 years.	Definitely yes Reason: Trial is registered (ISRCTN44347115). Primary and secondary outcomes are reported as pre-specified in the register.	Definitely yes Reason: No other problems noted.	**HIGH**

Table of excluded studies

Reference	Reason for exclusion
Vleggeert-Lankamp CLA, Janssen TMH, van Zwet E, Goedmakers CMW, Bosscher L, Peul W, Arts MP. The NECK trial: Effectiveness of anterior cervical discectomy with or without interbody fusion and arthroplasty in the treatment of cervical disc herniation; a double-blinded randomized controlled trial. Spine J. 2019 Jun;19(6):965-975. doi: 10.1016/j.spinee.2018.12.013. Epub 2018 Dec 21. PMID: 30583108.	5-year follow-up data is available and included (Goedmakers, 2023)
Gutman G, Rosenzweig DH, Golan JD. Surgical Treatment of Cervical Radiculopathy: Meta-analysis of Randomized Controlled Trials. Spine (Phila Pa 1976). 2018 Mar 15;43(6):E365-E372. doi: 10.1097/BRS.0000000000002324. PMID: 28700452.	Less complete/in accordance with PICO compared to Goedmakers (2019)
Latka D, Kozlowska K, Miekisiak G, Latka K, Chowaniec J, Olbrycht T, Latka M. Safety and efficacy of cervical disc arthroplasty in preventing the adjacent segment disease: a meta-analysis of mid- to long-term outcomes in prospective, randomized, controlled multicenter studies. Ther Clin Risk Manag. 2019 Mar 28;15:531-539. doi: 10.2147/TCRM.S196349. PMID: 30992666; PMCID: PMC6445235.	Less complete/in accordance with PICO compared to Goedmakers (2019)
MacDowall A, Skeppholm M, Lindhagen L, Robinson Y, Olerud C. Effects of preoperative mental distress versus surgical modality, arthroplasty, or fusion on long-term outcome in patients with cervical radiculopathy. J Neurosurg Spine. 2018 Oct;29(4):371-379. doi: 10.3171/2018.2.SPINE171378. Epub 2018 Jul 13. PMID: 30004317.	Less complete/in accordance with PICO compared to Goedmakers (2019)
Badhiwala JH, Platt A, Witiw CD, Traynelis VC. Cervical disc arthroplasty versus anterior cervical discectomy and fusion: a meta-analysis of rates of adjacent-level surgery to 7-year follow-up. J Spine Surg. 2020 Mar;6(1):217-232. doi: 10.21037/jss.2019.12.09. PMID: 32309660; PMCID: PMC7154351.	Less complete/in accordance with PICO compared to Goedmakers (2019)
Yang X, Janssen T, Arts MP, Peul WC, Vleggeert-Lankamp CLA. Radiological follow-up after implanting cervical disc prosthesis in anterior discectomy: a systematic review. Spine J. 2018 Sep;18(9):1678-1693. doi: 10.1016/j.spinee.2018.04.021. Epub 2018 May 8. PMID: 29751126.	Less complete/in accordance with PICO compared to Goedmakers (2019)
Katsuura Y, York PJ, Goto R, Yang J, Vaishnav AS, McAnany S, Albert T, Iyer S, Gang CH, Qureshi SA. Sagittal Reconstruction and Clinical Outcome Using Traditional ACDF, Versus Stand-alone ACDF Versus TDR: A Systematic Review and Quantitative Analysis. Spine (Phila Pa 1976). 2019 Oct 1;44(19):E1151-E1158. doi: 10.1097/BRS.0000000000003077. PMID: 31261280.	Less complete/in accordance with PICO compared to Goedmakers (2019)
Ghobrial GM, Lavelle WF, Florman JE, Riew KD, Levi AD. Symptomatic Adjacent Level Disease Requiring Surgery: Analysis of 10-Year Results From a Prospective, Randomized, Clinical Trial Comparing Cervical Disc Arthroplasty to Anterior Cervical Fusion. Neurosurgery. 2019 Feb 1;84(2):347-354. doi: 10.1093/neuros/nyy118. PMID: 29635520.	Wrong population (patients with myelopathy included; no subgroups)
Goedmakers CMW, Bartels RHMA, Donk RD, Arts MP, van Zwet EW, Vleggeert-Lankamp CLA. The Clinical Relevance of the Cervical Disc Prosthesis: Combining Clinical Results of Two RCTs. Spine (Phila Pa 1976). 2022 Jan 1;47(1):67-75. doi: 10.1097/BRS.0000000000004113. PMID: 34474447.	Used data of two RCTs published prior to 2017 (search date Goedmakers, 2019)
Gornet MF, Lanman TH, Burkus JK, Dryer RF, McConnell JR, Hodges SD, Schranck FW. Two-level cervical disc arthroplasty versus anterior cervical discectomy and fusion: 10-year outcomes of a prospective, randomized investigational device exemption clinical trial. J Neurosurg Spine. 2019 Jun 21:1-11. doi: 10.3171/2019.4.SPINE19157. Epub ahead of print. PMID: 31226684.	Wrong population (patients with myelopathy included; no subgroups)
Gornet MF, Lanman TH, Burkus JK, Hodges SD, McConnell JR, Dryer RF, Copay AG, Nian H, Harrell FE Jr. Cervical disc arthroplasty with	Wrong population (patients with myelopathy included; no subgroups)

the Prestige LP disc versus anterior cervical discectomy and fusion, at 2 levels: results of a prospective, multicenter randomized controlled clinical trial at 24 months. J Neurosurg Spine. 2017 Jun;26(6):653-667. doi: 10.3171/2016.10.SPINE16264. Epub 2017 Mar 17. PMID: 28304237.	
Lanman TH, Burkus JK, Dryer RG, Gornet MF, McConnell J, Hodges SD. Long-term clinical and radiographic outcomes of the Prestige LP artificial cervical disc replacement at 2 levels: results from a prospective randomized controlled clinical trial. J Neurosurg Spine. 2017 Jul;27(1):7-19. doi: 10.3171/2016.11.SPINE16746. Epub 2017 Apr 7. PMID: 28387616.	Published prior to search date of Goedmakers (2019)
MacDowall A, Skeppholm M, Lindhagen L, Robinson Y, Löfgren H, Michaëlsson K, Olerud C. Artificial disc replacement versus fusion in patients with cervical degenerative disc disease with radiculopathy: 5-year outcomes from the National Swedish Spine Register. J Neurosurg Spine. 2018 Nov 2;30(2):159-167. doi: 10.3171/2018.7.SPINE18657. PMID: 30485205.	Wrong design (cohort)
Rožanković M, Marasanov SM, Vukić M. Cervical Disk Replacement With Discover Versus Fusion in a Single-Level Cervical Disk Disease: A Prospective Single-Center Randomized Trial With a Minimum 2-Year Follow-up. Clin Spine Surg. 2017 Jun;30(5):E515-E522. doi: 10.1097/BSD.0000000000000170. PMID: 28525471.	Published prior to search date of Goedmakers (2019)
Sasso WR, Smucker JD, Sasso MP, Sasso RC. Long-term Clinical Outcomes of Cervical Disc Arthroplasty: A Prospective, Randomized, Controlled Trial. Spine (Phila Pa 1976). 2017 Feb 15;42(4):209-216. doi: 10.1097/BRS.0000000000001746. PMID: 28207654.	Published prior to search date of Goedmakers (2019)
Spivak JM, Zigler JE, Philipp T, Janssen M, Darden B, Radcliff K. Segmental Motion of Cervical Arthroplasty Leads to Decreased Adjacent-Level Degeneration: Analysis of the 7-Year Postoperative Results of a Multicenter Randomized Controlled Trial. Int J Spine Surg. 2022 Feb;16(1):186-193. doi: 10.14444/8187. Epub 2022 Feb 17. PMID: 35177528; PMCID: PMC9519082.	Wrong outcome (adjacent level degeneration)
Sundseth J, Fredriksli OA, Kolstad F, Johnsen LG, Pripp AH, Andresen H, Myrseth E, Müller K, Nygaard ØP, Zwart JA; NORCAT study group. The Norwegian Cervical Arthroplasty Trial (NORCAT): 2-year clinical outcome after single-level cervical arthroplasty versus fusion-a prospective, single-blinded, randomized, controlled multicenter study. Eur Spine J. 2017 Apr;26(4):1225-1235. doi: 10.1007/s00586-016-4922-5. Epub 2016 Dec 23. PMID: 28012081.	Included in Goedmakers (2019)
Yang W, Si M, Hou Y, Nie L. Superiority of 2-Level Total Disk Replacement Using a Cervical Disk Prosthesis Versus Anterior Cervical Diskectomy and Fusion. Orthopedics. 2018 Nov 1;41(6):344-350. doi: 10.3928/01477447-20180815-01. Epub 2018 Aug 21. PMID: 30125034.	Wrong population (patients with myelopathy included; no subgroups)
Yang X, Donk R, Arts MP, Bartels RHMA, Vleggeert-Lankamp CLA. Prosthesis in Anterior Cervical Herniated Disc Approach Does Not Prevent Radiologic Adjacent Segment Degeneration. Spine (Phila Pa 1976). 2020 Aug 1;45(15):1024-1029. doi: 10.1097/BRS.0000000000003453. PMID: 32675601; PMCID: PMC7373492.	Wrong population (patients with myeloradiculopathy included; no subgroups)

Literature search strategy

Zoekverantwoording
Algemene informatie

Cluster/richtlijn: Cervicaal Radiculair Syndroom	
Uitgangsvraag/modules: Wat is de plaats van ACDP (Anterieure Cervicale Discectomie met prothese) in vergelijking met ACDF (Anterieure Cervicale Discectomie en Fusie) als chirurgische therapie bij patiënten met CRS?	
Database(s): Embase.com, Ovid/Medline	Datum: 13 april 2023
Periode: vanaf 2016	Talen: geen restrictie
Literatuurspecialist: Alies van der Wal	
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting: Voor deze vraag is gezocht op de elementen: - Cervicaal Radiculair Syndroom - Anterieure Cervicale Discectomie met prothese - Anterieure Cervicale Discectomie en Fusie De genoemde sleutelartikelen worden gevonden met deze search	
Te gebruiken voor richtlijnen tekst: *Nederlands* In de databases Embase.com en Ovid/Medline is op 13 april 2023 systematisch gezocht naar systematische reviews en RCTs over Cervicaal Radiculair Syndroom en Anterieure Cervicale Discectomie met prothese of Anterieure Cervicale Discectomie en Fusie. De literatuurzoekactie leverde 190 unieke treffers op. *Engels* On the 13th of April 2023, a systematic search was performed in the databases Embase.com and Ovid/Medline for systematic reviews and RCTs on Cervical Radicular Syndrome and Anterior Cervical Discectomy with Prosthesis or Anterior Cervical Discectomy and Fusion. The search resulted in 190 unique hits.	

Zoekopbrengst

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR	50	46	58
RCT	117	69	132
Totaal	167	115	**190***

in Rayyan

Zoekstrategie

Embase.com

No.	Query	Results
#11	#7 AND #9 NOT #10 = RCT	117
#10	#7 AND #8 = SR	50
#9	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	3764385
#8	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab	916835

	OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	
#7	#6 AND [2016-2023]/py	506
#6	#5 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) NOT (('adolescent'/exp OR 'child'/exp OR adolescent*:ti,ab,kw OR child*:ti,ab,kw OR schoolchild*:ti,ab,kw OR infant*:ti,ab,kw OR girl*:ti,ab,kw OR boy*:ti,ab,kw OR teen:ti,ab,kw OR teens:ti,ab,kw OR teenager*:ti,ab,kw OR youth*:ti,ab,kw OR pediatr*:ti,ab,kw OR paediatr*:ti,ab,kw OR puber*:ti,ab,kw) NOT ('adult'/exp OR 'aged'/exp OR 'middle aged'/exp OR adult*:ti,ab,kw OR man:ti,ab,kw OR men:ti,ab,kw OR woman:ti,ab,kw OR women:ti,ab,kw))	1267
#5	#1 AND #4	1670
#4	#2 OR #3	20253
#3	'anterior cervical discectomy and fusion'/exp OR (('discectomy'/de OR 'decompression surgery'/exp) AND (fusion:ti,ab,kw OR cage*:ti,ab,kw)) OR ((anterior NEAR/5 (fusion* OR cage*)):ti,ab,kw) OR acdf:ti,ab,kw OR (((discectom* OR diskectom*) NEAR/5 (fusion* OR cage*)):ti,ab,kw)	18240
#2	('anterior cervical discectomy'/exp OR 'discectomy'/de OR 'decompression surgery'/exp OR ((anterior NEAR/3 (discectom* OR diskectom* OR decompress*)):ti,ab,kw) OR acdp:ti,ab,kw) AND ('cervical disk prosthesis'/exp OR 'disk prosthesis'/de OR 'prostheses and orthoses'/exp OR 'm6-c':ti,ab,kw OR 'secure-c':ti,ab,kw OR prosthes*:ti,ab,kw OR (((disc OR disk OR prodisc) NEAR/3 (artificial OR replac*)):ti,ab,kw))	3653
#1	'cervicobrachial neuralgia'/exp/mj OR cervicobrachial*:ti,ab,kw OR 'cervico brachial*':ti,ab,kw OR 'cervical brachial*':ti,ab,kw OR ((radiculalgia:ti,ab,kw OR radiculitis:ti,ab,kw OR radiculitides:ti,ab,kw OR radiculopath*:ti,ab,kw OR polyradiculopath*:ti,ab,kw OR neuralgia:ti,ab,kw OR 'herniated disc*':ti,ab,kw OR hernia:ti,ab,kw OR ((radicular NEAR/3 (pain* OR neuralgia* OR symptom*)):ti,ab,kw) OR (('nerve root' NEAR/3 (pain* OR inflammation* OR disorder* OR compression* OR avulsion* OR impingement)):ti,ab,kw)) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('radicular pain'/exp/mj OR 'radiculopathy'/exp/mj) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw))	11694

Ovid/Medline

#	Searches	Results
11	(7 and 9) not 10 = RCT	69
10	7 and 8 = SR	46
9	exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.	2575991
8	meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.	661270
7	limit 6 to yr="2016 -Current"	532
6	5 not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/) not ((Adolescent/ or Child/ or Infant/ or adolescen*.ti,ab,kf. or child*.ti,ab,kf. or schoolchild*.ti,ab,kf. or infant*.ti,ab,kf. or girl*.ti,ab,kf. or boy*.ti,ab,kf. or teen.ti,ab,kf. or teens.ti,ab,kf. or teenager*.ti,ab,kf. or youth*.ti,ab,kf. or pediatr*.ti,ab,kf. or paediatr*.ti,ab,kf. or puber*.ti,ab,kf.) not (Adult/ or adult*.ti,ab,kf. or man.ti,ab,kf. or men.ti,ab,kf. or woman.ti,ab,kf. or women.ti,ab,kf.))	1218
5	1 and 4	1232

4	2 or 3	15226
3	((exp Diskectomy/ or exp Decompression, Surgical/) and (fusion or cage*).ti,ab,kf.) or (anterior adj5 (fusion* or cage*)).ti,ab,kf. or acdf.ti,ab,kf. or ((discectom* or diskectom*) adj5 (fusion* or cage*)).ti,ab,kf.	13492
2	(exp Diskectomy/ or exp Decompression, Surgical/ or (anterior adj3 (discectom* or diskectom* or decompress*)).ti,ab,kf. or acdp.ti,ab,kf.) and (Total Disc Replacement/ or exp "Prostheses and Implants"/ or 'm6-c'.ti,ab,kf. or 'secure-c'.ti,ab,kf. or prosthes*.ti,ab,kf. or ((disc or disk or prodisc) adj3 (artificial or replac*)).ti,ab,kf.)	3841
1	((exp Radiculopathy/ or radiculalgia.ti,ab,kf. or radiculitis.ti,ab,kf. or radiculitides.ti,ab,kf. or radiculopath*.ti,ab,kf. or polyradiculopath*.ti,ab,kf. or neuralgia.ti,ab,kf. or 'herniated disc*'.ti,ab,kf. or hernia.ti,ab,kf. or (radicular adj3 (pain* or neuralgia* or symptom*)).ti,ab,kf. or ('nerve root' adj3 (pain* or inflammation* or disorder* or compression* or avulsion* or impingement)).ti,ab,kf.) and (exp Cervical Vertebrae/ or exp Neck/ or cervical.ti,ab,kf. or cervico*.ti,ab,kf. or neck.ti,ab,kf.)) or cervicobrachial*.ti,ab,kf. or 'cervico brachial*'.ti,ab,kf. or 'cervical brachial*'.ti,ab,kf.	7389

Module 3.4. Anterieure (micro)foraminotomie

Uitgangsvraag

Wat is de plaats van anterieure microforaminotomie in de behandeling van patiënten met CRS?

Inleiding

De standaard chirurgische behandeling van het cervicaal radiculair syndroom (CRS) zonder myelopathie is decompressie van de aangedane zenuw. Hiervoor zijn zowel anterieure als posterieure benaderingen te kiezen.

De meest verrichte benadering is de anterieure discectomie met of zonder cage plaatsing (ACDF) (Broekema, 2020; Saifi, 2018). Hierbij wordt de gehele tussenwervelschijf verwijderd om vervolgens de hernia/bulging te verwijderen ten einde de spinale zenuw vanuit de anterieure zijde te decomprimeren. Als gevolg van het verwijderen van de tussenwervelschijf zullen de belendende corpora gaan fuseren. Fusie kan als negatief gevolg hebben dat versnelde degeneratie op de belendende niveau's op kan treden met als resultaat adjacent segment disease (Donk, 2018). Bovendien wordt bij een ACDF veelal een kostbaar implantaat gebruikt. Aangezien er bij een CRS juist alleen compressie op de spinale zenuw bestaat is het wegnemen van de gehele tussenwervelschijf in theorie onnodig. Derhalve worden chirurgische alternatieven gezocht, die niet leiden tot fusie van het geopereerde segment (Broekema, 2020; Yang, 2019).

Een van de alternatieven is de anterieure microforaminotomie. Bij deze procedure, die mogelijk onterecht in de vergetelheid is geraakt, wordt enkel het laterale gedeelte van de discus en eventuele osteophyten die de wortel compromitteren, weggenomen. Hiermee blijft het grootste gedeelte van de discus intact, wordt er geen kostbaar implantaat geplaatst en zal geen fusie optreden. In deze module wordt de anterieure microforaminotomie in vergelijking met een volledige discectomie geëvalueerd.

Search and select

A systematic review of the literature was performed to answer the following question: *What is the effectiveness of micro foraminotomy (anterior) compared to anterior discectomy (with or without artificial disc/cage) in patients with CRS?*

P: Patients with CRS (no myelopathy)
I: (Micro)foraminotomy (anterior)
C: Anterior discectomy
O: Pain, disability, Odom criteria, re-operations, complications, adjacent disc disease (ADD), disc height, work status, quality of life, use of pain medication, patient satisfaction

<u>Relevant outcome measures</u>

The guideline development group considered pain and disability as *critical* outcome measures for decision making; and Odom criteria, re-operations, complications, adjacent disc disease, disc height, work status, quality of life, pain medication use, and patient satisfaction as *important* outcome measures for decision making.

The working group defined the outcome measures as follows:

- Pain: measured with visual analogue scale (VAS) or numerical rating scale (NRS)
- Disability: measured with Neck Disability Index (NDI)
- Quality of life: measured with 36-Item Short Form Health Survey (SF-36) or European Quality of Life - Five Dimension (EQ-5D)

For the other outcomes, the working group did not define the outcome measures listed above but used the definitions used in the studies.

The working group defined the following minimal clinically (patient) important differences:

- Pain:
  - Visual Analogue Scale (VAS, 0-10): ≥1
  - Numerical Rating Scale (NRS, 0-10): ≥1
- Disability:
  - Neck Disability Index (NDI, 0-50): ≥5

For the other outcomes, the working group defined 10% as a minimal clinically (patient) important difference for continuous outcomes and a RR of <0.91 or >1.1 for dichotomous outcomes.

Search and select (Methods)

The databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms until 17 January 2023. The detailed search strategy is depicted under the tab Methods. The systematic literature search resulted in 321 hits. Studies were selected based on the following criteria:

- systematic review and/or meta-analysis (with detailed search strategy, risk of bias assessment, and results of individual studies available), randomized controlled trials, or other comparative studies;
- patients aged ≥ 18 years;
- studies including ≥ 20 (10 in each study arm) patients;
- studies according to the PICO. (Micro)foraminotomy (anterior) as an intervention, and described anterior discectomy (with or without artificial disc/cage) as a comparison; and
- full-text English or Dutch language publication;

Initially, six studies were selected based on title and abstract screening. After reading the full text, four studies were excluded (see the table with reasons for exclusion under the tab Methods) and two studies were included.

Results

Two studies were included in the analysis of the literature. Important study characteristics and results are summarized in the evidence table. The assessment of the risk of bias is summarized in the risk of bias table.

Summary of literature

Description of studies

Akahori (2022) performed a retrospective cohort study to compare surgical and radiographic outcomes of transvertebral foraminotomy (TVF) with anterior cervical discectomy and fusion (ACDF) in patients with unilateral cervical spondylotic radiculopathy (CSR). Patients who were diagnosed with 1- or 2-level CSR and presented with neurological symptoms of unilateral neck or shoulder pain shooting down to the unilateral hands or fingers (compression corresponding to magnetic resonance imaging, computed tomography scans, and upright radiographs) were included. All patients suffered from CSR that was refractory to conservative treatment for more than 3 months. TVF was used to treat unilateral foraminal stenosis with minimum or no spinal cord compression, while ACDF was applied for unilateral foraminal stenosis with clear spinal cord compression. Patients with cervical myelopathy, developmental spinal canal stenosis, ossification of the posterior longitudinal ligament, spine trauma, spinal tumor, concomitant posterior fusion surgery,

previous surgery at the same level and stenosis as a result of postoperative adjacent segment disease were excluded.

In total, 72 patients were included of which 27 patients underwent TVF (mean age ± SD: 50.0 ± 11.3 years, 26% Female, follow-up 36 ± 10 months) and 45 patients underwent ACDF (mean age ± SD: 55.9 ± 11.6 years, 49% Female, follow-up 34 ± 10 months) with a minimum follow-up of 2 years. Groups were comparable at baseline. Outcomes of interest were pain and complications.

Yi (2009) performed a retrospective cohort study to assess the biomechanical effect of cervical arthroplasty and anterior cervical foraminotomy (ACF) in patients with unilateral cervical radiculopathy. Patients presenting with single-level cervical radiculopathy caused by a unilateral herniated cervical disk who underwent arthroplastie using Bryan disk and ACFs were included. Exclusion criteria were patients with signs of myelopathy or additional degenerative changes on plain radiography.

In total, 13 patients (mean age: 51.9 years, 38% Female, follow-up 13.8 months) underwent ACF and 15 patients (mean age: 41.9 years, 53% Female, follow-up 23.0 months) received arthroplastie. Groups were probably not comparable at baseline. The outcome of interest was the disc height.

Results

1. Pain (critical)

Only Akahori (2022) reported axial pain (neck and shoulder) and arm pain with the visual analogue scale (VAS) at the final follow-up (between 24 and 48 months). Besides, painful swallowing was reported with the VAS 1 week after surgery.

1.1. Axial pain

For axial pain, the postoperative VAS score at final follow-up was 0.4 (SD 0.5) and 0.8 (SD 1.3) for patients in the transvertebral foraminotomy (TVF) group and in the anterior cervical discectomy and fusion (ACDF) group, respectively. This resulted in a mean difference of -0.40 (95%CI -0.82 to 0.02), which was not clinically relevant.

1.2. Arm pain

For arm pain, the postoperative VAS score at final follow-up was 0.8 (SD 0.8) and 0.8 (SD 1.8) in the TVF-group and ACDF-group, respectively. This resulted in a mean difference of 0.0 (95%CI -0.61 to 0.61), which was not clinically relevant.

1.3. Painful swallowing

For painful swallowing, the postoperative VAS score 1 week after surgery was 0.7 (SD 1.0) and 1.9 (SD 1.4) in the TVF-group and ACDF-group, respectively. This resulted in a mean difference of -1.20 (95%CI -1.76 to -0.64). This difference was clinically relevant, favouring the TVF-group.

2. Complications (important)

Only Akahori (2022) reported early postoperative (within 7 days) and late postoperative (within 24 to 48 months) complications.

2.1 Early surgical complications

Hoarseness was experienced by 1 out of 27 patients (4%) in the TVF-group and 2 out of 45 patients (4%) in the ACDF-group. This resulted in a relative risk of 0.83 (95%CI 0.08 to 8.76). Horner syndrome was experienced by only 1 patient (2%) in the ACDF-group, while no cases were detected in the TVF-group. This resulted in a relative risk of 0.55 (95%CI 0.02 to 12.98).

When considering this difference, the very low number of cases and the large confidence interval should be considered.

2.2 Delayed surgical complications

Recurrence of radicular complaints due to recurrent compression at the operated level was reported by 2 out of 27 patients (7%) and 1 out of 45 patients (2%) in the TVF-group and ACDF-group, respectively. This resulted in a relative risk of 3.33 (95%CI 0.32 to 35.04). When considering this difference, the very low number of cases and the large confidence interval should be considered.

Recurrence of radicular complaints due to nerve root compression at the adjacent level was reported by 1 out of 27 patients (2%) in the ACDF-group and not in the TVF-group. This resulted in a relative risk of 0.55 (95%CI 0.02 to 12.98). When considering this difference, the very low number of cases and the large confidence interval should be considered.

Yi (2009) reported various adverse outcomes after ACF surgery, such as spondylotic change, lateral scoliotic tilt, anterior osteophyte formation, instability, and restricted motion at the operative level. However, since no absolute numbers were presented, no GRADE assessment could be performed.

3. Disc height (important)

Both studies reported on disc height. Akahori (2022) reported disc height postoperatively (time period not specified). Pre-operative was not reported, neither was the follow-up. The mean postoperative disc height was 5.3mm (SD 0.9) and 5.2mm (SD 1.0) in the TVF-group and ACDF-group, respectively. This difference was not clinically relevant (MD=0.10, 95%CI -0.35 to 0.55).

The Functional Spinal Unit (FSU) height was 35.2mm (SD 2.6) and 35.7mm (SD 3.5) in the TVF-group and ACDF-group, respectively. This difference was not clinically relevant (MD= -0.50, 95%CI -1.92 to 0.92).

Yi (2009) only reported the FSU height postoperatively (time period not specified). The FSU height was 32.8mm (SD 2.9) and 35.5mm (SD 3.4) in the ACF-group and arthroplasties-group, respectively. This difference was not clinically relevant (MD=-2.70, 95% CI -5.03 to -0.37).

4. Disability (critical); 5. Odom criteria (important); 6. Reoperations (important); 7. Adjacent disc disease (important); 8. Work status (important); 9. Quality of life (important); 10. Use of pain medication (important); 11. Patient satisfaction (important)

Not reported.

Level of evidence of the literature

1. The level of evidence regarding the outcome measure **pain** started as low because it was based on a retrospective cohort study and was downgraded to *very low* because of risk of bias (selection bias) and the very small sample size from only one study.

2. The level of evidence regarding the outcome measure **complications** started as low because it was based on a retrospective cohort study and was downgraded to *very low* because of risk of bias (selection bias) and the very low number of events.

3. The level of evidence regarding the outcome measure **disc height** started as low because it was based on a retrospective cohort study and was downgraded to *very low* because of risk of bias (groups probably not comparable at baseline, no correction for confounders, and selection bias) and the very small sample sizes.

The level of evidence regarding the outcome measures **disability, Odom criteria, reoperations, adjacent disc disease, work status, quality of life, use of pain medication,** and **patient satisfaction** could not be assessed.

Conclusions

1. Pain (critical)

Very low GRADE	The evidence is very uncertain about the effect of anterior (micro)foraminotomy on **pain** when compared with anterior discectomy in patients with cervical radiculopathy. *Source: Akahori, 2022*

2. Complications (important)

Very low GRADE	The evidence is very uncertain about the effect of anterior (micro)foraminotomy on **complications** when compared with anterior discectomy in patients with cervical radiculopathy. *Source: Akahori, 2022; Yi, 2009*

3. Disc height (important)

Very low GRADE	The evidence is very uncertain about the effect of anterior (micro)foraminotomy on **disc height** when compared with anterior discectomy in patients with cervical radiculopathy. *Source: Akahori, 2022; Yi, 2009*

4. Disability (critical); 5. Odom criteria (important); 6. Reoperations (important); 7. Adjacent disc disease (important); 8. Work status (important); 9. Quality of life (important); 10. Use of pain medication (important); 11. Patient satisfaction (important)

No GRADE	No evidence was found regarding the effect of anterior (micro)foraminotomy on **disability, Odom criteria, reoperations, adjacent disc disease, work status, quality of life, use of pain medication and patient satisfaction** when compared with anterior discectomy in patients with cervical radiculopathy.

Overwegingen – van bewijs naar aanbeveling

Voor- en nadelen van de interventie en de kwaliteit van het bewijs

Het doel van deze uitgangsvraag was om te achterhalen wat de plaats is van anterieure microforaminotomie in de behandeling van patiënten met cervicaal radiculair syndroom. Middels literatuuronderzoek zijn twee retrospectieve cohort studies gevonden; één vergelijkt een transvertebrale foraminotomie met ACDF (Akahori, 2022) en de andere vergelijkt anterieure foraminotomie met artroplastie (Yi, 2009). De bewijskracht voor de kritieke uitkomstmaat 'pijn' en de belangrijke uitkomstmaten 'complicaties' en 'schijf hoogte' was zeer laag vanwege methodologische beperkingen en kleine studiepopulaties. Dit betekent dat andere studies kunnen leiden tot nieuwe inzichten. Daarom kunnen er op basis van de literatuur geen harde conclusies geformuleerd worden. Voor de kritieke uitkomstmaat 'disability' en de belangrijke uitkomstmaten 'Odom criteria', 'heroperatie, 'adjacent disc disease', 'werkstatus', 'kwaliteit van leven', 'pijnmedicatiegebruik' en 'patiënttevredenheid' werd geen literatuur gevonden.

Niet iedere patiënt met een cervicaal radiculair syndroom zal in aanmerking komen voor een anterieure microforaminotomie. De beste indicatie voor een anterieure microforaminotomie is een unilaterale foraminale stenose en/of HNP zonder hoogte verlies van de discus. Dat betekent dat in het geval van een bilaterale stenosering van het foramen, een centrale HNP of in het geval van een standsafwijking van de cervicale wervelkolom waarschijnlijk een klassieke ACDF de voorkeur zal hebben.

Bij een microforaminotomie fuseren de wervels postoperatief niet. Er wordt enkel een decompressie verricht, waardoor het aannemelijk is dat de range of motion van de nek meer behouden zal blijven dan na een ACDF. Er zijn theorieën dat hierdoor de kans op een adjacent level disease kleiner is dan na een ACDF. Op basis van literatuuronderzoek is hier echter geen bewijs voor gevonden. Ditzelfde geldt voor slikklachten. De enige studie die hier naar heeft gekeken, zegt iets over slikproblemen één week postoperatief (Akahori, 2022). Dit is klinisch niet relevant. Interessanter zou zijn om slikproblemen op de wat langere termijn te bekijken. Een mogelijk nadeel van een microforaminotomie zou een recidief HNP kunnen zijn, maar ook hiervoor ontbreekt wetenschappelijk bewijs.

Er is in de voorhanden zijnde literatuur geen aandacht geschonken aan de degeneratie van de discus die partieel gelaedeerd is. Het is niet ondenkbaar dat de discus die deels is weggenomen dusdanig degenereert dat deze inzakt. Dit hoogteverlies kan leiden tot hernieuwde herniatie, maar nu van de gehele tussenwervelschijf, en tot immobiliteit die zich praktisch gezien als fusie manifesteert.

Waarden en voorkeuren van patiënten (en evt. hun verzorgers)

Voor patiënten kan een anterieure microforaminotomie aantrekkelijk zijn omdat fusie van de belendende corpora onwaarschijnlijk is en daarmee de kans op adjacent level disease verkleint. Wel moet hierbij worden aangetekend dat het optreden van adjacent level disease bij een ACDF ook niet onomstotelijk is bewezen. De keerzijde hiervan is dat op precies dit niveau een recidief HNP zou kunnen optreden. Dit dient goed besproken te worden in de spreekkamer. Indien er naast een cervicaal radiculair syndroom ook een standsafwijking van de nek bestaat die gecorrigeerd dient te worden, lijkt een ACDF waarbij immers ook een lichte standscorrectie kan worden verricht, de voorkeur te hebben.

Kosten (middelenbeslag)

De werkgroep is niet bekend met economische evaluaties of kosten-effectiviteitsstudies op dit gebied. Voor een anterieure microforaminotomie is het belang een microscoop danwel loupebril te gebruiken. Dit is iets wat de meeste wervelkolom chirurgen al gebruiken voor een operatieve behandeling voor een cervicaal radiculair syndroom. Echt grote financiële

investeringen lijken hierdoor niet nodig. Het voordeel van de anterieure microforaminotomie is dat er geen gebruik gemaakt wordt van een cage, maar een mogelijk nadeel is de langere operatietijd van een microforaminotomie.

Aanvaardbaarheid, haalbaarheid en implementatie

Gezien er geen studies zijn gedaan naar de aanvaardbaarheid en haalbaarheid van de anterieure microforaminotomie, is vervolgonderzoek hiernaar aangewezen. De werkgroep is van mening dat voor deze specifieke techniek zeker een learning curve aanwezig is waar rekening mee gehouden moet worden. Voor veel wervelkolom chirurgen in Nederland zal dit een nieuwe techniek zijn. Training van medische specialisten dient te gebeuren volgens de Leidraad 'Nieuwe interventies in de klinisch praktijk' (Federatie, 2014).

Aanbevelingen

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventies

Op basis van de beschikbare literatuur kan de werkgroep geen sterke aanbevelingen doen voor de anterieure microforaminotomie bij patiënten met een cervicaal radiculair syndroom. In theorie lijkt het een techniek die in de toekomst van aanvullende waarde kan zijn naast de bestaande operatieve technieken bij een CRS. Met name bij een unilaterale foraminale stenose en/of HNP zonder hoogteverlies van de discus lijkt de anterieure microforaminotomie een alternatief. Vervolgonderzoek naar deze techniek is dan ook gewenst.

Een anterieure microforaminotomie is een techniek die training en oefening nodig heeft. Het is van belang dat de operateur voldoende getraind en ervaren is in deze techniek.

Overweeg anterieure microforaminotomie in de behandeling van patiënten met CRS.

Adequate studies op dit gebied ontbreken, op basis van de theoretische voor- en nadelen is een dergelijke studie gewenst alvorens deze anterieure microforaminotomie op grotere schaal toe te passen.

Literatuur

Akahori S, Nishimura Y, Eguchi K, Nagashima Y, Ando R, Awaya T, Tanei T, Hara M, Kanemura T, Takayasu M, Saito R. Comparative Study of Anterior Transvertebral Foraminotomy and Anterior Cervical Discectomy and Fusion for Unilateral Cervical Spondylotic Radiculopathy. World Neurosurg. 2023 Mar;171:e516-e523. Doi: 10.1016/j.wneu.2022.12.053. Epub 2022 Dec 14. PMID: 36528318.

Broekema AEH, Groen RJM, Simões de Souza NF, Smidt N, Reneman MF, Soer R, et al. Surgical Interventions for Cervical Radiculopathy without Myelopathy: A Systematic Review and Meta-Analysis. J Bone Joint Surg Am. 2020;102(24):2182-96.

Donk RD, Verhagen WIM, Hosman AJF, Verbeek A, Bartels R. Symptomatic Adjacent Segment Disease After Anterior Cervical Discectomy for Single-level Degenerative Disk Disease. Clin Spine Surg. 2018;31(1):E50-e4.

Federatie, 2014. Leidraad NIKP: Nieuwe Interventies in de Klinische Praktijk. Oktober 2014. Link: https://demedischspecialist.nl/sites/default/files/Leidraad%20Nieuwe%20interventies%20in%20de%20klinische%20praktijk%20def.pdf.

Saifi C, Fein AW, Cazzulino A, Lehman RA, Phillips FM, An HS, et al. Trends in resource utilization and rate of cervical disc arthroplasty and anterior cervical discectomy and fusion throughout the United States from 2006 to 2013. Spine J. 2018;18(6):1022-9.

Yi S, Lim JH, Choi KS, Sheen YC, Park HK, Jang IT, Yoon DH. Comparison of anterior cervical foraminotomy vs arthroplasty for unilateral cervical radiculopathy. Surg Neurol. 2009

Jun;71(6):677-80, discussion 680. Doi: 10.1016/j.surneu.2008.06.017. Epub 2008 Sep 10. PMID: 18786707.

Yang X, Donk R, Arts MP, Arnts H, Walraevens J, Zhai Z, et al. Maintaining range of motion after cervical discectomy does not prevent adjacent segment degeneration. Spine J. 2019;19(11):1816-23.

Bijlagen bij module 'Anterieure microforaminotomie'

Implementatieplan

Aanbeveling	Tijdspad voor implementatie: < 1 jaar, 1 tot 3 jaar of > 3 jaar	Verwacht effect op kosten	Randvoorwaarden voor implementatie (binnen aangegeven tijdspad)	Mogelijke barrières voor implementatie[1]	Te ondernemen acties voor implementatie[2]	Verantwoordelijken voor acties[3]	Overige opmerkingen
Alle aanbevelingen	< 1 jaar	Beperkt.	Bekendheid met richtlijn.	Geen.	Vervolg onderzoek initiëren op het gebied van kennislacunes. Verspreiden van richtlijn.	Zorgprofessionals van instellingen. Beroepsverenigingen.	Geen.

[1] Barrières kunnen zich bevinden op het niveau van de professional, op het niveau van de organisatie (het ziekenhuis) of op het niveau van het systeem (buiten het ziekenhuis). Denk bijvoorbeeld aan onenigheid in het land met betrekking tot de aanbeveling, onvoldoende motivatie of kennis bij de specialist, onvoldoende faciliteiten of personeel, nodige concentratie van zorg, kosten, slechte samenwerking tussen disciplines, nodige taakherschikking, etc.

[2] Denk aan acties die noodzakelijk zijn voor implementatie, maar ook acties die mogelijk zijn om de implementatie te bevorderen. Denk bijvoorbeeld aan controleren aanbeveling tijdens kwaliteitsvisitatie, publicatie van de richtlijn, ontwikkelen van implementatietools, informeren van ziekenhuisbestuurders, regelen van goede vergoeding voor een bepaald type behandeling, maken van samenwerkingsafspraken.

[3] Wie de verantwoordelijkheden draagt voor implementatie van de aanbevelingen, zal tevens afhankelijk zijn van het niveau waarop zich barrières bevinden. Barrières op het niveau van de professional zullen vaak opgelost moeten worden door de beroepsvereniging. Barrières op het niveau van de organisatie zullen vaak onder verantwoordelijkheid van de ziekenhuisbestuurders vallen. Bij het oplossen van barrières op het niveau van het systeem zijn ook andere partijen, zoals de NZA en zorgverzekeraars, van belang.

Evidence table for intervention studies

Study reference	Study characteristics	Patient characteristics [2]	Intervention (I)	Comparison / control (C) [3]	Follow-up	Outcome measures and effect size [4]	Comments
Akahori, 2022	Type of study: Retrospective cohort study Setting and country: Nagoya University Hospital and Sakura General Hospital; Japan Funding and conflicts of interest: Funding not reported. The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.	Inclusion criteria: - 1- or 2-level cervical spondylotic radiculopathy (CSR) - Neurological symptoms of unilateral neck or shoulder pain shooting down to the unilateral hands or fingers, corresponding to magnetic resonance imaging, computed tomography scans, and upright radiographs - Required surgical intervention for CSR that was refractory to conservative treatment for more than 3 months Exclusion criteria: - Cervical myelopathy - Developmental spinal canal stenosis - Ossification of the posterior longitudinal ligament - Spine trauma - Spinal tumour - Concomitant posterior fusion surgery - Previous surgery at the same level - Stenosis as a result of postoperative adjacent segment disease N total at baseline: Intervention: 27 Control: 45 Important prognostic factors[2]: *Age ± SD:* I: 50.0 ± 11.3 years	Describe intervention (treatment/procedure/test): Transvertebral Foraminotomy The spine was approached from the symptomatic side using the standard anterior method.	Describe control (treatment/procedure/test): Anterior Cervical Discectomy and Fusion (ACDF)	Length of follow-up: Minimal 2 years Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Pain: postoperative VAS *Axial pain:* I: 0.4 ± 0.5 C: 0.8 ± 1.3 *Arm pain:* I: 0.8 ± 0.8 C: 0.8 ± 1.8 Pain: VAS of painful swallowing (postoperative) I: 0.7 ± 1.0 C: 1.9 ± 1.4 Complications *Early surgical complications (within 7 days postoperatively)* - Hoarseness I: 1 C: 2 - Horner syndrome I: 0 C: 1 *Delayed surgical complications (final follow-up)* - Recurrence of operated level I: 2 C: 1 - Recurrence of adjacent level I: 0 C: 1 Disc height I: 5.3 mm ± 0.9	Author's conclusion: TVF is as effective as ACDF for unilateral CSR and preserves whole cervical spine and segmental alignment. Limitations: - Small sample size - Selection bias

		C: 55.9 ± 11.6 years *Sex:* I: 26% F C: 49% F Groups comparable at baseline.				C: 5.2 mm ± 1.0 FSU height postoperatively I: 35.2 mm ± 2.6 C: 35.7 mm ± 3.5	
Yi, 2009	Type of study: Retrospective cohort study Setting and country: Seoul, Korea Funding and conflicts of interest: Not reported.	Inclusion criteria: - Patients with cervical radiculopathy caused by unilateral herniated cervical disk - Underwent arthroplasties using the Bryan disk and ACFs - Single-level disease and surgery Exclusion criteria: - Signs of myelopathy - Additional degenerative changes on plain radiography N total at baseline: Intervention: 13 Control: 15 Important prognostic factors[2]: *Age:* I: 51.9 years C: 41.9 years *Sex:* I: 38% F C: 53% F Groups probably not comparable at baseline.	Describe intervention (treatment/procedure/test): Anterior cervical foraminotomy (ACF)	Describe control (treatment/procedure/test): Arthroplasties	Length of follow-up: I: 13.8 months C: 23.0 months Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Disc height (FSU height) I: 32.8 mm ± 2.9 C: 35.5 mm ± 3.4 Adverse outcomes after ACF surgery - Spondylotic change - Lateral scoliotic tilt - Anterior osteophyte formation - Instability - Restricted motion at the operative level	Author's conclusion: In unilateral cervical radiculopathy, arthroplasty and ACF provided favourable clinical and radiological outcomes. Limitations: - Small sample size - No assessment of confounders

*FSU: functional spinal unit

Risk of bias table for interventions studies

Author, year	Selection of participants Was selection of exposed and non-exposed cohorts drawn from the same population?	Exposure Can we be confident in the assessment of exposure?	Outcome of interest Can we be confident that the outcome of interest was not present at start of study?	Confounding-assessment Can we be confident in the assessment of confounding factors?	Confounding-analysis Did the study match exposed and unexposed for all variables that are associated with the outcome of interest or did the statistical analysis adjust for these confounding variables?	Assessment of outcome Can we be confident in the assessment of outcome?	Follow up Was the follow up of cohorts adequate? In particular, was outcome data complete or imputed?	Co-interventions Were co-interventions similar between groups?	Overall Risk of bias
Akahori, 2022	Definitely yes Reason: Participants were selected based on their treatment (TVF or ACDF) at 2 institutions over the same time frame.	Definitely yes Reason: The received treatment was recorded at the institutions.	Definitely yes Reason: Outcomes were related to received treatment and therefore not present before.	Probably yes Reason: Baseline characteristics were reported.	Probably yes Reason: Performed statistical tests to assess differences in characteristics between both groups (which were non-significant).	No information Reason: Unclear about how data was collected.	Probably yes Reason: Follow up was adequate but different for both groups. Data was complete.	Probably yes Reason: No other interventions reported.	**Some concerns (postoperative complications; pain)**
Yi, 2009	Probably yes; Reason: Participants were selected based on treatment (ACF or ADR) in same time frame.	No information	Definitely yes; Reason: Outcomes were related to received treatment and therefore not present before.	Probably no; Reason: Baseline characteristics were limited.	Definitely no; Reason: No statistical tests for confounding.	Probably yes; Reason: Outcome was assessed using radiographs.	Probably yes; Reason: Follow up was adequate but different for both groups. Data was complete.	Probably yes; Reason: No other interventions reported.	**High (disc height)**

Table of excluded studies

Reference	Reason for exclusion
Gao, Q. Y. and Wei, F. L. and Zhu, K. L. and Zhou, C. P. and Zhang, H. and Cui, W. X. and Li, T. and Qian, J. X. and Hao, D. J. Clinical Efficacy and Safety of Surgical Treatments in Patients With Pure Cervical Radiculopathy. Frontiers in public health. 2022; 10:892042	Only one study included about anterior cervical foraminotomy but compared it with posterior cervical foraminotomy (Ebrahim 2011).
Alomar, S. A. and Maghrabi, Y. and Baeesa, S. S. and Alves, Ó L. Outcome of Anterior and Posterior Endoscopic Procedures for Cervical Radiculopathy Due to Degenerative Disk Disease: A Systematic Review and Meta-Analysis. Global Spine Journal. 2022; 12 (7) :1546-1560	No suitable studies about comparison anterior cervical foraminotomy with anterior discectomy. Compared anterior with posterior approach.
Matz, P. G. and Holly, L. T. and Groff, M. W. and Vresilovic, E. J. and Anderson, P. A. and Heary, R. F. and Kaiser, M. G. and Mummaneni, P. V. and Ryken, T. C. and Choudhri, T. F. and Resnick, D. K. Indications for anterior cervical decompression for the treatment of cervical degenerative radiculopathy. Journal of Neurosurgery: Spine. 2009; 11 (2) :174-182	No suitable studies about comparison anterior cervical foraminotomy with anterior discectomy; narrative description.
Ohtake, Y. and Hanakita, J. and Takahashi, T. and Minami, M. and Nakamura, H. and Kawaoka, T. Long-term radiological evidence of affected and adjacent segment disease after anterior cervical foraminotomy. Neurologia Medico-Chirurgica. 2020; 60 (10) :492-498	Wrong population: control group consists of patients with single-level degenerative cervical myelopathy

Literature search strategy

Cluster/richtlijn: Cervicaal Radiculair Syndroom	
Uitgangsvraag/modules: UV3d Wat is de plaats van anterieure microforaminotomie in de behandeling van patiënten met CRS?	
Database(s): Ovid/Medline, Embase.com	Datum: 17 januari 2023
Periode: geen restrictie	Talen: geen restrictie
Literatuurspecialist: Alies van der Wal	
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting: Voor deze vraag is gezocht op de elementen: - CRS - Anterieure (micro)foraminotomie In versie twee ook gezocht op foraminotomie en niet meer specifiek microforaminotomie. De sleutelartikelen worden gevonden met deze search.	
Te gebruiken voor richtlijnen tekst: *Nederlands* In de databases Embase.com en Ovid/Medline is op 17 januari 2023 met relevante zoektermen gezocht naar systematische reviews, RCTs, observationele en overige studies over anterieure (micro)foraminotomie bij patiënten met CRS. De literatuurzoekactie leverde 321 unieke treffers op. *Engels* On the 17th of January 2023, relevant search terms were used to search for systematic reviews, RCTs, observational and other studies about anterior (micro)foraminotomy for patients with CRS in the databases Embase.com and Ovid/Medline. The search resulted in 321 unique hits.	

Zoekopbrengst

	EMBASE	OVID/MEDLINE	Ontdubbeld
SR	24	21	28
RCT	15	12	17
Observationele studies	143	127	161
Overig	95	76	115
Totaal	277	236	**321**

5

Zoekstrategie

Embase.com

No.	Query	Results
#13	#4 NOT (#10 OR #11 OR #12) = overig	95
#12	#4 AND #9 NOT (#10 OR #11) = observationeel	143
#11	#4 AND #6 NOT #10 = RCT	15
#10	#4 AND #5 = SR	24
#9	#7 OR #8	15567450
#8	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	13776175
#7	'major clinical study'/de OR 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'comparative study'/de OR 'cohort	7451951

	analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti)	
#6	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	2006039
#5	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	893633
#4	#3 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	277
#3	#1 AND #2	337
#2	('foraminotomy'/exp OR 'anterior cervical foraminotomy'/exp OR foraminotom*:ti,ab,kw OR uncoforaminotom*:ti,ab,kw OR acf:ti,ab,kw OR microforaminotom*:ti,ab,kw OR macf:ti,ab,kw OR mecf:ti,ab,kw) NOT (posterior:ti NOT anterior:ti)	5129
#1	'cervicobrachial neuralgia'/exp/mj OR cervicobrachial*:ti,ab,kw OR 'cervico brachial*':ti,ab,kw OR 'cervical brachial*':ti,ab,kw OR ((radiculalgia:ti,ab,kw OR radiculitis:ti,ab,kw OR radiculitides:ti,ab,kw OR radiculopath*:ti,ab,kw OR polyradiculopath*:ti,ab,kw OR neuralgia:ti,ab,kw OR 'herniated disc*':ti,ab,kw OR hernia:ti,ab,kw OR ((radicular NEAR/3 (pain* OR neuralgia* OR symptom*)):ti,ab,kw) OR (('nerve root' NEAR/3 (pain* OR inflammation* OR disorder* OR compression* OR avulsion* OR impingement)):ti,ab,kw)) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('radicular pain'/exp/mj OR 'radiculopathy'/exp/mj) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw))	11560

Ovid/Medline

#	Searches	Results
13	4 not (10 or 11 or 12) = overig	76
12	(4 and 9) not (10 or 11) = observationeel	127
11	(4 and 6) not 10 = RCT	12
10	4 and 5 = SR	21
9	7 or 8	7111439
8	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or cohort*.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/	4379758
7	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,Kf. or (confounding adj6 adjust*).ti,Ab. or (versus or vs or compar*).ti. or ((exp cohort studies/ or epidemiologic studies/ or multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,Kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.))	5334164
6	(exp randomized controlled trial/ or randomized controlled trials as topic/ or random*.ti,Ab. or rct?.ti,Ab. or ((pragmatic or practical) adj "clinical trial*").ti,ab,Kf. or ((non-inferiority or noninferiority or superiority or equivalence) adj3 trial*).ti,ab,kf.)	1438935
5	meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,Kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,Kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,Kf. or (systemic* adj1 review*).ti,ab,Kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,Kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,Kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,Kf. or (("data extraction" or "data source*") and "study selection").ti,ab,Kf. or ("search strategy"	642861

	and "selection criteria").ti,ab,Kf. or ("data source*" and "data synthesis").ti,ab,Kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.	
4	3 not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/)	236
3	1 and 2	243
2	(Foraminotomy/ or foraminotom*.ti,ab,Kf. or uncoforaminotom*.ti,ab,Kf. or ACF.ti,ab,Kf. or microforaminotom*.ti,ab,Kf. or MACF.ti,ab,Kf. or MECF.ti,ab,kf.) not (posterior not anterior).ti.	3708
1	((exp Radiculopathy/ or radiculalgia.ti,ab,Kf. or radiculitis.ti,ab,Kf. or radiculitides.ti,ab,Kf. or radiculopath*.ti,ab,Kf. or polyradiculopath*.ti,ab,Kf. or neuralgia.ti,ab,Kf. or 'herniated disc*'.ti,ab,Kf. or hernia.ti,ab,Kf. or (radicular adj3 (pain* or neuralgia* or symptom*)).ti,ab,Kf. or ('nerve root' adj3 (pain* or inflammation* or disorder* or compression* or avulsion* or impingement)).ti,ab,kf.) and (exp Cervical Vertebrae/ or exp Neck/ or cervical.ti,ab,Kf. or cervico*.ti,ab,Kf. or neck.ti,ab,kf.)) or cervicobrachial*.ti,ab,Kf. or 'cervico brachial*'.ti,ab,Kf. or 'cervical brachial*'.ti,ab,kf.	7289

Module 4. Dorsale behandelingen

Uitgangsvraag

Wat is de plaats van de dorsale foraminotomie in vergelijking met de anterieure discectomie?

Inleiding

Momenteel wordt de anterieure discectomie steeds vaker toegepast in de praktijk. Reeds was aanbevolen dat anterieure benadering de voorkeur verdient (NVvN, 2010). Echter kennen zowel de dorsale als anterieure benadering voor- en nadelen. Anterieur kan leiden tot heesheid/stemproblematiek welke ongewenst is bij bepaalde beroepsgroepen. Hierdoor kan een dorsale foraminotomie de voorkeur hebben. Bij dorsale benadering ontbreekt het voordeel dat de chirurg een discusstuk kan wegnemen, wat het probleem in eerste instantie veroorzaakt (i.e. de hernia zelf). De vraag is echter of de uitgesproken voorkeur voor anterieure discectomie nog terecht is.

Search and select

A systematic review of the literature was performed to answer the following question: *What is the effectiveness of the dorsal foraminotomy compared to the anterior discectomy in patients with CRS?*

P: Patients with CRS (no myelopathy)
I: Dorsal foraminotomy (excluding laminectomy) (Posterior/Scoville)
C: Anterior discectomy (wide)
O: Pain, disability, Odom criteria (4-point rating scale), reoperations, complications (including dysphagia), adjacent disc disease (ADD), work status, quality of life, use of pain medication, patient satisfaction

<u>Relevant outcome measures</u>

The guideline development group considered pain and disability as critical outcome measures for decision making; and Odom criteria, reoperations, complications, adjacent disc disease, work status, quality of life, pain medication use, and patient satisfaction as important outcome measures for decision making.

The working group defined the outcome measures as follows:

- Pain: measured with visual analogue scale (VAS), McGill pain questionnaire, or numerical rating scale (NRS)
- Disability: measured with Neck Disability Index (NDI)
- Quality of life: measured with 36-Item Short Form Health Survey (SF-36) or European Quality of Life - Five Dimension (EQ-5D)

For the other outcomes, the working group did not define the outcome measures listed above but used the definitions used in the studies.

The working group defined the following minimal clinically (patient) important differences:

- Pain:
  - Visual Analogue Scale (VAS, 0-10): ≥1
  - Numerical Rating Scale (NRS, 0-10): ≥1
- Disability:
  - Neck Disability Index (NDI, 0-50): ≥5

For the other outcomes, the working group defined 10% as a minimal clinically (patient) important difference for continuous outcomes and a RR of <0.91 or >1.1 for dichotomous outcomes.

Search and select (Methods)

The databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms until 24 August 2022. The detailed search strategy is depicted under the tab Methods. The systematic literature search resulted in 340 hits. Studies were selected based on the following criteria:

- systematic review and/or meta-analysis, with detailed search strategy, risk of bias assessment, and results of individual studies available; randomized controlled trial (RCT); or other comparative studies;
- patients aged ≥ 18 years;
- studies including ≥ 20 patients (10 in each study arm);
- studies according to the PICO. Dorsal foraminotomy (excluding laminectomy) as an intervention, and described anterior discectomy as a comparison; and
- full-text English or Dutch language publication;

The search was updated for systematic reviews and RCTs on 16 January 2023 due to a new trial. A total of 5 new hits were found.

Initially, 28 studies were selected based on title and abstract screening. After reading the full text, 26 studies were excluded (see the table with reasons for exclusion under the tab Methods), and two studies were included (Broekema, 2020; Broekema, 2022). The systematic review of Broekema (2020) contained three RCTs matching with the PICO (Ebrahim, 2011; Ruetten, 2008; Wirth, 2000) which were included besides the RCT of Broekema (2022).

Results

Four studies were included in the analysis of the literature (Ebrahim, 2011; Ruetten, 2008; Wirth, 2000; Broekema, 2022). Important study characteristics and results are summarized in table 1 and the evidence table. The assessment of the risk of bias is summarized in the risk of bias table.

Summary of literature

Description of studies

Broekema (2022) performed a multicenter investigator-blinded noninferiority randomized controlled trial to assess the noninferiority of posterior versus anterior surgery in patients with cervical foraminal radiculopathy with regard to clinical outcomes after 1 year. Patients with an age between 18 and 80 years with 1-sided single-level cervical foraminal radiculopathy due to soft disc herniation or spondylotic changes requiring surgical decompression were included.

In total, 132 patients were randomized to posterior cervical foraminotomy (PCF) and 133 patients to anterior cervical discectomy with fusion (ACDF). Groups were comparable at baseline except for sex distribution (PCF-group: 55% Female vs. ACDF-group: 47% Female), radiological characteristics (PCF-group: 48% vs. ACDF-group: 57% combined discogenic and spondylotic) and comorbidities (PCF-group: 55% vs. ACDF-group: 46%). After 1 year of follow-up, 110 patients who received PCF and 118 patients who received ACDF were included in the analysis. Outcomes of interest were arm- and neck pain, disability, Odom criteria, reoperation, complications, work status, quality of life and patient satisfaction. For the Odom score, 98 patients treated with PCF and 106 patients treated with ACDF were included in the analysis.

Ebrahim (2011) performed a prospective randomized comparative study to assess clinical and radiological outcomes for the posterior (PCF) and anterior cervical foraminotomy (ACF) procedures in the treatment of patients with unilateral cervical radiculopathy. Patients with unilateral cervical radiculopathy that had not responded to conservative treatment for more than 6 weeks with imaging studies confirming pathoanatomic features (unilateral posterolateral disc herniation or osteophyte compression and foraminal stenosis) corresponding to the clinical symptoms without previous cervical spine surgery and no significant spondylotic stenosis causing spinal cord compromise were included. Exclusion criteria were cervical myelopathy, imaging studies showing central or paracentral stenosis, deformity or instability and previous cervical spine surgery. In total, 15 patients underwent PCF, and 15 patients underwent ACF. Groups were probably comparable at baseline. Outcomes of interest were neck and radicular pain, Odom criteria, complications, work status, and patient satisfaction.

Ruetten (2008) performed a prospective, randomized, controlled study to assess the results of cervical discectomy in lateral disc herniations in full-endoscopic technique via posterior foraminotomy and the conventional microsurgical ACDF. Patients with unilateral radiculopathy with arm pain, in MRI/CT lateral or foraminal localized monosegmental disc herniation of segments C2-C3-C7-Th1 were included. Besides, patients with cranio-caudal sequestering and patients with secondary foraminal stenosis were included as long as the lateral localization was maintained. Exclusion criteria were patients with clear instabilities or deformities, medial localization of disc herniation and isolated neck pain or foraminal stenosis without disc herniation. In total, 100 patients were randomized to PCF and 100 patients to ACDF. After 2 years of follow-up, 175 patients, of which 89 patients received PCF and 86 patients underwent ACDF, were included in the analysis. Groups were comparable at baseline. The outcomes of interest were arm- and neck pain and complications.

Wirth (2000) performed a randomized, prospective study to assess the efficacy of surgical procedures for the treatment of cervical radiculopathy. Patients with cervical radiculopathy caused by a unilateral herniated cervical disc with single-level disease were included. Exclusion criteria were patients with signs of myelopathy and additional degenerative changes on plain radiography. In total, 74 patients were randomized to PCF (n=23) or ACD/ACDF/ACDP (n=51). However, two patients (one in PCF-group and one in ACD-group) declined surgery. Therefore, 22 patients underwent PCF and 50 patients underwent ACD/ACDF/ACDP. Groups were comparable at baseline. Follow-up occurred at 2 months (office visit) and a delayed phone follow-up was performed at 60 months on average. Outcomes of interest were pain, reoperation, complications, work status, and use of pain medication.

Table 1. Description of included studies

Study	Intervention		Comparator		Follow-up	Outcomes
	Characteristics	**Intervention**	**Characteristics**	**Control**		
Broekema, 2022	**Arm 1 (n=119)** Mean age (SD): 51.6 ± 8.5 years Sex: 55% Female	PCF	**Arm 2 (n=124)** Mean age (SD): 51.0 ± 8.3 years Sex:47% Female	ACDF	12 months	Pain, disability, Odom criteria, reoperation, complications, work status, quality of life, patient satisfaction
Ebrahim, 2011	**Arm 1 (n=15)** Mean age (range): 46.7 years (29 to 62 years) Sex: 60% Female	PCF	**Arm 2 (n=15)** Mean age (range): 42 years (31 to 52 years) Sex: 47% Female	ACF	Up to 2 years: PCF: 15.4 months (5-24 months) ACF: 12.5 months (6-24 months)	Pain, Odom criteria, reoperation, complications, work status, patient satisfaction
Ruetten, 2008	**Arm 1 (n=89)** Mean age (range): NR Sex: NR	PCF	**Arm 2 (n=86)** Mean age (range): NR Sex: NR	ACDF	2 years	Pain, complications, reoperation, patient satisfaction
Wirth, 2000	**Arm 1 (n=22)** Median age (range): 43.8 years (30–66) Sex: 59% Female	PCF	**Arm 2 (n=25)** Median age (range): 45.0 years (30–67) Sex:48% Female **Arm 3 (n=25)** Mean age (range): 41.7 years (28–63) Sex:44% Female	ACD ACDF	2 months and at 60 months on average: PCF: 53 months ACD: 56 months ACDF: 69 months	Pain, reoperation, complications, work status, use of pain medication

Abbreviations: PCF=posterior cervical foraminotomy; ACD=anterior cervical discectomy; ACDF=anterior cervical discectomy with fusion; ACF=anterior cervical foraminotomy

Results

1. PCF versus ACD/ACDF/ACDP (Broekema, 2022; Ruetten, 2008; Wirth, 2000)

1.1. Pain (critical)

1.1.1 Arm pain

Broekema (2022) reported that the 1-year postoperative VAS score for arm pain was 18.6 (SD=22.9) in the PCF-group as compared to 15.8 (SD=23.7) in the ACDF-group. This resulted in a mean difference of 2.80 (95%CI -3.06 to 8.66), which was clinically relevant favoring ACDF.

Ruetten (2008) reported that the 2-year postoperative VAS score for arm pain was 7 in the PCF-group and 8 in the ACDF-group. However, since no standard deviations were presented, no GRADE assessment could be performed.

1.1.2. Neck pain

Broekema (2022) reported that the 1-year postoperative VAS score for neck pain was 24.4 (SD=27.5) in the PCF-group as compared to 21.7 (SD=26.1) for the ACDF-group. This resulted in a mean difference of 2.70 (95%CI -4.05 to 9.45), which was clinically relevant favoring ACDF.

Ruetten (2008) reported that the 2-year postoperative VAS score for neck pain was 16 in the PCF-group and 17 in the ACDF-group. However, since no standard deviations were presented, no GRADE assessment could be performed.

1.1.3. Radicular pain

Ruetten (2008) reported the radicular pain after 2 years. No radicular pain was reported by 79 of the 89 patients (89%) in the PCF-group and by 76 of the 86 patients (88%) in the ACDF-group. This resulted in a relative risk of 1.00 (95%CI 0.90 to 1.12), which was not clinically relevant.

Wirth (2000) reported the pain improvement (defined as complete relief or partial improvement of radicular pain) peri-operative, at 2 months and at 60 months on average.

- *Peri-operative*

All patients had 100% pain improvement on the first post-operative day. Nine of the 22 patients (41%) in the PCF-group had a complete relief of pain as compared to 24 of the 50 patients (48%) in the ACD/ACDF/ACDP/ACDP-group. A relative risk of 0.85 (95%CI 0.48 to 1.52) was found, which was clinically relevant favoring ACD/ACDF/ACDP/ACDP.

- *2 months follow-up*
  At 2 months, the pain improvement declined to 98% in the ACD/ACDF/ACDP-group, while in the PCF-group, it remained 100%. Seventeen of the 22 patients (77%) in the PCF-group reported complete pain relief at 2 months, as compared to 37 of the 50 patients (74%) in the ACD/ACDF/ACDP-group. This resulted in a relative risk of 1.04 (95%CI 0.79 to 1.38), which was not clinically relevant.
- *60 months follow-up*
  At telephone follow-up, the pain improvement remained 100% for patients in the PCF-group, while it declined to 97% in the ACD/ACDF/ACDP-group. Complete pain relief was reported by seven of the 14 patients (50%) in the PCF-group at 53 months and 16 of the 29 patients (55%) in the ACD/ACDF/ACDP-group at 62.5 months on average. This resulted in a relative risk of 0.91 (95%CI 0.49 to 1.68), which was not clinically relevant.

1.2. Disability (critical)

Broekema (2022) reported disability with the Neck Disability Index (NDI). The NDI score was 17.6 (SD=14.6) in the PCF-group as compared to 19.2 (SD=16.5) in the ACDF-group. This resulted in a mean difference of -1.60 (95%CI -5.51 to 2.31), which was not clinically relevant.

1.3. Odom criteria (important)

Broekema (2022) reported the proportion of patients with a successful outcome at 1-year follow-up with a score of excellent or good on the modified Odom criteria 4-point rating scale. For the PCF-group, 86 of the 98 patients (88%) had a successful outcome as compared to 81 of the 106 patients (76%) in the ACF-group. This resulted in a relative risk of 1.15 (95%CI 1.01 to 1.31), which was clinically relevant favoring PCF.

1.4. Reoperations (important)

Three studies reported reoperations (Broekema, 2022; Wirth, 2000; Ruetten, 2008) (Figure 1).

Broekema (2022) reported in the PCF-group, 6 of the 119 patients (5%) had a reoperation as compared to 4 of the 124 patients (3%) in the ACDF-group. This resulted in a relative risk of 1.56 (95%CI 0.45 to 5.40), which was clinically relevant favoring ACDF.

Ruetten (2008) reported recurrences/revisions. Three of the 89 patients (3.4%) in the PCF-group and three of the 86 patients (3.5%) in the ACDF-group had recurrences/revisions. This resulted in a relative risk of 0.97 (95%CI 0.20 to 4.66), which was not clinically relevant.

Wirth (2020) reported that reoperation was required in 6 of the 22 patients (27%) in the PCF-group and in 10 of the 50 patients (20%) in the ACD/ACDF/ACDP-group. This resulted in a relative risk of 1.36 (95%CI 0.57 to 3.28), which was clinically relevant favoring ACD/ACDF/ACDP.

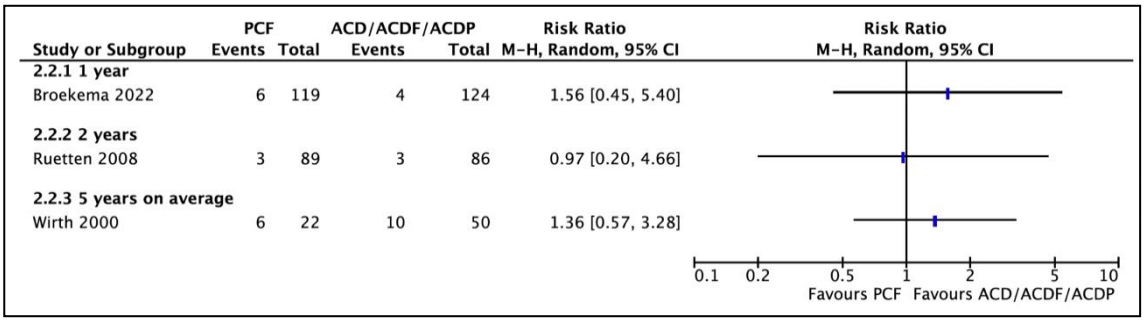

Figure 1. Forest plot for reoperation.

1.5. Complications (important)

Three studies reported complications (Broekema, 2022; Wirth, 2000; Ruetten, 2008) Broekema (2022) reported overall adverse events and serious adverse events at 1 year. Besides, the serious surgery-associated adverse events dysphagia, wound infection, and hoarseness were reported.

- *Adverse events*
  Thirty-six of the 119 patients (30%) in the PCF-group and 35 of the 124 patients (28%) in the ACDF-group reported adverse events (Broekema, 2022). This resulted in a relative risk of 1.07 (95%CI 0.72 to 1.59), which was not clinically relevant.
- *Serious adverse events*
  Thirteen of the 119 patients (11%) in the PCF-group and 17 of the 124 patients (14%) in the ACDF-group reported serious adverse events (Broekema, 2022). This resulted in a relative risk of 0.80 (95%CI 0.40 to 1.57), which was clinically relevant favoring PCF.
- *Serious surgery-associated adverse events*
  Dysphagia or globus sensation was experienced by 1 of the 119 patients (0.8%) in the PCF-group as compared to 6 of the 124 patients (4.8%) in the ACDF-group (Broekema, 2022). This resulted in a relative risk of 0.17 (95%CI 0.02 to 1.42), which was clinically relevant favoring PCF.
  Wound infections were experienced by 5 of the 119 patients (4.2%) in the PCF-group as compared to 2 of the 124 patients (1.6%) in the ACDF-group (Broekema, 2022). This resulted in a relative risk of 2.61 (95%CI 0.52 to 13.17), which was clinically relevant favoring ACDF.
  Hoarseness was experienced by one of 119 patients (0.8%) in the PCF-group as compared to two of the 124 patients (1.6%) in the ACDF-group (Broekema, 2022). This resulted in a relative risk of 0.52 (95%CI 0.05 to 5.67), which was clinically relevant favoring PCF.

Ruetten (2008) reported perioperative complications. In the PCF-group, three patients had transient, dermatoma-related hypesthesia. In the ACDF-group, three patients experienced transient difficulty swallowing, one patient had surface hematoma and one patient had scar distortion which was cosmetically disruptive.

Wirth (2000) reported the perioperative complications new weakness and new numbness. New weakness was reported by 3 of the 22 patients (14%) in the PCF-group and by 4 of the 50 patients (8%) in the ACD/ACDF/ACDP-group. This resulted in a relative risk of 1.70 (95% CI 0.42 to 6.98), which was clinically relevant favoring ACD/ACDF/ACDP. New numbness was reported by 2 of the 22 patients (9%) in the PCF-group and in 3 of the 50 patients (6%) in the ACD/ACDF/ACDP-group. This resulted in a relative risk of 1.52 (95% CI 0.27 to 8.44), which was clinically relevant favoring ACD/ACDF/ACDP. No hoarseness was reported in the PCF- and ACD/ACDF/ACDP-group.

1.6. Work status (important)

Two studies reported about work status (Broekema, 2022; Wirth, 2000).

Broekema (2022) reported the Work Ability Index (Single-item) with higher scores indicating better work ability. The mean Work Ability Index was 6.7 (SD=2.3) in the PCF-group and 6.7 (SD=2.6) in the ACDF-group. This resulted in a mean difference of 0.0 (95%CI -0.62 to 0.62), which was not clinically relevant.

Wirth (2000) reported return to work at 2 months and at telephone follow-up of on average 60 months.

- *2 months follow-up*
  At 2-months, 20 of the 22 patients (91%) in the PCF-group and 45 of the 50 patients (90%) in the ACD/ACDF/ACDP-group returned to work. This resulted in a relative risk of 1.01 (95%CI 0.86 to 1.19), which was not clinically relevant.
- *60 months follow-up*
  At telephone follow-up, return to work was reported in 11 of the 14 patients (79%) in the PCF-group at 53 months and in 25 of the 29 patients (86%) in the ACD/ACDF/ACDP-group at 62.5 months on average. This resulted in a relative risk of 0.91 (95%CI 0.67 to 1.24), which was not clinically relevant.

1.7. Quality of life (important)

Broekema (2022) reported the quality of life with the EQ-5D. The mean EQ-5D score in the PCF-group was 0.84 (SD=0.15) as compared to 0.82 (SD=0.14) in the ACDF-group. This resulted in a mean difference of 0.02 (95%CI -0.02 to 0.06), which was not clinically relevant.

1.8. Use of pain medication (important)

Wirth (2000) reported the required postoperative analgesic medication (injections and oral medication). This was 15.9 (SD=12.6) for the PCF-group and 12.8 (SD=35.7) for patients in the ACD/ACDF/ACDP-group. This resulted in a mean difference of 3.10 (95% CI -8.11 to 14.31), which was clinically relevant favoring ACDF.

1.9. Patient satisfaction (important)

Two studies reported patient satisfaction (Broekema, 2022; Ruetten, 2008). Broekema (2022) reported that 70 of the 96 patients (73%) in the PCF-group were satisfied or very satisfied after 1 year follow-up as compared to 76 of the 99 patients (77%) in the ACDF-group. This resulted in a relative risk of 0.95 (95%CI 0.81 to 1.12), which was not clinically relevant.

Ruetten (2008) reported that 86 of the 89 patients (96%) in the PCF-group were satisfied as compared to 78 of the 86 patients (91%) in the ACDF-group. This resulted in a relative risk of 1.07 (95%CI 0.99 to 1.15), which was not clinically relevant.

1.10. Adjacent disc disease (important)

Not reported.

Level of evidence of the literature

1.1.1 The level of evidence regarding the outcome measure **arm pain** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about blinding (-1, risk of bias) and the optimal information size was not achieved (-2, imprecision).

1.1.2 The level of evidence regarding the outcome measure **neck pain** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about blinding (-1, risk of bias) and the optimal information size was not achieved (-2, imprecision).

1.1.3 The level of evidence regarding the outcome measure **radicular pain** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about randomization and blinding (-1, risk of bias) and the 95% confidence interval crossed the lines of no (clinically relevant) effect (-2, imprecision).

1.2 The level of evidence regarding the outcome measure **disability** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about blinding (-1, risk of bias) and the optimal information size was not achieved (-2, imprecision).

1.3 The level of evidence regarding the outcome measure **Odom criteria** started as high because it was based on a RCT and was downgraded by two levels to *low* because of concerns about blinding (-1, risk of bias) and 95% confidence interval crossed the line of no (clinically relevant) effect (-1, imprecision).

1.4 The level of evidence regarding the outcome measure **reoperations** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about randomization and blinding (-1, risk of bias) and the 95% confidence interval crossed the lines of no (clinically relevant) effect (-2, imprecision).

1.5 The level of evidence regarding the outcome measure **complications** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about randomization and blinding (-1, risk of bias) and the 95% confidence interval crossed the lines of no (clinically relevant) effect (-2, imprecision).

1.6 The level of evidence regarding the outcome measure **work status** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about randomization and blinding (-1, risk of bias) and the 95% confidence interval crossed the lines of no (clinically relevant) effect (-2, imprecision).

1.7 The level of evidence regarding the outcome measure **quality of life** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about blinding (-1, risk of bias) and the optimal information size was not achieved (-2, imprecision).

1.8 The level of evidence regarding the outcome measure **use of pain medication** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about randomization and blinding (-1, risk of bias) and the optimal information size was not achieved (-2, imprecision).

1.9 The level of evidence regarding the outcome measure **patient satisfaction** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about randomization and blinding (-1, risk of bias) and the 95% confidence interval crossed the lines of no (clinically relevant) effect (-2, imprecision).

The level of evidence regarding the outcome measure **adjacent disc disease** was not assessed.

1. Conclusions PCF versus ACD/ACDF/ACDP

1.1. Pain (critical)

Very low GRADE	The evidence is very uncertain about the effect of dorsal foraminotomy on **arm pain** and **neck pain** when compared with anterior cervical discectomy (with fusion) in patients with cervical radiculopathy. *Source: Broekema, 2022*
Very low GRADE	The evidence is very uncertain about the effect of dorsal foraminotomy on **radicular pain** when compared with anterior cervical discectomy (with fusion) in patients with cervical radiculopathy. *Source: Ruetten, 2008; Wirth, 2000*

1.2. Disability (critical)

Very low GRADE	The evidence is very uncertain about the effect of dorsal foraminotomy on **disability** when compared with anterior cervical discectomy (with fusion) in patients with cervical radiculopathy. *Source: Broekema, 2022*

1.3. Odom criteria (important)

Low GRADE	The evidence suggests that dorsal foraminotomy increases the **Odom criteria** when compared with anterior cervical discectomy (with fusion) in patients with cervical radiculopathy. *Source: Broekema, 2022*

1.4. Reoperations (important)

Very low GRADE	The evidence is very uncertain about the effect of dorsal foraminotomy on **reoperations** when compared with anterior cervical discectomy (with fusion) in patients with cervical radiculopathy. *Source: Broekema, 2022; Ruetten, 2008; Wirth, 2000*

1.5. Complications (important)

Very low GRADE	The evidence is very uncertain about the effect of dorsal foraminotomy on **complications** when compared with anterior cervical discectomy (with fusion) in patients with cervical radiculopathy. *Source: Broekema, 2022; Ruetten, 2008; Wirth, 2000*

1.6. Work status (important)

Very low GRADE	The evidence is very uncertain about the effect of dorsal foraminotomy on **work status** when compared with anterior cervical discectomy (with fusion) in patients with cervical radiculopathy. *Source: Broekema, 2022; Wirth, 2000*

1.7. Quality of life (important)

Very low GRADE	The evidence is very uncertain about the effect of dorsal foraminotomy on **quality of life** when compared with anterior cervical discectomy (with fusion) in patients with cervical radiculopathy. *Source: Broekema, 2022*

1.8. Use of pain medication (important)

Very low GRADE	The evidence is very uncertain about the effect of dorsal foraminotomy on **use of pain medication** when compared with anterior cervical discectomy (with fusion) in patients with cervical radiculopathy. *Source: Wirth, 2000*

1.9. Patient satisfaction (important)

Very low GRADE	The evidence is very uncertain about the effect of dorsal foraminotomy on **patient satisfaction** when compared with anterior cervical discectomy (with fusion) in patients with cervical radiculopathy. *Source: Broekema, 2022; Ruetten, 2008*

1.10. Adjacent disc disease (important)

No GRADE	No evidence was found regarding the effect of dorsal foraminotomy on **adjacent disc disease** when compared with anterior cervical discectomy (with fusion) in patients with cervical radiculopathy. *Source: -*

2. PCF versus ACF (Ebrahim, 2011)

2.1 Pain (critical)

2.1.1 Neck pain

Ebrahim (2011) reported that neck pain was resolved for 27.3% in the PCF-group and 50% in ACF-group at the postoperative follow-up of two years. Besides, a statistically significant difference in neck pain at time of discharge of 3.1 (SD=2.5) was demonstrated. However, since no absolute numbers were presented, no GRADE assessment could be performed.

2.1.2. *Radicular pain*

Ebrahim (2011) reported that radicular pain was resolved for 66.7% in the PCF-group and 73.3% in the ACF-group. However, since no absolute numbers were presented, no GRADE assessment could be performed.

2.2. Odom criteria (important)

Ebrahim (2011) reported that an excellent or good score on the Odom criteria was experienced in 14 of the 15 patients (93%) receiving either PCF or ACF. This resulted in a relative risk of 1.00 (95%CI 0.83 to 1.21), which is not clinically relevant.

2.3. Reoperations (important)

Ebrahim (2011) reported that reoperations were required in one of the 15 patients (6.7%) receiving either PCF or ACF. This resulted in a relative risk of 1.00 (95%CI 0.07 to 14.55), which is not clinically relevant.

2.4. Complications (important)

Ebrahim (2011) reported operative complications. For patients who underwent PCF, one patient experienced superficial wound infection and one patient had an intraoperative cerebrospinal fluid leak. Patients in the ACF-group did not experience permanent surgery-related morbidity; no cases of Horner's syndrome or wound-related problems were reported. No GRADE assessment could be performed.

2.5. Work status (important)

Ebrahim (2011) reported that 12 of the 15 patients (80%) in the PCF-group returned to work or their baseline level of activity within 6 weeks postoperatively, while in the ACF-group this was percentage was achieved within 3 weeks postoperatively. However, since no data was provided at the same follow-up period, no GRADE assessment could be performed.

2.6. Patient satisfaction (important)

Ebrahim (2011) measured patient satisfaction with the patient satisfaction index (PSI). Fourteen of the 15 patients receiving either PCF or ACF were satisfied or very satisfied. This resulted in a relative risk of 1.00 (95%CI 0.83 to 1.21), which is not clinically relevant.

2.7. Disability (critical); 2.8. Adjacent disc disease (important); 2.9. Quality of life (important); 2.10. Use of pain medication

Not reported.

Level of evidence of the literature

2.2. The level of evidence regarding the outcome measure **Odom criteria** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about randomization and blinding (-1, risk of bias) and the 95% confidence interval crossed the lines of no (clinically relevant) effect (-2, imprecision).

2.3 The level of evidence regarding the outcome measure **reoperations** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about randomization and blinding (-1, risk of bias) and the 95% confidence interval crossed the lines of no (clinically relevant) effect (-2, imprecision).

2.6 The level of evidence regarding the outcome measure **patient satisfaction** started as high because it was based on a RCT and was downgraded by three levels to *very low* because of concerns about randomization and blinding (-1, risk of bias) and the 95% confidence interval crossed the lines of no (clinically relevant) effect (-2, imprecision).

The level of evidence regarding the outcome measures **pain, disability, complications, adjacent disc disease, work status, quality of life,** and **use of pain medication** were not assessed.

2. Conclusions PCF versus ACF

2.2. Odom criteria (important)

Very low GRADE	The evidence is very uncertain about the effect of dorsal foraminotomy on **Odom criteria** when compared with anterior cervical foraminotomy in patients with cervical radiculopathy. *Source: Ebrahim, 2011*

2.3. Reoperations (important)

Very low GRADE	The evidence is very uncertain about the effect of dorsal foraminotomy on **reoperations** when compared with anterior cervical foraminotomy in patients with cervical radiculopathy. *Source: Ebrahim, 2011*

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2.6. Patient satisfaction (important)

Very low GRADE	The evidence is very uncertain about the effect of dorsal foraminotomy on **patient satisfaction** when compared with anterior cervical foraminotomy in patients with cervical radiculopathy. *Source: Ebrahim, 2011*

2.1 Pain (critical); 2.7. Disability (critical); 2.8. Adjacent disc disease (important); 2.9. Quality of life (important); 2.10. Use of pain medication

No GRADE	No evidence was found regarding the effect of dorsal foraminotomy on **pain, disability, complications, adjacent disc disease, work status, quality of life,** and **use of pain medication** when compared with anterior cervical foraminotomy in patients with cervical radiculopathy. *Source: -*

10

Overwegingen – van bewijs naar aanbeveling

Voor- en nadelen van de interventie en de kwaliteit van het bewijs

Het doel van deze uitgangsvraag was om te achterhalen wat de plaats is van dorsale foraminotomie in vergelijking met anterieure discectomie in de behandeling van patiënten met een cervicaal radiculair syndroom. Er zijn in totaal vier RCTs (Ebrahim, 2011; Ruetten, 2008; Wirth, 2000; Broekema, 2022) geïncludeerd met twee vergelijkingen. Samenvattend kunnen andere studies leiden tot nieuwe inzichten. Daarom kunnen er op basis van de literatuur alleen geen harde conclusies geformuleerd worden.

- *PCF versus ACD/ACDF/ACDP*
  Voor de vergelijking tussen posterieure cervicale foraminotomie (PCF) en anterieure cervicale discecotomie (met fusie) (ACD/ACDF/ACDP) werd voor de cruciale uitkomstmaten pijn en disability een zeer lage bewijskracht gevonden. Posterieure cervicale foraminotomie lijkt te resulteren in een iets grotere verbetering van de Odom criteria in vergelijking met anterieure cervicale discectomie (met fusie).
- *PCF versus ACF*
  Voor de vergelijking tussen posterieure cervicale foraminotomie en anterieure cervicale foraminotomie werd voor de cruciale uitkomstmaten pijn en disability *geen* bewijs gevonden.

De literatuur toont geen verschil in uitkomsten tussen de behandeling van een unilateraal radiculair syndroom met ACD(F) of PCF. Een voorkeur op basis van de literatuur is wat betreft de werkgroep dan ook niet te geven. De verrichte RCT's over dit onderwerp zijn niet gepowered om andere verschillen (bijvoorbeeld in complicaties) tussen deze twee operatietechnieken te tonen. Gezien de verschillen in techniek, is het logisch dat een ACDF vaker tot een postoperatieve dysfagie leidt en een PCF tot meer wondinfecties leidt. Dit wordt wel gesuggereerd door de resultaten van de geïncludeerde studies (Broekema, 2022; Ruetten, 2008; Wirth, 2000).

Een ander verschil in techniek is het nastreven van fusie bij de ACD(F), wat niet gebeurt bij PCF. Indien hierbij een implantaat geplaatst wordt, maakt dit de ACDF duurder dan de PCF (wegens de kosten gerelateerd aan het implantaat).

Het theoretische voordeel van het verwijderen van de degeneratieve discus, is dat het betreffende segment fuseert en in de toekomst mogelijk minder kans geeft op compressiesyndromen. Daarentegen zorgt deze fusie mogelijk voor toegenomen belasting van de boven en ondergelegen discus. De vraag blijft of dit daadwerkelijk tot toename van klinische symptomen door degeneratie van deze boven- en ondergelegen disci leidt of dat dit zonder de fusie ook gebeurt (Hilibrand, 2004; Yang, 2022). Tevens geeft het gebruik van een implantaat kans op mogelijke hardware failure, iets wat overigens niet uit de geïncludeerde studies blijkt (Broekema, 2022; Ruetten, 2008; Wirth, 2000). De werkgroep is van mening dat deze theoretische voor- en nadelen onvoldoende zijn om voorkeur voor de ACD(F) of PCF uit te kunnen spreken. Met betrekking tot een unilateraal radiculair syndroom kunnen beide technieken gekozen worden. Bij multilevel CRS zijn er geen studies van goede kwaliteit verricht. Enkele retrospectieve studies geven aanwijzingen dat de resultaten tussen beide operaties overeenkomen (Lee, 2017; Ng, 2022). Wel wordt een langere opnameduur en een groter aantal infecties gezien bij PCF dan bij ACD(F) (Lee, 2017; Ng, 2022)

Waarden en voorkeuren van patiënten (en evt. hun verzorgers)

Qua ervaren pijn, hersteltijd en/of complicaties laat de literatuur geen klinisch relevante verschillen zien tussen de anterieure en posterieure benadering. Wel kennen de beide benaderingen verschillende (kleine) operatie gerelateerde risico's die een voorkeur voor de

ene of andere techniek kunnen geven. Voor patiënten is dan ook een goede en volledige toelichting van beide operaties essentieel.

Kosten (middelenbeslag)

Gezien bij PCF geen gebruik wordt gemaakt van een cage en bij de ACDF wel, lijkt op korte termijn de PCF goedkoper in vergelijking met ACDF (Broekema, 2022). Echter ontbreken kosteneffectiviteitsstudies over dit onderwerp en zijn ook lange termijn resultaten onbekend. Op lange termijn kunnen mogelijk beide operatietechnieken leiden tot re-operaties die de kosteneffectiviteit doen veranderen. Zo kan de ACDF in theorie leiden tot adjacent segment disease en de PCF tot same level pathologie. Ook omvatten de RCT's relatief kleine studiepopulaties met een unilateraal en single level disease, met een relatief korte follow-up. Dit maakt de kosteneffectiviteit van beide operaties een hypothetisch onderwerp. De werkgroep is daardoor van mening dat voorkeur voor het een of ander niet op basis van kosten kan geschieden.

Aanvaardbaarheid, haalbaarheid en implementatie

In de huidige praktijk wordt de ACDF vaker uitgevoerd dan de PCF. De werkgroep verwacht echter geen grote problemen met aanvaardbaarheid, haalbaarheid en implementatie van deze aanbeveling. Neurochirurgen die kennis hebben gemaakt met beide technieken gedurende hun opleiding, zullen hiervoor openstaan en tot middelen beschikken om beide operatietechnieken uit te voeren.

Aanbevelingen

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventies

Op basis van de bestaande literatuur kan de werkgroep geen sterke aanbevelingen doen ten aanzien van de plaats van de dorsale foraminotomie in vergelijking met de anterieure discectomie bij patiënten met een cervicaal radiculair syndroom vast te stellen. Gezien de lage bewijskracht en overwegingen, acht de werkgroep beide benaderingen gelijkwaardig.

Baseer de keuze voor anterieure of dorsale benadering op basis van patiëntkarakteristieken (bijvoorbeeld patiënten die beroepsmatig hun stem gebruiken) en voorkeur van patiënt en chirurg. De werkgroep acht de benaderingen gelijkwaardig.

Overweeg bij patiënten met persisterend CRS (met congruente MRI-afwijking) na eerdere anterieure discectomie een dorsale foraminotomie te verrichten, mits doorbouw van bot na anterieure benadering is aangetoond. Eveneens kan een anterieure benadering overwogen worden indien een dorsale foraminotomie niet tot afdoende decompressie heeft geleid.

Literatuur

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Bijlagen bij module ‘Anterieur versus dorsaal’

Implementatieplan

Aanbeveling	Tijdspad voor implementatie: < 1 jaar, 1 tot 3 jaar of > 3 jaar	Verwacht effect op kosten	Randvoorwaarden voor implementatie (binnen aangegeven tijdspad)	Mogelijke barrières voor implementatie[1]	Te ondernemen acties voor implementatie[2]	Verantwoordelijken voor acties[3]	Overige opmerkingen
Alle aanbevelingen	< 1 jaar	Beperkt	Bekendheid met de richtlijn	Geen	• Voldoende kennis bij / scholing voor zorgverleners. • Vervolg onderzoek. • Verspreiden van richtlijn.	• Zorgprofessionals van instellingen. • Beroepsverenigingen.	Niet van toepassing.

[1] Barrières kunnen zich bevinden op het niveau van de professional, op het niveau van de organisatie (het ziekenhuis) of op het niveau van het systeem (buiten het ziekenhuis). Denk bijvoorbeeld aan onenigheid in het land met betrekking tot de aanbeveling, onvoldoende motivatie of kennis bij de specialist, onvoldoende faciliteiten of personeel, nodige concentratie van zorg, kosten, slechte samenwerking tussen disciplines, nodige taakherschikking, etc.

[2] Denk aan acties die noodzakelijk zijn voor implementatie, maar ook acties die mogelijk zijn om de implementatie te bevorderen. Denk bijvoorbeeld aan controleren aanbeveling tijdens kwaliteitsvisitatie, publicatie van de richtlijn, ontwikkelen van implementatietools, informeren van ziekenhuisbestuurders, regelen van goede vergoeding voor een bepaald type behandeling, maken van samenwerkingsafspraken.

[3] Wie de verantwoordelijkheden draagt voor implementatie van de aanbevelingen, zal tevens afhankelijk zijn van het niveau waarop zich barrières bevinden. Barrières op het niveau van de professional zullen vaak opgelost moeten worden door de beroepsvereniging. Barrières op het niveau van de organisatie zullen vaak onder verantwoordelijkheid van de ziekenhuisbestuurders vallen. Bij het oplossen van barrières op het niveau van het systeem zijn ook andere partijen, zoals de NZA en zorgverzekeraars, van belang.

Evidence table

Study reference	Study characteristics	Patient characteristics [2]	Intervention (I)	Comparison / control (C) [3]	Follow-up	Outcome measures and effect size [4]	Comments
Broekema, 2022	Type of study: Multicenter investigator-blinded noninferiority randomized clinical trial Setting and country: 9 hospitals in the Netherlands Funding and conflicts of interest: Funded by Netherlands Organisation for Health Research and Development (ZonMW). Conflicts of interest were reported (not serious)	Inclusion criteria: - Age between 18 and 80 years - Cervical foraminal stenosis due to a soft disc component causing monoradiculopathy of C4, C5, C6, or C7 and requiring decompression of neuroforamen - No response to conservative treatment for eight weeks or presence of progressive symptoms or signs of nerve root compression in the face of conservative treatment. - Soft disc/Spondylitic foraminal stenosis (determined by MRI and CT and/or right or left oblique Xray of the cervical spine) at the treatment level correlating to primary symptoms. - Psychosocially, mentally, and physically able to fully comply with this protocol, including adhering to scheduled visits, treatment plan, completing forms, and other study procedures. - Patient has sufficient mastery of the Dutch language to fill out the questionnaires. - Signed and dated	Describe intervention (treatment/procedure/test): Posterior surgery (posterior cervical foraminotomy) Partial hemilaminectomy and foraminotomy of the involved level was performed. Soft disc herniations and osteophytes were removed when necessary. No additional plate fixation or postsurgical neck brace was applied in either technique	Describe control (treatment/procedure/test): Anterior surgery (anterior cervical discectomy with fusion) After discectomy, with reduction of the uncovertebral joint if needed, a cage or bone cement was applied in the intervertebral space	Length of follow-up: 12 months Loss-to-follow-up: Intervention: 9 (8%) Reasons: no information available on Odom score and VAS-arm score Control: 6 (5%) Reasons: no information available on Odom score and VAS-arm score Incomplete outcome data: Missing data for baseline characteristics, but infrequent in both intervention and control group	Arm pain (VAS) I: 18.6 ± 22.9 C: 15.8 ± 23.7 MD=2.80, 95%CI -3.06 to 8.66 Neck pain (VAS) I: 24.4 ± 27.5 C: 21.7 ± 26.1 MD=2.70, 95% CI -4.05 to 9.45 Disability (NDI) I: 17.6 ± 14.6 C: 19.2 ± 16.5 MD=-1.60, 95%CI -5.51 to 2.31 Successful score (excellent or good) on Odom-criteria I: 88% (86 of 98) C: 76% (81 of 106) RR=1.15, 95%CI 1.01 to 1.31 Reoperation I: 6 (5%) C: 4 (3%) RR=1.56, 95%CI 0.45 to 5.40 Complications *All adverse events* I: 36 (30%) C: 35 (28%) RR=1.07, 95%CI 0.72 to 1.5913 *All serious adverse events* I: 13 (11%) C: 17 (14%) RR=0.80, 95%CI 0.40 to 1.57	Author's conclusion: The 1-year clinical effectiveness results demonstrate noninferiority of success rate and arm pain in posterior versus anterior surgery at 1-year follow-up. Decrease in arm pain as well as all secondary outcomes had small between-group differences indicating comparable results between groups. Limitations: - Predefined sample size was not reached - Inability to blind surgeons and patients - Selection bias

		informed consent document prior to any study-related procedures <u>Exclusion criteria</u>: - Pure axial neck pain without radicular pain - Multisegmental CRS - Median located disc protrusion or osteophytic protrusion. - Foraminal compression of C8. - Spinal cord compression with clinical myelopathy. - Radiological myelopathy. - History of cervical spine surgery. - Malignant obesity (BMI > 30). - Osteoporosis / chronic use of corticosteroids. - ASA 4 and 5 patients (serious ill patients). - Pregnancy - Active malignancy - Abundant use of alcohol, drugs, narcotics and recreational drugs. - Contra-indications for anesthesia or surgery - Patient has used another investigational drug or device within the 30 days prior to surgery - Incapability to speak and write the Dutch language <u>N total at baseline</u>: Intervention: 119 Control: 124				*Dysphagia* I: 1 (0.8%) C: 6 (4.8%) RR=0.17 (95%CI 0.02 to 1.42 *Wound infection* I: 5 (4.2%) C: 2 (1.6%) RR=2.61 (95%CI 0.52 to 13.17) *Hoarseness* I: 1 (0.8%) C: 2 (1.6%) RR=0.52 (95%CI 0.05 to 5.67) <u>Work status (work ability index score)</u> I: 6.7 ± 2.3 C: 6.7 ± 2.6 MD=0.0, 95%CI -0.62 to 0.62 <u>Quality of life (EQ-5D):</u> I: 0.84 ± 0.15 C: 0.82 ± 0.14 MD=0.02, 95%CI -0.02 to 0.06 <u>Satisfaction (satisfied or very satisfied):</u> I: 70 (73%) C: 76 (77%) RR=0.96, 95%CI 0.78 to 1.18	

		Important prognostic factors[2]: *Age ± SD:* I: 51.6 ± 8.5 C: 51.0 ± 8.3 *Sex:* I: 55% F C: 47% F *Radiological characteristics (combined discogenic and spondylotic)* I: 57 (48%) C: 70 (57%) *Number of comorbidities* I: 66 (55%) C: 57 (46%) Groups comparable at baseline except for sex distribution, radiological characteristics and comorbidities.					
Ebrahim, 2011	Type of study: Prospective randomized comparative study Setting and country: Ain Shams University Hospital, Egypt Funding and conflicts of interest: Not reported	Inclusion criteria: - Unilateral cervical radiculopathy that had not responded to conservative treatment for more than 6 weeks - Imaging studies confirming pathoanatomic features (unilateral posterolateral disc herniation or osteophyte compression and foraminal stenosis) corresponding to the clinical symptoms. - No previous cervical spine surgery. - No significant spondylotic	Describe intervention (treatment/procedure/test): Posterior cervical foraminotomy (PCF)	Describe control (treatment/procedure/test): Anterior cervical foraminotomy (ACF)	Length of follow-up: Up to 2 years: I: 15.4 months C: 12.5 months Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Neck pain (10-point VAS) *Resolved (at end of postoperative follow-up)* I: 27.3% C: 50% Difference at time of discharge: 3.1 (SD=2.5) Radicular pain (10-point VAS) *Resolved (at end of postoperative follow-up)* I: 66.7% C: 73.3% Odom criteria (excellent or good) I: 14 (93%)	Author's conclusion: Anterior or posterior cervical foraminotomy for cervical radiculopathy is an effective and safe minimally invasive treatment for unilateral cervical radiculopathy in well selected patients. They can be performed as alternatives to traditional standard anterior cervical discectomy and fusion (ACDF), especially in younger patients avoiding potential fusion-related problems, motion

		stenosis causing spinal cord compromise. Exclusion criteria: - Cervical myelopathy - Imaging studies showing central or paracentral stenosis; deformity or instability - Previous cervical spine surgery N total at baseline: Intervention: 15 Control: 15 Important prognostic factors[2]: *Age (range):* I: 46.7 years (29 to 62 years) C: 42 years (31 to 52 years) *Sex:* I: 60% F C: 47% F Groups probably comparable at baseline.				C: 14 (93%) Reoperation I: 1 (6.7%) C: 1 (6.7%) Complications PCF: superficial wound infection (n=1) and intraoperative cerebrospinal fluid leak (n=1) Return to work or baseline level of activity I: 12 (80%) within 6 weeks C: 12 (80%) within 3 weeks Patient satisfaction (patient satisfaction index) *Very satisfied or satisfied* I: 14 (93%) C: 14 (93%)	limitation and long-term adjacent segment disease which could result from ACDF. Limitations: - Very small sample sizes - No information about randomization/blinding
Ruetten, 2008	Type of study: Prospective, randomized, controlled study Setting and country: Germany Funding and conflicts of interest: No funds were	Inclusion criteria: - Unilateral radiculopathy with arm pain - In MRI/CT lateral or foraminal localized monosegmental disc herniation - Segments C2-C3-C7-Th1 - Patients with cranio-caudal sequestering and patients with secondary foraminal stenosis (as long as the lateral localization was maintained)	Describe intervention (treatment/procedure/test): Full-endoscopic posterior cervical foraminotomy (PCF)	Describe control (treatment/procedure/test): Anterior cervical decompression and fusion (ACDF)	Length of follow-up: 2 years Loss-to-follow-up: 2 patients moved away and left no forwarding address, 13 patients did not respond to letters or telephone calls, 10 patients underwent revision surgery with conventional ACDF.	VAS arm pain (2 years) I: 7 C: 8 VAS neck pain (2 years) I: 16 C: 17 Radicular pain (no pain after 2 years) I: 79 of the 89 patients (89%) C: 76 of the 86 patients (88%) Perioperative complications	Author's conclusion: The recorded results show that the full endoscopic posterior foraminotomy is a sufficient and safe supplement and alternative to conventional procedures when the indication criteria are fulfilled. At the same time, it offers the advantages of a minimally invasive intervention.

	received in support of this work. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of the manuscript	Exclusion criteria: - Clear instabilities or deformities - Medial localization of disc herniation - Isolated neck pain or foraminal stenosis without disc herniation N total at baseline: Intervention: 100 Control: 100 Important prognostic factors[2]: Not reported for FPCF and ACDF separately. Groups comparable at baseline.			Incomplete outcome data: Not reported	I: 3 (3%) had transient, dermatoma-related hypesthesia C: 3 (4%) had transient difficulty swallowing; 1 (1%) surface hematoma and 1 (1%) scar distortion which was cosmetically disruptive Reoperation I: 3/89 C: 3/86 Patient satisfaction I: 86 of the 89 (96%) C: 78 of the 86 (91%)	Limitations: - No characteristics presented for PCF and ACDF separately
Wirth, 2000	Type of study: Randomized, prospective study Setting and country: USA Funding and conflicts of interest: Not reported	Inclusion criteria: - Patients presenting with cervical radiculopathy caused by unilateral herniated cervical disc - Single-level disease Exclusion criteria: Signs of myelopathy and additional degenerative changes on plain radiography. N total at baseline: Intervention: 22 Control: 25 (ACD) and 25 (ACDF) Important prognostic factors[2]: *Age (range):*	Describe intervention (treatment/procedure/test): Posterior cervical foraminotomy (PCF)	Describe control (treatment/procedure/test): Anterior cervical discectomy (ACD) or anterior cervical discectomy with fusion (ACDF)	Length of follow-up: At 2-months office visit Telephone follow-up at 60 months on average PCF: 53 months ACD: 56 months ACDF: 69 months Loss-to-follow-up: No loss to follow-up at 2 months At telephone follow-up PCF: 8 (36%) ACD: 12 (48%) ACDF: 9 (36%)	Postoperative analgesic medication required (injections plus oral) PCF: 15.9±12.6 ACD: 13.0±9.2 ACDF: 12.5±50.2 Analgesic medication requests PCF: mean 9.2 ACD: mean 6.0 ACDF: mean 6.4 Pain improvement (complete relief or partial improvement of radicular pain) *Peri-operative pain improvement (%complete relief):* PCF: 100% (41%) ACD: 100% (72%) ACDF: 100% (64%) *Pain improvement (%complete*	Author's conclusion All three of the procedures were successful for treatment of cervical radiculopathy caused by a herniated cervical disc. Although the numbers in this study were small, none of the procedures could be considered superior to the others. This study suggests that the selection of surgical procedure may reasonably be based on the preference of the surgeon and tailored to the individual patient. Limitation

		PCF: 43.8 years (30–66) ACD: 45.0 years (30–67) ACDF: 41.7 years (28–63) *Sex:* PCF: 59% F ACD: 48% F ACDF: 44% F Groups comparable at baseline			Incomplete outcome data: Not reported.	*relief) at 2-months* PCF: 100% (77%) ACD: 100% (72%) ACDF: 96% (76%) *Pain improvement (%complete relief) at phone follow-up* PCF: 100% (50%) ACD: 92% (69%) ACDF: 100% (44%) Complications: *New weakness* PCF: 3 (14%) ACD: 2 (8%) ACDF: 2 (8%) *New numbness* PCF: 2 (9%) ACD: 2 (8%) ACDF: 1 (4%) No hoarseness Return to work *2-months* PCF: 91% ACD: 88% ACDF: 92% *Telephone follow-up* PCF: 11 (79%) ACD: 12 (92%) ACDF: 13 (81%) Reoperation PCF: 6 (27%) ACD: 3 (12%) ACDF: 7 (28%)	- Small sample size - Limited information about randomization and blinding

Risk of bias table for interventions studies

Study reference	Was the allocation sequence adequately generated?	Was the allocation adequately concealed?	Blinding: Was knowledge of the allocated interventions adequately prevented? Were patients blinded? Were healthcare providers blinded? Were data collectors blinded? Were outcome assessors blinded? Were data analysts blinded?	Was loss to follow-up (missing outcome data) infrequent?	Are reports of the study free of selective outcome reporting?	Was the study apparently free of other problems that could put it at a risk of bias?	Overall risk of bias If applicable/necessary, per outcome measure
Broekema, 2022	Definitely yes; Reason: Web-based block randomization design was used.	Probably yes; Reason: Independent institute web-based block randomization design was used.	Probably yes; Reason: Blinding of patients and surgeons was not possible. Interviewer that assessed outcomes was blinded.	Probably yes; Reason: Loss to follow-up was infrequent in intervention and control group. Sensitivity analyses were performed to account for the missing data.	Probably yes; Reason: All relevant outcomes were reported.	Probably no; Reason: Selection bias in enrolment of participants	**LOW (reoperation, complications)** **Some concerns (pain, disability, Odom criteria, work status, quality of life, patient satisfaction)**
Ebrahim, 2011	No information	No information	No information	Probably yes; Reason: No loss to follow-up reported.	Probably yes; Reason: All relevant outcomes were reported.	Probably no; Reason: No information about funding or conflicts of interest.	**HIGH (pain, Odom criteria, patient satisfaction)** **Some concerns (reoperation, complications, return to work)**
Ruetten, 2008	Probably no; Reason: Randomization by alternation in the	Probably no; Reason: Randomization was open.	Probably no; Reason: Blinding of patients and surgeons	Probably no; Reason: Lost to follow-up of 12.5% and	Probably no; Reason: Not all outcomes described in	Probably yes; Reason: No other problems reported.	**HIGH (pain, patient satisfaction)** **Some concerns**

	order of presentation by nondoctors assisting in the study.		not possible. Examinators were blinded.	unclear if it differs between treatment groups.	the results section were mentioned in the methods.		**(reoperation, complications)**
Wirth, 2000	No information	Definitely yes; Reason: Randomized by sealed envelope.	No information	Probably yes; Reason: No lost to follow-up at 2-months and long-term lost to follow-up was similar in treatment groups.	Probably yes; Reason: All relevant outcomes were reported.	Probably no; Reason: No information about funding or conflicts of interest.	**HIGH (pain)** **Some concerns (pain medication use, complications, return to work, reoperation)**

Table of excluded studies

Reference	Reason for exclusion
Alvin 2014	Included only 1 rct including patients with myelopathy, and less recent and complete than Broekema (2020) (wrong population, wrong study design)
Caridi 2011	nonsystematic review (wrong study design)
Guo 2022	systematic review with network meta-analysis, but multiple anterior interventions in network, not anterior versus posterior (wrong study design)
Liu 2016	less recent and complete than Broekema (lacking Ebrahim, 2011)
Skovrlj 2017	nonsystematic review (wrong study design)
Sahai 2019	less recent and complete than Broekema (lacking Wirth 2011; Ebrahim, 2011)
Platt 2021	Search date unknown but less complete than Broekema (lacking Wirth 2011; Ebrahim, 2011)
Alomar 2021	less recent and complete than Broekema (lacking Wirth 2011; Ebrahim, 2011)
Zhang 2020	less recent and complete than Broekema (lacking Wirth 2011; Ebrahim, 2011)
Fehlings 2009	nonsystematic review (wrong study design)
Gutman 2018	less recent and complete than Broekema (lacking Wirth 2011; Ebrahim, 2011)
Ament 2018	nonsystematic review (wrong study design)
Foster 2019	retrospective design (wrong study design)
Tschugg 2014	study protocol (wrong study design)
Holy 2021	study protocol (wrong study design)
Hohl 2011	nonsystematic review (wrong study design)
Broekema 2017	study protocol (wrong study design)
Calvanese 2022	narrative review (wrong study design)
Shaban 2022	two forms of posterior compared (wrong intervention)
Zou 2022	Less complete than Broekema (lacking Wirth 2011; Ebrahim, 2011)
Fang 2020	meta-analysis included observational studies, no possiblity to substract experimental data (wrong study design)
Gao 2022	same relevant RCTs but less transparent reporting compared to Broekema2020
Holy 2022	correction to Holy (2021)

Literature search strategy

5

Cluster/richtlijn: Cervicaal Radiculair Syndroom	
Uitgangsvraag/modules: Wat is de plaats van de dorsale foraminotomie in vergelijking met de anterieure discectomie?	
Database(s): Ovid/Medline, Embase.com	Datum: 24 augustus 2022 (update op 16 januari 2023)
Periode: geen restrictie	Talen: Engels, Nederlands
Literatuurspecialist: Miriam van der Maten	
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting: Deze vraag is geupdatet voor SR en RCT i.v.m. een nieuwe trial. In totaal werden er 5 nieuwe hits gevonden. Voor deze vraag is gezocht op de elementen: - CRS - Dorsale foraminotomie	
Te gebruiken voor richtlijnen tekst: *Nederlands* In de databases Embase.com en Ovid/Medline is op 24 augustus 2022 met relevante zoektermen gezocht naar systematische reviews, RCT en observationele studies over de plaats van de dorsale foraminotomie in vergelijking met de anterieure discectomie bij patiënten met CRS De literatuurzoekactie leverde 340 unieke treffers op. *Engels* On the 24th of August 2022, relevant search terms were used to search for systematic reviews, RCT and observational studies about the place of posterior foraminotomy compared to anterior discectomy for patients with CRS in the databases Embase.com and Ovid/Medline. The search resulted in 340 unique hits.	

Zoekopbrengst

	EMBASE	OVID/MEDLINE	Ontdubbeld
SRs	38	34	43 (+2)
RCT	26	22	28 (+3)
Observationele studies	250	187	269
Totaal	314	243	**340**

Zoekstrategie

Embase.com

No.	Query	Results
#15	#12 OR #13 OR #14	314
#14	#8 AND #11 NOT (#12 OR #13) **= observationeel vergelijkend**	250
#13	#8 AND #10 NOT #12 **= RCT**	26
#12	#8 AND #9 **= SR**	38
#11	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	13382133
#10	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	1948645
#9	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	733409
#8	#6 AND #7 AND ([english]/lim OR [dutch]/lim) NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	585
#7	'discectomy'/exp AND posterior:ti,ab,kw OR ('foraminotomy'/exp AND posterior:ti,ab,kw) OR 'posterior cervical foraminotomy'/exp OR (((posterior OR dorsal) NEAR/3 (foraminotom* OR discectom* OR diskectom*)):ti,ab,kw) OR pcf:ti,ab,kw OR frynkholm*:ti,ab,kw OR scoville*:ti,ab,kw OR ((posterior NEAR/7 (surg* OR operat* OR procedure* OR approach)):ti,ab,kw)	42974
#6	'cervicobrachial neuralgia'/exp/mj OR cervicobrachialgia:ti,ab,kw OR ((radiculalgia:ti,ab,kw OR radiculitis:ti,ab,kw OR radiculitides:ti,ab,kw OR radiculopath*:ti,ab,kw OR polyradiculopath*:ti,ab,kw OR neuralgia:ti,ab,kw OR 'herniated disc*':ti,ab,kw OR hernia:ti,ab,kw OR ((radicular NEAR/3 (pain* OR neuralgia* OR symptom*)):ti,ab,kw) OR (('nerve root' NEAR/3 (pain* OR inflammation* OR disorder* OR compression* OR avulsion* OR impingement)):ti,ab,kw)) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('radicular pain'/exp/mj OR 'radiculopathy'/exp/mj) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw))	10860

5 **Ovid/Medline**

#	Searches	Results
17	14 or 15 or 16	243
16	(10 and 13) not (14 or 15) **= observationeel vergelijkend**	187
15	(10 and 12) not 14 **= RCT**	22
14	10 and 11 **= SR**	34

13	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or ((exp cohort studies/ or epidemiologic studies/ or multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.))	5231141
12	exp randomized controlled trial/ or randomized controlled trials as topic/ or random*.ti,ab. or rct?.ti,ab. or ((pragmatic or practical) adj "clinical trial*").ti,ab,kf. or ((non-inferiority or noninferiority or superiority or equivalence) adj3 trial*).ti,ab,kf.	1540100
11	meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.	613417
10	limit 9 to (english language or dutch)	515
9	8 not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	554
8	6 and 7	560
7	(exp Diskectomy/ and posterior.ti,ab,kf.) or (exp Foraminotomy/ and posterior.ti,ab,kf.) or ((posterior or dorsal) adj3 (foraminotom* or discectom* or diskectom*)).ti,ab,kf. or pcf.ti,ab,kf. or frynkholm*.ti,ab,kf. or scoville*.ti,ab,kf. or (posterior adj7 (surg* or operat* or procedure* or approach)).ti,ab,kf.	32775
6	((exp Radiculopathy/ or radiculalgia.ti,ab,kf. or radiculitis.ti,ab,kf. or radiculitides.ti,ab,kf. or radiculopath*.ti,ab,kf. or polyradiculopath*.ti,ab,kf. or neuralgia.ti,ab,kf. or 'herniated disc*'.ti,ab,kf. or hernia.ti,ab,kf. or (radicular adj3 (pain* or neuralgia* or symptom*)).ti,ab,kf. or ('nerve root' adj3 (pain* or inflammation* or disorder* or compression* or avulsion* or impingement)).ti,ab,kf.) and (exp Cervical Vertebrae/ or exp Neck/ or cervical.ti,ab,kf. or cervico*.ti,ab,kf. or neck.ti,ab,kf.)) or cervicobrachialgia.ti,ab,kf.	6630

Module 5. AI gebaseerde predictiemodellen

Uitgangsvraag

Wat is de rol van predictiemodellen gebaseerd op AI bij het maken van behandelbeslissingen?

Introductie

Hoewel chirurgie voor een CRS door wervelkolomchirurgen over het algemeen wordt beschouwd als een procedure met een hoog succespercentage, blijkt uit verschillende studies dat ongeveer 25% van de patiënten na de ingreep een lage tevredenheid meldt (Hessler, 2012; Wichmann, 2021). Het preoperatief identificeren van deze patiënten kan onnodige procedures voorkomen en leiden tot kostenbesparingen. Desondanks blijft het zeer uitdagend om vooraf te bepalen welke groep patiënten baat zal hebben bij de operatie en welke groep niet (Iyer, 2016).

Predictiemodellen kunnen wervelkolomchirurgen mogelijk beter inzicht geven in het succes van chirurgie voor een specifieke patiënt. Op basis van patiëntkarakteristieken, radiologische en/of klinische parameters kan een voorspelling worden gedaan over het verwachte resultaat voor de patiënt. Dit zou zorgverleners in staat stellen een betere beslissing te nemen over het aanbieden van de operatie aan de patiënt en de patiënt een beter idee geven van het verwachte resultaat. Deze module evalueert de rol van predictiemodellen bij het maken van behandelbeslissingen bij patienten met CRS.

Search and select

A systematic review of the literature was performed to answer the following question: *Which model predicts clinical outcomes and complications (adjacent segment disease/ continued opioid use) in patients with cervical radiculopathy and what is the predictive value of this model?*

P: Patients with cervical radiculopathy undergoing ACDF surgery
I: Validated prediction model based on machine learning/deep learning principles
C: Model based on clinical judgement or classical statistical methods (e.g. regression-analysis)
O: Model performance (predictive value, fit, discrimination parameters (AUC), Brier score, F1 score) for predicting complications (adjacent segment disease/sustained opioid prescription) or clinical outcomes (e.g. disability or pain)
T/S: Based on pre-operative data predicting postoperative outcomes, in-hospital setting

<u>Relevant outcome measures</u>

The guideline development group considered discrimination parameters (such as area under curve) as a critical outcome measure for decision making; and all other outcomes as an important outcome measure for decision making.

The working group defined the outcomes measures as follows:

- Disability: Neck disability index (NDI)
- Pain: Visual analogue scale (VAS) or numerical rating scale (NRS)

For other outcomes, the working group did not define the outcome measures listed above but used the definitions used in the studies.

The working group defined the performance of the included models as follows (Habibzadeh, 2016; Ludemann, 2006; Obuchowski, 2003; Metz, 1978):

- AUC <0.6: failed

- 0.6 ≤ AUC<7: poor
- 0.7≤AUC<0.8: acceptable,
- 0.8≤AUC<0.9: excellent,
- AUC≥0.9: outstanding.

Search and select (Methods)

In the first step, the databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms until February 1sth, 2023. The detailed search strategy is depicted under the tab Methods. The systematic literature search resulted in 153 hits. Studies were initially selected based on the following criteria:

- Reporting prediction model with complication or clinical outcome as dependent variable and risk factors based on machine learning/deep learning as independent variables, the described model(s) were internally and externally validated,
- Studies were full text available in English or Dutch, and
- Studies according to the PICO.

Twenty-three studies were initially selected based on title and abstract screening. After reading the full text, all studies were excluded (see the table with reasons for exclusion under the tab Methods), and no studies were included.

Results

No studies were included in the analysis of the literature.

Level of evidence of the literature

No studies were included in the analysis of the literature.

Conclusions

All outcomes

No GRADE	No evidence was found regarding the performance of models based on machine learning/deep learning in predicting clinical outcomes/complications when compared with clinical judgement or a models based on classical statistical methods in patients with cervical radiculopathy undergoing ACDF-surgery.

Overwegingen – van bewijs naar aanbeveling

Voor- en nadelen van de interventie en de kwaliteit van het bewijs

Er werd geen bewijs gevonden over de waarde van predictiemodellen gebaseerd op machine learning/deep learning in vergelijking met predictiemodellen gebaseerd op het klinisch oordeel of klassieke statistische methoden, bij patiënten met CRS. Er werden geen studies gevonden die voldoen aan de PICO en dus is er geen GRADE beoordeling uitgevoerd.

- Er werden wel twee studies gevonden met twee predictiemodellen, die op basis van baseline data een predictie geven voor de uitkomst van chirurgie (Goedmakers, 2021; Liew, 2020). In *Tabel 1* weergeeft een samenvatting van studieresultaten. *Goedmakers (2021)* rapporteerde over drie AI-modellen (VGGNet19, ResNet18 and ResNet50) die kunnen helpen om post-operatief adjacent segment diasease (ASD) te voorspellen op basis van preoperatieve T2 saggitale MRI-beelden. De predictieve waarde van de modellen werd vergeleken met een voorspelling gebaseerd op klinisch oordeel met behulp van de Matsumoto MRI grading scale. De waarde van het model is weergegeven in tabel 1 in de vorm van sensitiviteit, specificiteit, positief voorspellende waarde en

negatief voorspellende waarde, F1 score en AUC. Reflecterend op de AUC-waarde, scoorde het ResNet50 model het best met een AUC van 0.89. Coëfficiënten werden niet gerapporteerd omdat de modellen zich baseren op T2 MRI-beelden.

- *Liew (2020)* rapporteerde over drie AI-methoden (least absolute shrinikage and selection operator (LASSO), boosting en multivariate adaptive regression splines (MUaRS)) om postoperatieve disability, arm-pijn en nek-pijn 12 maanden na ACDF-chirurgie bij patiënten met cervicaal radiculair syndroom (CRS) te voorspellen. Model fit is gepresenteerd met behulp van de root mean squared error (RMSE), waarbij lagere waarden een betere model-fit weergeven. Gezien het feit dat RMSE-waarden grafisch zijn gerapporteerd, is voor alle uitkomsten gebruik gemaakt van de web-applicatie WebPlotDigitizer. De laagste RMSE waarden zijn gevonden voor een klassiek model resulterend uit stapsgewijze selectie waarmee nekpijn kon worden voorspeld (RMSE 25.2, 95% BI 18.2 tot 32.2[1]) en een model gebaseerd op stapsgewijze selectie waarmee disability werd voorspeld (RMSE 7.90, 95% BI 6.78 tot 9.01[2]). Voor het voorspellen van armpijn, vertoonde een model ontwikkeld met behulp van LASSO de beste waarden (RMSE 24.6, 95% BI 20.8 tot 28.5[3]).

Het eerste model (Goedmakers, 2021) maakt gebruik van baseline MRI beelden om adjacent segment disease na een median follow-up 19 maanden (IQR: 12-38 maanden) te voorspellen. Het model is intern gevalideerd met data van het eigen centrum, dit betekent dat het model matig valide is (AUC: 0.69). Voordat een predictiemodel gebruikt kan worden in de klinische praktijk, dient de prestatie van het model te worden bestudeerd in nieuwe patiënten (externe validiteit). Een externe validatie ontbreekt echter voor het model van Goedmakers (2021).
Het tweede model (*Liew, 2020)* voorspelt disability, arm-pijn en/of nek-pijn 12 maanden na ACDF-chirurgie op basis van baseline klinische data (zie *voetnoten 1-3*). Ook dit model is slechts intern gevalideerd, waardoor het model niet bruikbaar is in de klinische praktijk.

Gezien het feit dat de twee predictiemodellen niet extern gevalideerd zijn, dienen deze uitkomsten met de nodige voorzichtigheid te worden geïnterpreteerd.
Het literatuuronderzoek laat ook zien dat er wel regelmatig met behulp van machine learning modellen algoritmen worden ontworpen. In *Tabel 2* staan overige op AI gebaseerde predictiemodellen die in de systematische search gevonden werden. Deze predictiemodellen waren geen volledige match met de vooraf opgestelde PICO (ontbreken controlegroep, bredere patiëntenpopulatie), maar geven wel de omvang van het aantal intern gevalideerde modellen in het veld weer.
Indien onderzoekers of zorgverleners predictiemodellen voor patiënten met CRS verder willen ontwikkelen, dan adviseert werkgroep om gebruik te maken van de reeds bestaande predictiemodellen en die toe te passen op de eigen data. Op die manier kunnen bestaande predictiemodellen extern gevalideerd worden en daarmee waarde krijgen voor algemene toepasbaarheid.

Tabel 1. Samenvatting van studieresultaten (Engelstalig)

Study	Population (design, n)	Outcome of interest	AI-model(s) evaluated	AI model performance	Comparison model	Comparison model performance
Goedmakers, 2021	Patients with cervical radiculopathy undergoing ACDF (retrospective chart review, 340)	ASD Prevalence at final clinical follow-up (median follow-up 19 months (IQR: 12-38 months): 16%	VGGNet19 trained using T2 sagittal MRI	F1, sensitivity, specificity, PPV, NPV: NR	Prediction by clinical expert, using the Matsumoto MRI grading scale	F1: 0.32 (95% CI NR) PPV: 27 (95% CI NR) Sensitivity: 60 (95% CI NR) Specificity: 58 (95% CI NR) NPV: 88 (95% CI NR)
				AUC: 0.69 (95% CI NR)		AUC: NR
			ResNet18 trained using T2 sagittal MRI	F1, Sensitivity, specificity, PPV, NPV: NR		
				AUC: 0.86 (95% CI NR)		
			ResNet50 trained using T2 sagittal MRI	F1: 0.83 (95% CI NR)		
				Sensitivity: 80 (95% CI NR)		
				Specificity: 97 (95% CI NR)		
				PPV: 86 (95% CI NR)		
				NPV: 96 (95% CI NR)		
				AUC: 0.89 (95% CI NR)		
Liew, 2020	Patients with cervical radiculopathy undergoing ACDF or PCF (prospective cohort dataset, 201)	NDI neck pain intensity, and present arm pain intensity at follow-up (12 months post-surgery)	LASSO	RMSE NDI: 8.13 (95% CI 6.90 to 9.34)	Two stage stepwise linear regression	RMSE NDI: 7.90 (95% CI 6.78 to 9.01)*
				RMSE Neck pain: 23.0 (95% CI 19.4 to 26.6)		
				RMSE Arm pain: 24.6 (95% CI 20.8 to 28.5)*		RMSE Arm pain: 25.2 (95% CI 18.2 to 32.2)
			Boosting	RMSE NDI: 8.16 (95% CI 6.93 to 9.37)		
				RMSE Neck pain: 22.9 (95% CI 19.2 to 26.6)		RMSE Neck pain: 21.7 (95% CI 18.3 to 25.1)*
				RMSE Arm pain: 25.0 (95% CI 20.9 to 29.2)		
			MuARS	RMSE NDI: 8.19 (95% CI 6.93 to 9.44)		
				RMSE Neck pain: 23.5 (95% CI 19.2 to 27.8)		
				RMSE Arm pain: 24.6 (95% CI 20.1 to 29.1)		

Abbreviations: ASD, adjacent segment disease; AUC, area under the ROC-curve; LASSO, least absolute shrinkage and selection operator; MUaRS, multivariate adaptive regression splines; NDI, neck disability index; NPV, negative predictive value; PPV, positive predictive value; RMSE, root mean squared error
*lowest RMSE

Tabel 2. Overige predictiemodellen (Engelstalig)

Study ID	Population	Model(s) intervention	Model(s) control	Outcome	Reported measures for accuracy
Schroerder, 2017	Patients with radiculopathy or myeloradiculopathy undergoing TDR with Mobi-C cervical artificial disc or ACDF	LASSO logistic regression	NR	Patient satisfaction	AUC
Rodigues, 2022	Patients who underwent ACDF procedures	Traditional machine learning algorithms, LR and SVM	NR	Postoperative complications, unfavorable 90-day readmissions, and two-year reoperations	AUC
Karhade, 2019	Patients who underwent inpatient and outpatient ACDF. 25.4% of the patients had myelopathy and 36.2% had radiculopathy	Random forest, SGB, neural network, SVM, elastic-net penalized logistic regression	NR	Sustained opioid prescription	dc-statistic), calibration slope/intercept, and Brier score
Arvind, 2018	Patients undergoing ACDF	ANN, SVM, and random forest decision tree (RF) model	compared to the ASA physical status classification system	Surgical complications	AUC
Wang, 2021	Patients undergoing ACDF	artificial neural network (ANN) using preoperative variables	legacy risk-stratification measures: ASA and Charlson Comorbidity Index (CCI)	Complications within one week of index surgery	AUC
Veeramani, 2022	Patients undergoing ACDF	LR, Decision Tree (DT), RF, Gradient Boosting (GB), Extreme Gradient Boosting (XGB), and a Neural Network (NN)	NR	Unplanned intubation	AUC, Brier-score
Rudisill, 2022	Patients undergoing ACDF	extreme gradient boost (XGBoost)	NR	Early-onset adjacent segment degeneration	F1, AUC
Karhade, 2021	Patients undergoing ACDF	RF, SGB, neural network, SVM, elastic-net penalized logistic regression	NR	Lenght of stay >1 day after index	AUC, calibration, c-statistic, Brier-score
Gowd, 2022	Patients undergoing ACDF	LR, gradient boosting trees, RF, and decision tree	A predictive linear regression model constructed solely from comorbidity indices (ASA classification and frailty index) was used as comparison	Complications	AUC
Wong, 2020	Patients undergoing ACDF for degenerative cervical spine pathology	support vector machine algorithm	NR	early onset adjacent segment degeneration	AUC

Abbreviations: ANN, artificial neural network; ASD, adjacent segment disease; AUC, area under the ROC-curve; LASSO, least absolute shrinkage and selection operator; LR, logistic regression; MUaRS, multivariate adaptive regression splines; NDI, neck disability index; NPV, negative predictive value; PPV, positive predictive value; RF, random forest; SGB, stochastic gradient boosting; SVM, support vector machine

Waarden en voorkeuren van patiënten (en evt. hun verzorgers)

Indien patiënten vragen hebben over de voorspelling van behandeluitkomsten die betrekking hebben op hun eigen klinische situatie, dan is het van groot belang om patiënten goed te infomeren over het feit dat bestaande predictiemodellen slechts intern (of niet) gevalideerd zijn en dus niet betrouwbaar toepasbaar zijn in de klinische praktijk. Het ligt in de lijn der verwachting dat in de komende jaren externe validatie van predictiemodellen zal volgen.

Kosten (middelenbeslag)

De werkgroep is niet beken met kosten-effectiviteitsstudies op het gebied van predictiemodellen bij patiënten met CRS. Over de mogelijke kosten kan de werkgroep in stadium nog geen inschatting geven.

Aanvaardbaarheid, haalbaarheid en implementatie

Het moet worden aangetekend dat voor het laten 'draaien' van dergelijke predictiemodellen programma's moeten worden gedownload (zoals R of Python) die niet in elk ziekenhuis voorhanden zijn en/of die niet door de ICT van het ziekenhuis worden ondersteund. Het ligt sterk in de lijn der verwachting dat deze randvoorwaarde voor het in de praktijk toepasbaar laten zijn voor predictiemodellen de komende jaren aandacht zal krijgen.

Voetnoten:

NDI, C7 level pinprick on right (left) normal and Achilles (triceps brachii) muscle reflex on right normal.

NDI, level light touch on right normal, level pinprick on right normal and achilles (triceps brachii) muscle reflex on right normal

VAS-arm worst, NDI, MSPQ, EQ5D, cervical flexion (extension) active range of motion, cervical flexion (right rotation) active range of motion, head reposition accuracy from right to neutral, right hand grip strength, Romberg, Figure 8, coping strategies questionnaire, coping subscale, C5 level light touch on right normal, C6 level light touch on right normal and C7 level pinprick on right normal.

Aanbevelingen

Rationale van de aanbeveling: weging van argumenten voor en tegen de diagnostische procedure

Gezien de afwezigheid externe gevalideerde predictiemodellen en het slechts zeer beperkt aanwezig zijn van intern gevalideerde predictiemodellen kunnen aanbevelingen alleen met veel reserve worden gegeven. Op basis van de beschikbare gegevens adviseert de werkgroep om terughoudend te zijn met het bepalen van prognoses op basis van de predictiemodellen.

Geef geen prognoses aan patiënten met CRS op basis van predictiemodellen die niet extern gevalideerd zijn.

Wees terughoudend met het ontwikkelen van nieuwe predictiemodellen. Gebruik reeds gepubliceerde intern gevalideerde modellen alleen in onderzoekverband op eigen data ten behoeve van de externe validatie.

Literatuur

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Bijlagen bij module ‘AI gebaseerde predictiemodellen’

Implementatieplan

Aanbeveling	Tijdspad voor implementatie: <1 jaar, 1-3 jaar of >3 jaar	Verwacht effect op kosten	Randvoorwaarden voor implementatie (binnen aangegeven tijdspad)	Mogelijke barrières voor implementatie[1]	Te ondernemen acties voor implementatie[2]	Verantwoordelijken voor acties[3]	Overige opmerkingen
Wees terughoudend met het geven van prognoses aan patiënten met CRS op basis van predictiemodellen	<1 jaar	Geen	Geen	Geen	Verspreiden van richtlijn	Betrokken zorgprofessionals Beroepsverenigingen	-
Wees terughoudend met het ontwikkelen van nieuwe predictiemodellen. Gebruik reeds gepubliceerde intern gevalideerde modellen alleen in onderzoekverband op eigen data ten behoeve van de externe validatie.	1-3 jaar	Onderzoek financiering	*ICT van onderzoeksgroepen moet worden ingericht op effectueren van testen van modellen *Intern gevalideerde modellen dienen eerst extern gevalideerd te zijn	*Tekort aan personeel, onvoldoende financiering voor onderzoek *Vanwege bovengenoemde barrières nog onvoldoende getest zijn van slecht intern gevalideerde modellen	Gelden beschikbaar stellen om modellen in de praktijk te kunnen testen en daarmee tevredenheid van patiëntgroepen te evalueren	Betrokken zorgprofessionals. Onderzoek financiers.	Indien bestaande modellen extern gevalideerd zijn kunnen zij nadien geoptimaliseerd worden of inzicht geven in de richting van nieuw te ontwikkelen modellen

[1] Barrières kunnen zich bevinden op het niveau van de professional, op het niveau van de organisatie (het ziekenhuis) of op het niveau van het systeem (buiten het ziekenhuis). Denk bijvoorbeeld aan onenigheid in het land met betrekking tot de aanbeveling, onvoldoende motivatie of kennis bij de specialist, onvoldoende faciliteiten of personeel, nodige concentratie van zorg, kosten, slechte samenwerking tussen disciplines, nodige taakherschikking, etc.

[2] Denk aan acties die noodzakelijk zijn voor implementatie, maar ook acties die mogelijk zijn om de implementatie te bevorderen. Denk bijvoorbeeld aan controleren aanbeveling tijdens kwaliteitsvisitatie, publicatie van de richtlijn, ontwikkelen van implementatietools, informeren van ziekenhuisbestuurders, regelen van goede vergoeding voor een bepaald type behandeling, maken van samenwerkingsafspraken.

[3] Wie de verantwoordelijkheden draagt voor implementatie van de aanbevelingen, zal tevens afhankelijk zijn van het niveau waarop zich barrières bevinden. Barrières op het niveau van de professional zullen vaak opgelost moeten worden door de beroepsvereniging. Barrières op het niveau van de organisatie zullen vaak onder verantwoordelijkheid van de ziekenhuisbestuurders vallen. Bij het oplossen van barrières op het niveau van het systeem zijn ook andere partijen, zoals de NZA en zorgverzekeraars, van belang.

Zoekverantwoording

Algemene informatie

Cluster/richtlijn: NVvN Cervicaal radiculair syndroom	
Uitgangsvraag/modules: UV6 Wat is de rol/plaats van predictiemodellen bij het maken van behandelbeslissingen?	
Database(s): Embase.com, Ovid/Medline	Datum: 1 februari 2023
Periode: vanaf 2010	Talen: geen restrictie
Literatuurspecialist: Alies van der Wal	
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting: Voor deze vraag is gezocht op de elementen: - (chirurgie voor) CRS - machine/ deep learning, AI, prediction model De sleutelartikelen worden gevonden met deze search (vallen binnen de observationele studies). Sensitief RCT filter gebruikt.	
Te gebruiken voor richtlijnen tekst: *Nederlands* In de databases Embase.com en Ovid/Medline is op 1 februari 2023 systematisch gezocht naar systematische reviews, RCTs (en observationele studies) over CRS en machine/ deep learning, AI en prediction models. De literatuurzoekactie leverde 153 unieke treffers op. *Engels* On the 1st of February 2023, a systematic search was performed for systematic reviews, RCTs, (and observational studies) about machine/ deep learning, AI and prediction models in the databases Embase.com and Ovid/Medline. The search resulted in 153 unique hits.	

5 ***Zoekopbrengst***

	EMBASE	**OVID/MEDLINE**	**Ontdubbeld**
SR	43	31	50
RCT	92	49	103
Observationele studies	201	137	243
Totaal	135	80	**153***

in Rayyan

Zoekstrategie

Embase.com

No.	**Query**	**Results**
#13	#5 AND #10 NOT (#11 OR #12) = observationeel	201
#12	#5 AND #7 NOT #11 = RCT	92
#11	#5 AND #6 = SR	43
#10	#8 OR #9	15608484
#9	'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo*:ti,ab,kw OR 'sham-control*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind* OR masked)):ti,ab,kw) OR nonrandom*:ti,ab,kw OR 'non-random*':ti,ab,kw OR 'quasi-experiment*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case* NEAR/6 (matched OR control*)):ti,ab,kw) OR ((match* NEAR/6 (pair OR pairs OR cohort* OR control* OR group* OR healthy OR age OR sex OR gender OR patient* OR subject* OR participant*)):ti,ab,kw) OR ((propensity NEAR/6 (scor* OR match*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar*:ti OR ((compar* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort*:ti,ab,kw OR 'follow	13813526

	up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal*:ti,ab,kw OR prospective*:ti,ab,kw OR retrospective*:ti,ab,kw OR observational*:ti,ab,kw OR 'cross sectional*':ti,ab,kw OR cross?ectional*:ti,ab,kw OR multicent*:ti,ab,kw OR 'multi-cent*':ti,ab,kw OR consecutive*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar*:ti,ab,kw OR 'odds ratio*':ab OR 'relative odds':ab OR 'risk ratio*':ab OR 'relative risk*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab)))	
#8	'major clinical study'/de OR 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'comparative study'/de OR 'cohort analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti)	6767914
#7	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti	3718234
#6	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR (((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	733409
#5	#4 AND [2010-2023]/py	421
#4	#3 NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	524
#3	#1 AND #2	729
#2	'machine learning'/exp OR 'artificial intelligence'/exp OR 'deep learning model'/exp OR 'deep learning algorithm'/exp OR 'data classification'/exp OR 'algorithm'/exp OR 'prediction model'/exp OR 'prediction algorithm'/exp OR 'prediction'/exp OR 'computer prediction'/exp OR 'predictor variable'/exp OR 'predictive model'/exp OR (((machine OR deep OR algorithm* OR future OR representation) NEAR/3 learn*):ti,ab,kw) OR 'artificial intelligence':ti,ab,kw OR 'artificial neural network':ti,ab,kw OR 'machine intelligence':ti,ab,kw OR datamining:ti,ab,kw OR 'data mining':ti,ab,kw OR 'random forest*':ti,ab,kw OR 'random decision forest*':ti,ab,kw OR algorithm*:ti,ab,kw OR metric*:ti,ab,kw OR 'predict* model*':ti,ab,kw OR 'multilayer perceptron*':ti,ab,kw OR ((bayes* NEAR/3 network*):ti,ab,kw) OR 'support vector*':ti,ab,kw OR 'svc':ti,ab,kw OR 'svm':ti,ab,kw OR 'svr':ti,ab,kw OR 'nearest neighbor*':ti,ab,kw OR 'elastic net':ti,ab,kw OR (((kernel OR ensemble OR bagging OR bagged OR boosting OR boosted OR fuzzy) NEAR/3 (model* OR tree* OR algorithm*)):ti,ab,kw)	1530765
#1	'cervicobrachial neuralgia'/exp/mj OR cervicobrachial*:ti,ab,kw OR 'cervico brachial*':ti,ab,kw OR 'cervical brachial*':ti,ab,kw OR ((radiculalgia:ti,ab,kw OR radiculitis:ti,ab,kw OR radiculitides:ti,ab,kw OR radiculopath*:ti,ab,kw OR polyradiculopath*:ti,ab,kw OR neuralgia:ti,ab,kw OR 'herniated disc*':ti,ab,kw OR hernia:ti,ab,kw OR ((radicular NEAR/3 (pain* OR neuralgia* OR symptom* OR syndrom*)):ti,ab,kw) OR (('nerve root' NEAR/3 (pain* OR inflammation* OR disorder* OR compression* OR avulsion* OR impingement)):ti,ab,kw)) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('radicular pain'/exp/mj OR 'radiculopathy'/exp/mj) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('decompression surgery'/exp OR 'discectomy'/exp OR 'foraminotomy'/exp OR decompress*:ti,ab,kw OR discectom*:ti,ab,kw OR diskectom*:ti,ab,kw OR 'disc fusion':ti,ab,kw OR foraminotomy*:ti,ab,kw OR microforaminotom*:ti,ab,kw) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR 'anterior cervical discectomy'/exp OR 'anterior cervical discectomy and fusion'/exp	27360

Ovid/Medline

#	Searches	Results
13	(5 and 10) not (11 or 12) = observationeel	137
12	(5 and 7) not 11 = RCT	49
11	5 and 6 = SR	31
10	8 or 9	7129344
9	Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar* adj (study or studies)) or ((control or controlled) adj1 active) or "open label*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat* adj10 (arm or arms)) or placebo* or "sham-control*" or ((single or double or triple or assessor) adj1 (blind* or masked)) or nonrandom* or "non-random*" or "quasi-experiment*" or "parallel group*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case* adj6 (matched or control*)) or (match* adj6 (pair or pairs or cohort* or control* or group* or healthy or age or sex or gender or patient* or subject* or participant*)) or (propensity adj6 (scor* or match*))).ti,ab,kf. or (confounding adj6 adjust*).ti,ab. or (versus or vs or compar*).ti. or ((exp cohort studies/ or epidemiologic studies/ or multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort* or 'follow up' or followup or longitudinal* or prospective* or retrospective* or observational* or multicent* or 'multi-cent*' or consecutive*).ti,ab,kf.) and ((group or groups or subgroup* or versus or vs or compar*).ti,ab,kf. or ('odds ratio*' or 'relative odds' or 'risk ratio*' or 'relative risk*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.))	5357587
8	Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective*.tw. or prospective*.tw. or consecutive*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/	4365195
7	exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo*.tw.	2553963
6	meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.	649558
5	limit 4 to yr="2010 -Current"	304
4	3 not (comment/ or editorial/ or letter/) not ((exp animals/ or exp models, animal/) not humans/)	380
3	1 and 2	387
2	exp Machine Learning/ or exp Artificial Intelligence/ or exp Algorithms/ or exp Pattern Recognition, Automated/ or exp Decision Making, Computer-Assisted/ or ((machine or deep or algorithm* or future or representation) adj3 learn*).ti,ab,kf. or 'artificial intelligence'.ti,ab,kf. or 'artificial neural network'.ti,ab,kf. or 'machine intelligence'.ti,ab,kf. or datamining.ti,ab,kf. or 'data mining'.ti,ab,kf. or 'random forest*'.ti,ab,kf. or 'random decision forest*'.ti,ab,kf. or algorithm*.ti,ab,kf. or metric*.ti,ab,kf. or 'predict* model*'.ti,ab,kf. or 'multilayer perceptron*'.ti,ab,kf. or (bayes* adj3 network*).ti,ab,kf. or 'support vector*'.ti,ab,kf. or 'svc'.ti,ab,kf. or 'svm'.ti,ab,kf. or 'svr'.ti,ab,kf. or 'nearest neighbor*'.ti,ab,kf. or 'elastic net'.ti,ab,kf. or ((kernel or ensemble or bagging or bagged or boosting or boosted or fuzzy) adj3 (model* or tree* or algorithm*)).ti,ab,kf.	915581
1	((exp Radiculopathy/ or radiculalgia.ti,ab,kf. or radiculitis.ti,ab,kf. or radiculitides.ti,ab,kf. or radiculopath*.ti,ab,kf. or polyradiculopath*.ti,ab,kf. or neuralgia.ti,ab,kf. or 'herniated disc*'.ti,ab,kf. or hernia.ti,ab,kf. or (radicular adj3 (pain* or neuralgia* or symptom* or syndrom*)).ti,ab,kf. or ('nerve root' adj3 (pain* or inflammation* or disorder* or compression* or avulsion* or impingement)).ti,ab,kf.) and (exp Cervical Vertebrae/ or exp Neck/ or cervical.ti,ab,kf. or cervico*.ti,ab,kf. or neck.ti,ab,kf.)) or cervicobrachial*.ti,ab,kf. or 'cervico brachial*'.ti,ab,kf. or 'cervical brachial*'.ti,ab,kf. or ACDF.ti,ab,kf. or ((exp Decompression, Surgical/ or exp Diskectomy/ or	19743

	exp Foraminotomy/ or decompress*.ti,ab,kf. or foraminotom*.ti,ab,kf. or microforaminotom*.ti,ab,kf. or dis*ectom*.ti,ab,kf. or 'disc fusion*.ti,ab,kf. or microdiscectom*.ti,ab,kf.) and (exp Cervical Vertebrae/ or exp Neck/ or cervical.ti,ab,kf. or cervico*.ti,ab,kf. or neck.ti,ab,kf.))	

Module 6. Postoperatief beleid

Uitgangsvraag

Wat is het advies postoperatief ten aanzien van belastbaarheid van de nek voor patiënten met CRS?

Inleiding

Bij patiënten met het cervicaal radiculair syndroom (CRS) die een operatie ondergaan is er veel variatie in het advies aangaande de restricties en belastbaarheid van de nek in het postoperatieve beleid. De huidige klinische praktijk is niet gestandaardiseerd ten aanzien van belastbaarheidsadviezen en fysio-/oefenherapeutische nabehandeling. Hierin heerst praktijkvariatie. Ten grondslag aan de praktijkvariatie ligt het feit dat momenteel onduidelijk is welke postoperatieve adviezen rondom fysieke belastbaarheid na de operatie zouden moeten zijn. Deze module evalueert welk postoperatief beleid ten aanzien van belastbaarheid van de nek met meest passend is voor patiënten met CRS.

Search and select

A systematic review of the literature was performed to answer the following questions:

PICO 1: *What are the effects of postoperative advice of activity limitations compared to no physical restrictions in patients who have undergone surgery for CRS, in the acute postoperative phase (first 6 weeks after surgery)?*

- P: Patients who underwent surgery for CRS
- I: Advice within first 6 weeks after surgery: activity limitations
- C: Advice within first 6 weeks after surgery: no activity limitations/no physical restrictions
- O: Quality of life, global perceived effect, pain, disability, return to work, adjacent level disease

PICO 2: *What are the effects of postoperative advice of activity limitations compared to no physical restrictions in patients who have undergone surgery for CRS, after an initial postoperative recovery period (starting 6 weeks after surgery)?*

- P: Patients who underwent surgery for CRS
- I: Advice starting 6 weeks after surgery: activity limitations (after initial postoperative recovery)
- C: Advice starting 6 weeks after surgery: no activity limitations/no physical restrictions (after initial postoperative recovery)
- O: Quality of life, global perceived effect, pain, disability, return to work, adjacent level disease

<u>Relevant outcome measures</u>

The guideline development group considered quality of life and global perceived effect as *critical* outcome measures for decision making; and pain, disability, return to work and adjacent level disease as *important* outcome measures for decision making. The working group defined the outcome measures as in *Table 1*.

The working group defined a 10% difference for continuous outcome measures (weighted mean difference), 20% for dichotomous outcome measures informing on relative risk (RR ≤ 0.91 and ≥ 1.25), and 0.5 for Cohen's d in standardized mean difference (SMD ≤-0.5 and ≥ 0.5) as minimal clinically (patient) important differences.

Table 1. Definitions and instruments of researched outcome measures

Outcome	Instrument	Abbreviation	Explanation/Definition	Scale
Quality of Life	Short Form 36	SF-36	A multidimensional instrument consisting of 36 questions; higher scores indicating a better health status. It can generate 2 summary scores: Physical (PCS) and Mental Component Score (MCS).	0 to 100
	Short Form 12	SF-12	Questionnaire with 12 questions; higher scores indicating a better health status. It can generate scores on the physical (PCS) and mental health subscale (MCS).	0 to 100
	EuroQoL-5D	EQ-5D	This questionnaire generates an index score based on 5 questions on quality of life and has a VAS for current health state. Higher scores represent better (perceived) health.	Index: 0 to 1 VAS: 0 to 100
Global perceived effect	Global perceived effect (GPE)	GPE-DV	Questionnaire to measure patients' assessment of change in main complaint, on a scale from "fully recovered" (low score) to "much worse" (high score)	1 to 7 or 1 to 9
Pain	Visual Analog Scale	VAS	Line on which patients can indicate their pain from 0 (no pain) to 100 (worst pain imaginable)	0 to 100mm or 10cm
	Numerical (Pain) Rating Scale	N(P)RS	An 11-point scale on which patients can indicate their pain from 0 (no pain) to 10 (worst pain imaginable)	0 to 10
Disability	Neck Disability Index	NDI	Ten 5-point questions, after which total score is multiplied by 2 (seldom exceptions). Disability increases with increasing score.	0 to 100 (*or* 0 to 50)
Return to work	-	-	*Was not defined a priori by the working group, instead the definitions used in the studies were used.*	-
Adjacent level disease	-	-	*Was not defined a priori by the working group, instead the definitions used in the studies were used.*	-

Search and select (Methods)

The databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms from 1990 until 17 August 2022. The detailed search strategy is available upon request. The systematic literature search resulted in 382 hits. Studies were selected based on the following criteria:

1. Systematic review and/or meta-analysis, with detailed search strategy, risk of bias assessment, and results of individual studies available; or randomized controlled trial (RCT);
2. Patients aged ≥ 18 years;
3. studies including ≥ 20 (10 in each study arm) patients;
4. studies according to the PICOs (found under the heading "Search and select");
5. Follow-up period for PICO 1 of 6 weeks, 12 weeks or 3 months, and/or 12 months; and for PICO 2 a period of 3 months/12 weeks and/or 12 months;

- full-text English or Dutch language publication

Thirteen studies were initially selected based on title and abstract screening. After reading the full text, nine studies were excluded (see the table with reasons for exclusion under the heading "Evidence Tables") and four studies were included (PICO 1 n=3; PICO 2 n=1).

Results

Four studies were included in the analysis of the literature, three RCTs for PICO 1 and one RCT for PICO 2. Important study characteristics and results are summarized in the evidence tables. The assessment of the risk of bias is summarized in the risk of bias tables.

Summary of literature

Description of studies - PICO 1 (acute postoperative phase)

Abbott (2013) investigated the physical, functional, and quality of life-related outcomes of patients undergoing anterior cervical discectomy and fusion (ACDF), with and without post-operative activity restrictions (i.e. collar usage). To this end, patients aged 18 to 65 years planned to undergo ACDF were randomized before surgery into the intervention group (n = 17) or the control group (n = 16). During the first days after surgery, both groups received respiratory and circulatory exercises, training of transfers, walking, and activities of daily living by a physiotherapist. Patients in the intervention group received a rigid cervical collar

to be worn during daytime over a 6-week period and **restrictions** from certain activities in the first 3 months after the operation (restricted from activities such as contact sports, running, heavy lifting, driving, and outer-range cervical spine movements). The control group received no postoperative neck movement restrictions. The outcomes quality of life (SF-36), pain (Borg CR-10), and disability (NDI) were assessed after 6 weeks, 3 months, 6 months, 12 months, and 24 months.

Coronado (2020) performed an RCT to examine the acceptability and outcome effects of an early **self-directed home exercise program** (HEP) within the first 6 weeks after ACDF. Patients aged 21 or older undergoing ACDF were included and randomized to the early HEP (n = 15) or usual care (n = 15). Usual care was administered to both groups and comprised:

- medication,
- cervical collar as indicated (9 patients in HEP-group (60%) and 11 patients in usual care group (73%)),
- driving restrictions (varying from 2 to 6 weeks after surgery), or
- lifting restrictions (not more than 15 pounds or perform sudden or extreme neck movements).

The early HEP was a 6-week self-directed program directly after surgery with walking, sleeping instructions, and range of motion and strengthening exercises performed daily, with personalized adaption by the physiotherapist every 2 weeks. After 6 weeks, 6 months and 12 months, quality of life was measured through the SF-12, arm and neck pain through the NRS, and disability through the NDI.

McFarland (2020) compared clinical outcomes between **early cervical spine stabilizer (ECS) training** and usual care in patients after ACDF in an RCT. Randomization of patients aged 30 to 75 years and scheduled to undergo ADCF surgery for MRI-confirmed cervical nerve root compression causing radiculopathy took place. Patients were either randomly allocated to ECS training for 6 weeks (n = 20), or usual care for 6 weeks (n = 20). ECS comprised specific instructions with pictures and descriptions of 10 exercises (performed daily with increasing repetitions) for achieving correct positioning and movement; and a walking program. Usual care consisted of a DVD with general spine surgery precautions, and instructions in proper posture, use of cervical collar if applicable, and safety with transfers and walking. Pain (NPRS) and disability (NDI) were the outcomes assessed after 6 and 12 weeks.

Results – PICO 1

1a. Quality of life

Rest versus no rest

Quality of life was reported by Abbott (2013) after 6 weeks, 3 months and 12 months through the SF-36, for patients receiving movement restrictions (secured by prescribing a rigid collar) post-operative compared to patients receiving no advice with regard to activity restrictions.

Exercise versus usual care

Coronado (2020) reported quality of life after 6 weeks and 12 months for patients receiving an early home exercise program and patients receiving usual care, measured through the SF-12. The mean differences in quality of life for the physical (PCS) and mental component score (MCS) between rest and no rest, and exercise and usual care, is depicted in *Figure 1a*.

For the comparison "*rest versus no rest*", rest (movement restrictions and collar) seems to positively affect the PCS (statistically significant), yet possibly negatively affect the MCS; however, this effect on the MCS has disappeared after 12 months. For the comparison "*Exercise versus usual care*", a training program does not seem to affect PCS and negatively

affect MCS. However, none of the observed differences in PCS and MCS in both comparisons exceed the borders for clinical relevance.

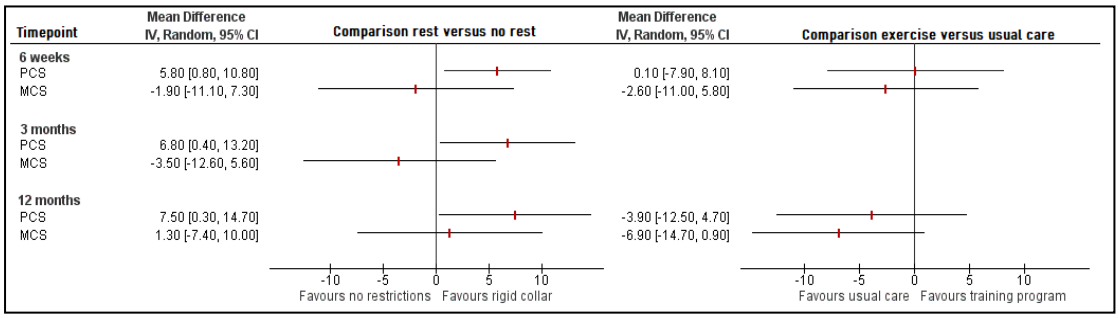

Figure 1a. Mean differences in quality of life outcomes for the comparisons "rest versus no rest" and "exercise versus usual care". Higher scores indicate better outcomes.

1b. Global perceived effect

No studies reported on the outcome measure global perceived effect.

1c. Pain

Rest versus no rest

Abbott (2013) reported average pain intensity over 24 hours in the neck and shoulder/arm region on the Borg CR-10 scale. This scale was not previously defined (under the heading "Search and select", subheading "Relevant outcome measures"), yet ranges from 0 (least intense pain) to 10 (most intense pain), and correlates with the VAS (Harms-Ringdahl, 1986). Therefore, the outcomes are reported and depicted in *Figure 1b1*. Point estimates of pain scores show a clinically relevant effect in favour of movement restrictions, however the confidence interval crosses the border of clinical relevance and significance, implying different inferences.

Exercise versus usual care

Both Coronado (2020) and McFarland (2020) reported pain outcomes through the NRS, after 6 weeks and 12 months, and 6 weeks and 3 months, respectively. Both studies compare an early training programme (home exercise program or cervical spine stabilizer training) to usual care. The results are depicted in *Figure 1b2*. Observed differences in pain are not statistically significant, nor clinically relevant.

1d. Disability

Rest versus no rest

Abbott (2013) reported disability through the Neck Disability Index (NDI) on a scale of 0 to 50 for patients receiving movement restrictions post-operative compared to patients receiving no advice with regard to activity restrictions. Mean differences are shown in *Figure 1d1*. Despite being statistically significant at 6 weeks, none of the observed differences in disability are clinically relevant.

Exercise versus usual care

Both Coronado (2020) and McFarland (2020) reported disability outcomes through the NDI: the former on a scale from 0 to 50 after 6 weeks and 12 months; the latter on a scale from 0 to 100 afters 6 weeks and 3 months, respectively. The results are depicted in *Figure 1d2*. For reading and interpretation purposes the score of McFarland have been divided by 2. No observed differences were statistically significant or clinically relevant.

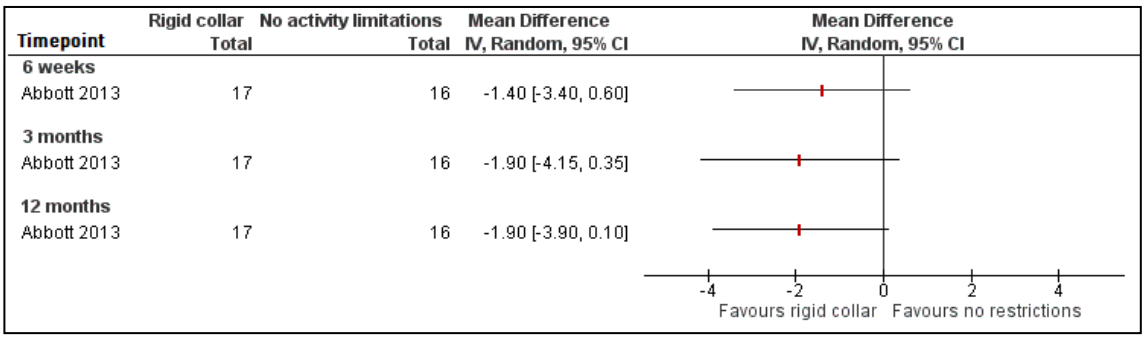

Figure 1c1. Mean differences in pain outcomes for "rest versus no rest" 6 weeks postoperative, 6 weeks after end of intervention (3 months), and 12 months.

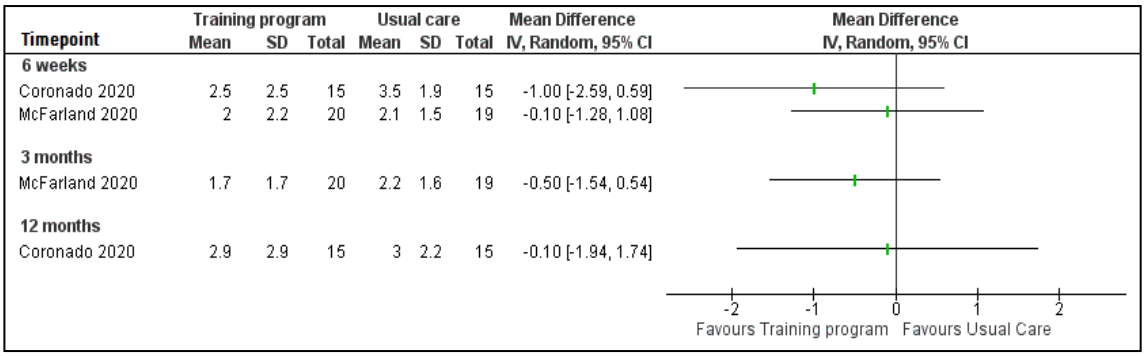

Figure 1c2. Mean differences in pain outcomes for "training versus usual care" 6 weeks postoperative, 6 weeks after end of intervention (3 months), and 12 months.

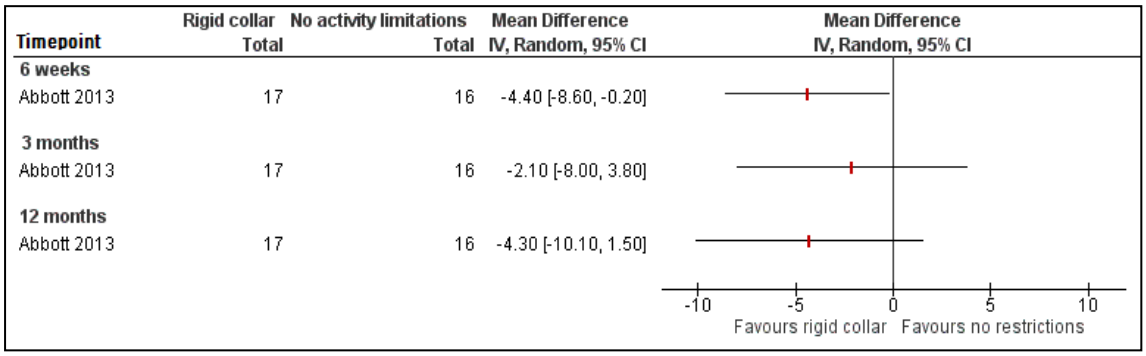

Figure 1d1. Mean differences in disability outcomes (scale 0 to 50) for "rest versus no rest" 6 weeks postoperative, 6 weeks after end of intervention (3 months), and 12 months

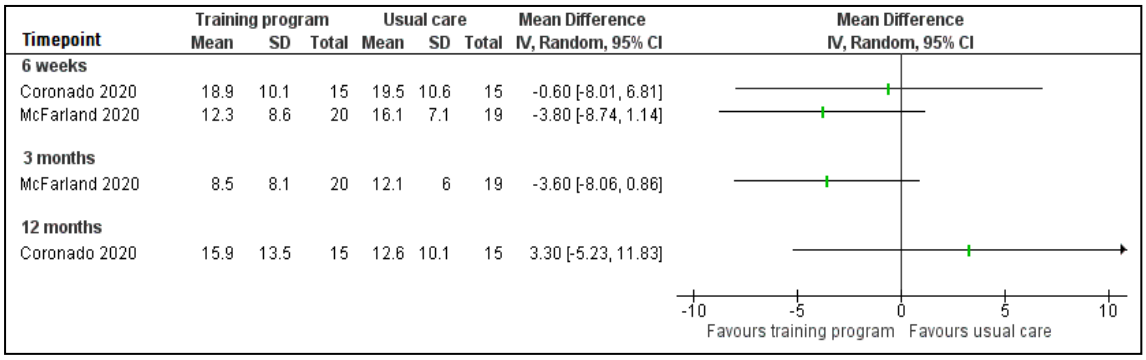

Figure 1d2. Mean differences in disability outcomes (scale 0 to 50) for "training versus usual care" 6 weeks postoperative, 6 weeks after end of intervention (3 months), and 12 months.

5

1e. Return to work; and
No studies reported on the outcome measure return to work.

1f. Adjacent level disease
Coronado (2020) did not specifically report adjacent level disease but noted that no participants underwent revision surgery during follow-up.

Level of evidence of the literature – PICO 1

1a. Quality of life (critical)
The level of evidence regarding the outcome measure *quality of life* was downgraded:

6. For *Rest versus no rest* by 4 levels because of unclear randomization, no blinding, and a large proportion loss to follow-up (-2, risk of bias); and the inclusion of a single study, with confidence intervals of the estimate crossing the border of clinical relevance (-2, imprecision).
7. For *Exercise versus usual care* by 4 levels because of unclear randomization in one study, insufficient blinding, and selective reporting in one study (-1, risk of bias); not comparing relative rest to no activity restrictions (-1, bias due to indirectness); and the inclusion of a single study, with confidence intervals of the estimate crossing the border of clinical relevance (-2, imprecision).

No downgrading took place for inconsistency or publication bias.

1b. Global perceived effect (critical)
The outcome global perceived effect was not reported and could not be graded.

1c. Pain (important)
The level of evidence regarding the outcome measure *pain* was downgraded by 3 levels:

8. For *Rest versus no rest* because of unclear randomization, no blinding, and a large proportion loss to follow-up (-2, risk of bias); and the inclusion of a single study, with confidence intervals of the estimate crossing the border of clinical relevance (-1, imprecision).
9. For *Exercise versus usual care* because of unclear randomization in one study, insufficient blinding, and selective reporting in one study (-1, risk of bias); not comparing relative rest to no activity restrictions (-1, bias due to indirectness); the confidence intervals of the clinical estimates crossing the border of clinical relevance (-1, imprecision).

No downgrading took place for inconsistency or publication bias.

1d. Disability (important)
The level of evidence regarding the outcome measure *disability* was downgraded by 4 levels:

10. For *Rest versus no rest* because of unclear randomization, no blinding, and a large proportion loss to follow-up (-2, risk of bias); and the inclusion of a single study, with confidence intervals of the estimate crossing the border of clinical relevance (-2, imprecision).
11. For *Exercise versus usual care* because of unclear randomization in one study, insufficient blinding, and selective reporting in one study (-1, risk of bias); not comparing relive rest to no activity restrictions (-1, bias due to indirectness); and the confidence intervals of the estimates crossing both borders of clinical relevance (-2, imprecision).

No downgrading took place for inconsistency or publication bias.

1e. Return to work (important); and 1f. Adjacent level disease (important)
The outcomes return to work and adjacent level disease were not reported and could not be graded.

Description of studies - PICO 2 (initial postoperative recovery period)

The RCT by Peolsson (2019) investigated the additional benefits of structured postoperative rehabilitation programme (SPT) over a standard approach (SA). Patients with MRI evidence of disc herniation and concomitant clinical signs of cervical radiculopathy for which they underwent surgery, were randomized to either the SPT group (n = 101) or the SA (n = 100) group. Both groups underwent equal postoperative care within the first 6 weeks after surgery. The SPT programme included physiotherapy sessions (from 6 weeks after surgery up until 24 weeks) with individually and progressively adjusted neck-specific exercises and a behavioural approach. The standard postoperative approach comprised usual care with the possibility to seek physiotherapy upon the patient's own initiative. Outcomes were quality of life, pain, and disability, after 3 months, 6 months, 12 months and 24 months.

Results – PICO 2

2a. Quality of life

Peolsson (2019) reported the quality of life through the EQ-5D questionnaire, scoring from 0 to 1. Mean differences after 3 and 12 months are depicted in *Figure 2a* (per-protocol analysis). The SMD from ANOVA intention-to-treat analysis between groups was 0.02, indicating no difference in effect between SPT and SA.

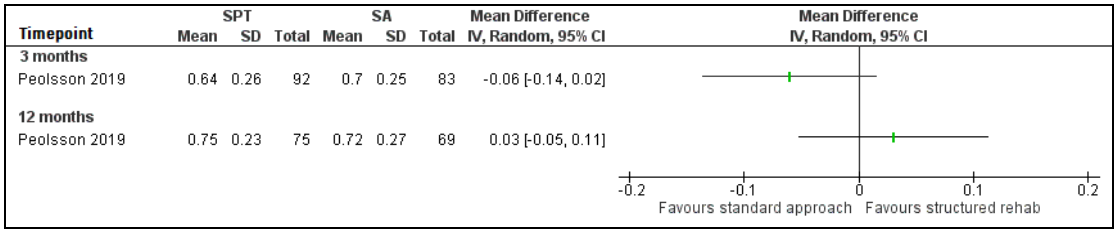

Figure 2a. Mean differences in quality of life outcomes between a standardized postoperative rehabilitation program (SPT) and a standard postoperative approach (SA), per-protocol. Higher scores indicate better outcomes.

2b. Global perceived effect

No studies reported on the outcome measure global perceived effect.

2c. Pain

Pain was reported by Peolsson (2019) through the VAS from 0 to 100 mm. The mean difference (from per-protocol data) at 3 months between SPT and SA was 3.0 (95%CI -3.5 to 9.5); and at 12 months 0 (95% CI -7.7 to 7.7). This is not statistically significant nor clinically relevant. The SMD from ANOVA intention-to-treat analysis between groups was 0.07, indicating no difference in effect between SPT and SA.

2d. Disability

The outcome disability was reported after 3 and 12 months through the NDI, on a scale from 0 to 100% (Peolsson, 2019). After 3 months, disability (per-protocol data) was higher in the SPT group (mean difference 4.0; 95% CI -1.0 to 9.0), but after 12 months higher in the SA group (mean difference -2.0; 95% CI -7.8 to 3.8). These differences are not statistically significant, nor clinically relevant. The SMD from ANOVA intention-to-treat analysis between groups was 0.03, indicating no difference in effect between SPT and SA.

2e. Return to work; and 2f. Adjacent level disease

The outcome measures return to work or adjacent level disease were not reported.

Level of evidence of the literature – PICO 2

2a. Quality of life (critical)

The level of evidence regarding the outcome measure *quality of life* was downgraded by 4 levels because of insufficient blinding, frequent loss to follow-up, and dilution of potential effect due to study methods (-1, risk of bias); not comparing relative rest to no activity restrictions (-1, bias due to indirectness); and the inclusion of a single study, with confidence intervals of the estimate crossing the border of clinical relevance (-2, imprecision). No downgrading took place for inconsistency or publication bias.

2b. Global perceived effect (critical)

The outcome global perceived effect was not reported and could not be graded.

2c. Pain (important)

The level of evidence regarding the outcome measure *pain* was downgraded by 3 levels because of insufficient blinding, frequent loss to follow-up, and dilution of potential effect due to study methods (-1, risk of bias); not comparing relative rest to no activity restrictions (-1, bias due to indirectness); and the inclusion of a single study that was underpowered for this comparison (-1, imprecision). No downgrading took place for inconsistency or publication bias.

2d. Disability (important)

The level of evidence regarding the outcome measure *disability* was downgraded by 3 levels because of insufficient blinding, frequent loss to follow-up, and dilution of potential effect due to study methods (-1, risk of bias); not comparing relative rest to no activity restrictions (-1, bias due to indirectness); and the inclusion of a single study that was underpowered for this comparison (-1, imprecision). No downgrading took place for inconsistency or publication bias.

2e. Return to work (important); 2f. Adjacent level disease (important)

The outcomes return to work and adjacent level disease were not reported and could not be graded.

Conclusions – PICO 1

What are the effects of postoperative advice of activity limitations compared to no physical restrictions in patients who have undergone surgery for CRS, in the acute postoperative phase (first 6 weeks after surgery)?

1a. Quality of life (critical)

Very low GRADE	The possible beneficial effect of activity restrictions within the first 6 weeks after ACDF surgery on the physical component of quality of life is very uncertain, as is the effect on the mental component of quality of life, compared to no activity restrictions. *Source: Abbott (2013), Coronado (2020)*

1b. Global perceived effect (critical)

- GRADE	The outcome global perceived effect was not reported and could not be graded.

1c. Pain (important)

Very low GRADE	The possible beneficial effect on pain outcomes of activity restrictions within the first 6 weeks after ACDF surgery compared to no activity restrictions is very uncertain. *Source: Abbott (2013), Coronado (2020), McFarland (2020)*

1d. Disability (important)

Very low GRADE	The evidence is very uncertain about the effect of activity restrictions within the first 6 weeks after ACDF surgery compared to no activity restrictions on disability. *Source: Abbott (2013), Coronado (2020), McFarland (2020)*

1e. Return to work (important); 1f. Adjacent level disease (important)

- GRADE	The outcomes return to work and adjacent level disease were not reported and could not be graded.

Conclusions – PICO 2

What are the effects of postoperative advice of activity limitations compared to no physical restrictions in patients who have undergone surgery for CRS, after an initial postoperative recovery period (starting 6 weeks after surgery)?

2a. Quality of life (critical)

Very low GRADE	The evidence is very uncertain about the effect of activity limitations starting 6 weeks after ACDF surgery on quality of life compared to no activity restrictions, for patients with CRS. *Source: Peolsson (2019)*

2b. Global perceived effect (critical)

- GRADE	The outcome global perceived effect was not reported and could not be graded.

2c. Pain (important)

Very low GRADE	The evidence is very uncertain about the effect of activity limitations starting 6 weeks after ACDF surgery on pain outcomes compared to no activity restrictions, for patients with CRS. *Source: Peolsson (2019)*

2d. Disability (important)

Very low GRADE	The evidence is very uncertain about the effect of activity limitations starting 6 weeks after ACDF surgery compared to no activity restrictions on disability in patients with CRS. *Source: Peolsson (2019)*

2e. Return to work (important); f. Adjacent level disease (important)

- GRADE	The outcomes return to work and adjacent level disease were not reported and could not be graded.

Overwegingen – van bewijs naar aanbeveling

Voor- en nadelen van de interventie en de kwaliteit van het bewijs

Het doel van deze module was om te achterhalen wat het optimale postoperatieve beleid is ten aanzien van belastbaarheid van de nek voor patiënten met CRS. De module is opgedeeld in twee subvragen. In *deel 1* is gekeken naar de effectiviteit van het geven van advies om de fysieke belastbaarheid te beperken op korte termijn (binnen 6 weken postoperatief). Er zijn drie studies gevonden. Er lijkt geen voordeel te zijn voor de kwaliteit van leven bij het ontvangen van advies voor restricties in activiteit in vergelijking met geen advies tot activiteit restricties in de eerste 6 weken na operatie, bij patiënten die geopereerd zijn voor CRS. De bewijskracht voor de cruciale uitkomstmaat kwaliteit van leven is *zeer laag*, omdat dit op slechts enkele kleine studies is gebaseerd met risico op bias. De cruciale uitkomstmaat 'global perceived effect' wordt niet gerapporteerd.

In *deel 2* is gekeken naar de effectiviteit van het geven van advies om de fysieke belastbaarheid te beperken op de lange termijn (vanaf 6 weken postoperatief). Er is één studie gevonden. Intensieve revalidatie met fysieke en mentale begeleiding na een initiële postoperatieve fase van 6 weken heeft geen klinisch relevant effect op de kwaliteit van leven, pijnuitkomsten of functioneren. De gevonden bewijskracht is hiervoor zeer laag, volgend uit indirect bewijs met risico op bias. Samenvattend is de bewijskracht voor de kritieke uitkomstmaten was *zeer laag*. Dit betekent dat andere studies kunnen leiden tot nieuwe inzichten.

Uit de literatuur blijkt dat er geen direct antwoord is te geven op de uitgangsvraag. De werkgroep adviseert (op basis van expert opinie en praktijkervaring) om werk en sport geleidelijk hervatten met uiteindelijk doel de patiënt geen beperkingen op te leggen. Om dit advies indirect te toetsen, is de vraag onderzocht of restricties van activiteiten of extra oefeningen in de vroege fase (binnen 6 weken) effect hebben op de uitkomst na chirurgie. Abott (2013) toont dat het geven van restricties in de eerste 3 maanden na operatie (geen contactsporten, rennen, zwaar tillen, autorijden) niet leidt tot een betere uitkomst. Coronado (2000) concludeert dat rek- en spierkrachtoefeningen direct na de operatie niet leiden tot een betere (of slechtere) uitkomst. McFarland (2020) laat zien dat dagelijkse oefeningen met cervicale retractie in de eerste 6 weken niet leidt tot meer pijn of functieverlies, maar ook niet tot verbetering van de uitkomst.

In de regel herstellen patiënten na operatieve behandeling van een CRS snel. Daarom meent de werkgroep dat snelle hervatting van alle activiteiten op geleide van de pijn mogelijk is. Een mogelijk gevaar schuilt echter in het *te snel* hervatten van activiteiten, waarbij snelle nekbewegingen nodig zouden kunnen zijn (zoals autorijden en fietsen). De literatuur toont echter niet dat het geven van restricties helpt. Hier ligt een kennislacune. Beter onderzoek is nodig met gebruik van performance-tests zoals de FIT-HaNSA (McGee, 2019). Ook vanuit de richtlijnen 'Geïnstrumenteerde wervelkolomchirurgie'- (NOV, 2017) en 'Lumbosacraal radiculair syndroom' (NVN, 2020) is geen informatie voorhanden die te extrapoleren is naar patiënten met CRS. Ten aanzien van restrictie met autorijden is alleen een survey onder chirurgen na spinale chirurgie in de brede zin van het woord bekend, waarbij de grootste groep (58%) als advies geeft hervatten autorijden na 3 tot 6 weken (McGregor, 2006). Enige beperking ten aanzien van werk of andere activiteiten bestaat uiteindelijk niet. Aanvankelijk kunnen nekklachten een beperkende factor zijn, waardoor de werkomgeving indien mogelijk aangepast moet worden. Ook de mogelijkheid om regelmatig van houding te kunnen wisselen of van activiteit te veranderen draagt bij aan een snellere volledige werkhervatting, zo blijkt uit de praktijk.

De werkgroep acht het van belang dat pre-operatief de patiënt bewust is van realistische verwachtingen ten aanzien van werkhervatting en eventuele tijdelijke restricties. Dit moet goed besproken worden met de patiënt. Hervatting van autorijden en werk zijn hierbij

belangrijke punten. Hierbij kan bijvoorbeeld een concreet plan ten aanzien van hervatting van activiteiten bij helpen.

Waarden en voorkeuren van patiënten (en evt. hun verzorgers)

Het doel is om de patiënt zo snel als mogelijk is, alles weer te laten doen zónder risico op complicaties. Daarbij is het ook van belang om te voorkomen dat de patiënt de nek te veel belast kort na de operatie en daarmee een geprolongeerd herstel bewerkstelligt. De patiënt is gediend bij het geven van adviezen die zo concreet als mogelijk zijn en al worden gegeven voor de operatie plaatsvindt. De patiënt zal echter moeten omgaan met het feit dat er onzekerheid is of de postoperatieve adviezen zinvol zijn en dat het ook een kwestie is van 'gezond verstand'. Autorijden en werkhervatting zijn belangrijke aspecten om te bespreken.

Kosten (middelenbeslag)

Kosten-effectiviteitsstudies rondom dit onderwerp zijn de werkgroep niet bekend. Sneller minder restricties zal een snellere hervatting van dagelijkse activiteiten en werkhervatting betekenen, wat zeer waarschijnlijk zal resulteren in lagere kosten.

Aanvaardbaarheid, haalbaarheid en implementatie

Er is geen onderzoek bekend dat heeft gekeken naar de aanvaardbaarheid en haalbaarheid van de postoperatieve adviezen. Gezien het ontbreken van een standaard dient de operateur de adviezen goed en op tijd af te stemmen met de patiënt. De werkgroep voorziet geen barrières op het gebied van aanvaardbaarheid, haalbaarheid of implementatie.

Aanbevelingen

Rationale van de aanbeveling: weging van argumenten voor en tegen de interventies

Uit de literatuur is geen sterk bewijs gevonden over postoperatieve adviezen. In de regel herstellen patiënten na operatieve behandeling van een CRS snel. Daarom meent de werkgroep dat snelle hervatting van alle activiteiten mogelijk is. Het is hierbij van belang dat preoperatief ene plan en/of verwachtingen met de patiënt worden afgestemd. Postoperatief is het van belang te streven naar het snel oppakken van activiteiten. Nader onderzoek op dit gebied is gewenst.

Preoperatief

Maak de patiënt voor de operatie bewust van realistische verwachtingen ten aanzien van werkhervatting en eventuele tijdelijke restricties (denk bijvoorbeeld aan autorijden, intensiteit van werk, sport).

Postoperatief

Adviseer de patiënt om activiteiten van het dagelijks leven weer op te pakken, zonder al te veel restricties, op geleide van de pijn.

Leg tijdens het herstel focus op de mogelijk ontstane beperkingen van de nek en/of arm. Overweeg actieve gerichte oefentherapie (geen massage).

Literatuur

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Bijlagen bij module ‘post-operatief beleid’

Implementatieplan

Aanbeveling	Tijdspad voor implementatie: < 1 jaar, 1 tot 3 jaar of > 3 jaar	Verwacht effect op kosten	Randvoorwaarden voor implementatie (binnen aangegeven tijdspad)	Mogelijke barrières voor implementatie[1]	Te ondernemen acties voor implementatie[2]	Verantwoordelijken voor acties[3]	Overige opmerkingen
Alle aanbevelingen	< 1 jaar	Beperkt	Bekendheid met de richtlijn.	Geen	• Voldoende kennis bij / scholing voor zorgverleners. • Vervolg onderzoek. • Verspreiden van richtlijn.	• Zorgprofessionals van instellingen. • Beroepsverenigingen.	Niet van toepassing.

[1] Barrières kunnen zich bevinden op het niveau van de professional, op het niveau van de organisatie (het ziekenhuis) of op het niveau van het systeem (buiten het ziekenhuis). Denk bijvoorbeeld aan onenigheid in het land met betrekking tot de aanbeveling, onvoldoende motivatie of kennis bij de specialist, onvoldoende faciliteiten of personeel, nodige concentratie van zorg, kosten, slechte samenwerking tussen disciplines, nodige taakherschikking, etc.

[2] Denk aan acties die noodzakelijk zijn voor implementatie, maar ook acties die mogelijk zijn om de implementatie te bevorderen. Denk bijvoorbeeld aan controleren aanbeveling tijdens kwaliteitsvisitatie, publicatie van de richtlijn, ontwikkelen van implementatietools, informeren van ziekenhuisbestuurders, regelen van goede vergoeding voor een bepaald type behandeling, maken van samenwerkingsafspraken.

[3] Wie de verantwoordelijkheden draagt voor implementatie van de aanbevelingen, zal tevens afhankelijk zijn van het niveau waarop zich barrières bevinden. Barrières op het niveau van de professional zullen vaak opgelost moeten worden door de beroepsvereniging. Barrières op het niveau van de organisatie zullen vaak onder verantwoordelijkheid van de ziekenhuisbestuurders vallen. Bij het oplossen van barrières op het niveau van het systeem zijn ook andere partijen, zoals de NZA en zorgverzekeraars, van belang.

Evidence tables

PICO1

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Abbot, 2013	Type of study: RCT Setting and country: Single academic centre, Sweden Funding and conflicts of interest: authors report "no declaration of interest", funding information not disclosed in article.	Inclusion criteria: (1) Aged 18-65 years, (2) clinical and radiological signs of cervical root compression with corresponding pain distribution for >3 months, for which conservative treatment had failed, (3) primary diagnosis of cervical spondylosis, disc herniation or degenerative disc disease, (4) planned to undergo ACDF Exclusion criteria: (1) Inability to understand Swedish, (2) previous ACDF surgery N total at baseline: 33 Intervention (I): 17 Control (C): 16 Important prognostic factors: *age ± SD:* I: 53.4 ± 13 C: 47.3 ± 11 *Sex (% M):* I: 53%| C: 69% Groups comparable at baseline? Yes	During first days after surgery: respiratory and circulatory exercises, training of transfers, walking and activities of daily living relevant for the patient by physiotherapist. Before discharge instruction for home training program for shoulder and thoracic mobility, stabilization of cervical spine and walking. Rigid cervical collar at daytime over a 6-week period. In first 3 weeks both in- and outdoors, in second 3 weeks collar could be removed when sitting indoors with the neck supported. Restriction from certain activities in first 3 months after the operation.	No postoperative neck movement restrictions.	Length of follow-up: 6 weeks, 3 months, 6 months, 12 months, and 24 months Loss-to-follow-up: Intervention: 9 (53%) Control: 9 (56%) *Reasons*: not reported Incomplete outcome data: Up until 6 months: 9 (I: 5, C: 4) Up until 1 year: 13 (I: 7, C: 6) Up until 2 years: 18 (I: 9, C: 9)	Outcome measures and effect size (including 95%CI): Quality of Life (SF-36) *Mean difference (95% CI)* 6w PCS 5.8 (0.8 to 1.07) MCS -1.9 (-11.1 to 7.4) 3m PCS 6.8 (0.4 to 13.1) MCS -3.5 (-12.6 to 5.6) 12m PCS 7.5 (0.3 to 14.6) MCS 1.3 (-7.4 to 10.1) Pain (Borg CR-10 scale) *Neck pain, mean difference (95% CI)* 6w: -1.4 (-3.4 to 0.6) 3m: -1.9 (-4.1 to 0.4) 12m: -1.9 (-3.9 to 0.01) Disability (NDI) *Mean difference (95% CI)* 6w: -4.4 (-8.6 to -0.2) 3m: -2.1 (-8.0 to 3.8) 12m: -4.3 (-10.1 to 1.5)	Author's conclusion: short-term cervical collar use post ACDF with interbody cage may help certain patients cope with initial post-operative pain and disability. Remarks: imprecise; post-hoc analyses without sample size calculation
Coronado, 2020	Type of study: RCT Setting and country: Single academic centre, United States of America Funding and conflicts of interest: two non-commercial grants, consultancy grants and expert	Inclusion criteria: (1) Patients aged ≥21, (2) undergoing ACDF for cervical stenosis, spondylosis, degenerative spondylolisthesis, or disc herniation Exclusion criteria: (1) Surgery secondary to trauma, fracture, tumor, infection or spinal deformity, (2) undergoing cervical corpectomy, (3) N total at baseline: 30 Intervention (I): 15 Control (C): 15 Important prognostic factors: *age ± SD:* I: 51.8 ± 10.3	Usual postoperative care, including medication, cervical collar as indicated, and driving (2 to 6 weeks) or lifting restrictions (not >15 pounds). Early self-directed Home Exercise program for 6 weeks directly after surgery with walking, and sleeping instructions and range of motion and strengthening exercises, performed daily, progressing in intensity every 2 weeks. Support was through weekly phone calls by the physiotherapist giving personalized adaptation.		Length of follow-up: 6 weeks, 6 months and 12 months Loss-to-follow-up: 2 Intervention: 1 (6.7%) Control: 1. (6.7%) *Reasons:* not reported Incomplete outcome data: See above.	Outcome measures and effect size (including 95%CI): Quality of Life (SF-12) *Mean difference (95% CI)* 6w P 0.1 (-7.9 to 8.1) M -2.6 (11.0 to 5.8) 12m P -3.9 (-12.5 to 4.7) M -6.9 (-14.7 to 0.9) Pain (NRS) *Neck pain, mean difference (95% CI)* 6w: -1.0 (-2.6 to 0.6) 12m: -0.1 (-1.9 to 1.7)	Authors' conclusion: exercise may be an effective pain management approach in the short-term, with potential for long-term reductions in opioid utilization Remarks: underpowered (pilot design)

	testimony.	C: 49.3 ± 11.9 *Sex (% M)* I: 40.0% | C: 53.3% Groups comparable at baseline? Yes				Disability (NDI) *Mean difference (95% CI)* 6w: -0.6 (-8.0 to 6.8) 12m: 3.3 (-5.2 to 11.8)	
McFarland, 2020	Type of study: RCT Setting and country: Single centre, United States of America Funding and conflicts of interest: authors report no conflict of interest, funding information not disclosed in article.	Inclusion criteria: (1) Age 30-75 years, (2) scheduled to undergo ACDF surgery, (3) cervical radiculopathy verified using MRI Exclusion criteria: (1) musculoskeletal or systemic disorders that would limit activity required for the study, (2) pain >8 (out of 10) on NPRS, (3) prior cervical spine surgery N total at baseline: 40 Intervention (I): 20 Control (C): 20 Important prognostic factors: *age ± SD:* I: 54.7 ± 10.5 C: 56.0 ±9.8 *Sex (%M)* I: 30% | C: 50% Groups comparable at baseline? Yes	*Early cervical spine stabilizer training for 6 (+ 6) weeks*: specific instructions with pictures and descriptions of 10 exercises for achieving correct positioning and movement. Performed daily, increasing exercise by one repetition every other day until 30 repetitions (without aggravating symptoms). Plus a walking program with written instructions and attention to proper posture, having to record walking distance	*Usual care for 6 weeks:* instructions in proper posture (head neutral position and avoiding looing up), use of cervical collar if applicable, and safety with transfers and gait. A DVD with general spine surgery precautions and instructions. Nonpharmacological pain management instructions (ice pack, deep breathing, walking) Plus general instructions to walk.	Length of follow-up: 6 and 12 weeks Loss-to-follow-up: Intervention: 3 (15%) Control: 4 (20%) *Reasons:* Withdrew from study (n = 1), did not return for follow-up (n = 5), discontinued due to medical complications (n = 1) Incomplete outcome data: Intervention: 5 (25%) Control: 7 (35%) *Reasons:* see loss to follow-up, plus 5 patients released by surgeon and followed-up on phone.	Outcome measures and effect size (including 95%CI): Pain (NPRS) *Mean difference (95% CI)* 6w: -0.1 (--1.3 to 1.1) 3m: -0.5 (-1.5 to 0.5) Disability (NDI) *Mean difference (95% CI)* 6w: -7.6 (-17.5 to 2.3) 3m: -7.3 (-16.2 to 1.6)	Authors' conclusion: Because both the UC training and ECS training resulted in the same amount of improvements at 6 and 12 weeks, UC training may be sufficient for the patient's first three months of recovery after ACDF surgery. Remarks: imputation under unreasonable assumption (imprecise)

PICO2

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Peolsson, 2019	Type of study: RCT Setting and country: Single academic centre, Sweden Funding and conflicts of interest: authors report no conflict interest", funding from mainly non-commercial parties.	Inclusion criteria: (1) having undergone surgery based on (1a) clinical findings of nerve root compression, confirmed through MRI, (1b) radiculopathy, (1c) ≥ 2 months of persistent nerve root pain; (2) age 18-70 years Exclusion criteria: (1) myelopathy, (2) previous fracture, subluxation or surgery of cervical column, (3) malignancy, (4) spinal infection, (5) systemic disease or trauma that contra-indicates the treatment program, (6) severe psychiatric disorder or known drug abuse, (7) inability to understand Swedish N total at baseline: 201 Intervention (I): 101 Control (C): 100 Important prognostic factors: *age ± SD:* I: 50 ± 8.2 C: 50 ± 8.7 *Sex (% M):* I: 51%| C: 54% Groups comparable at baseline? Intervention group had a longer median duration of neck pain before surgery	Regular postoperative care during first 5 weeks (information and advice about posture and ergonomics, mobility exercises for the shoulders and avoidance of certain tasks that may have a negative effect on the healing process or pain) and one routine visit to physiotherapist at 6 weeks postoperative *Structured postoperative rehabilitation (SPT) programme:* physiotherapy session with neck-specific exercises, individually and progressively adjusted by physiotherapist. Once weekly for 6 weeks, then twice weekly for 12 weeks, with additional home exercises and encouragement to increase overall physical activity level. A behavioural approach was applied.	*Standard postoperative approach (SA):* comprised usual care, without referral to a physiotherapist after surgery, but patients could seek physiotherapy themselves.	Length of follow-up: 3 months, 6 months, 12 months, and 24 months Loss-to-follow-up: Intervention: 30 (30%) Control: 38 (38%) *Reasons*: unknown Incomplete outcome data: Up until 3 months: 26 (I: 9, C: 17) Up until 6months: 29 (I: 11, C: 18) Up until 1 years: 57 (I: 26, C: 31)	Outcome measures and effect size (including 95%CI): Quality of Life (EQ-5D) *Mean difference (95% CI)* 3m: -0.06 (-0.14 to 0.02) 12m: 0.03 (-0.05 to 0.11) Cohen's d for ANOVA between-group difference ITT over time: 0.02 Pain (VAS) *Neck pain, mean difference (95% CI)* 3m: 3.0 (-3.5 to 9.5) 12m: 0.0 (-7.7 to 7.7) Cohen's d for ANOVA between-group difference ITT over time: 0.07 Disability (NDI) *Mean difference (95% CI)* 3m: 4.0 (-1.0 to 9.0) 12m: -2.0 (7.8 to 3.8) Cohen's d for ANOVA between-group difference ITT over time: 0.03	Author's conclusion: postoperative SPT offered no additional benefits over SA in patients who had undergone CR. All patients improved over time for all of the outcome variables, and the results show that patients with CR can tolerate postoperative loading of the neck exercises Remarks: Mean differences calculated on per-protocol data

Abbreviations: 12m: 12 months, 3m: 3 months, 6w: 6 weeks, ACDF: anterior cervical discectomy and fusion, CI: confidence interval, ITT: intention to treat, M: male, MCS: mental component score, MRI: magnetic resonance imaging, NPRS: numeric pain rating scale, PCS: physical component score, RCT: randomized controlled trial, SD: standard deviation

Risk of bias table for intervention studies

Study reference	Was the allocation sequence adequately generated?	Was the allocation adequately concealed?	Blinding: Was knowledge of the allocated interventions adequately prevented? • Were patients blinded? • Were healthcare providers blinded? • Were data collectors blinded? • Were outcome assessors blinded? • Were data analysts blinded?	Was loss to follow-up (missing outcome data) infrequent?	Are reports of the study free of selective outcome reporting?	Was the study apparently free of other problems that could put it at a risk of bias?	Overall risk of bias If applicable/necessary, per outcome measure
Abbot, 2013	No information; *Reason:* authors reported "random concealed allocation was the method used to form the groups"	No information; *Reason:* Method for concealment not reported.	Definitely no; *Reason:* Patients, health care providers and outcome assessors were not blinded (blinding of data collectors and analysts not reported)	Definitely no; *Reason:* Loss to follow-up was frequent in both groups. Intention to treat principle used for analysis, but unclear how missing data were handled.	Probably yes; *Reason:* no protocol available. All outcome measures from methods are described in the results.	No information; *Reason*: Largely underpowered, no other limitations described.	**HIGH** - Unclear randomization and allocation concealment - No blinding - Large proportion of loss to follow-up
Coronado, 2020	Definitely yes; *Reason:* Computer generated scheme in a 1:1 ratio in blocks stratified by age and number of fusion levels	Probably yes; *Reason:* authors report "in a concealed manner using a computer generated scheme", by personnel not responsible for recruitment	Definitely no *Reason:* Patients and health care providers not blinded, outcome assessors blinded. The blinding of data collectors and analysts is not reported.	Probably yes *Reason:* Loss to follow-up was infrequent in intervention and control group. Unclear whether adequate imputation methods were used	Definitely no *Reason:* deviation from protocol: no movement accelerometery and no fusion rate reported; yet opioid use is additionally reported.	No information; *Reason:* Underpowered, no other limitations described.	**Some concerns** - No blinding - Deviation in outcome reporting from protocol
McFarland, 2020	Probably no *Reason:* randomization procedure not adequately described.	Definitely no; *Reason:* Study coordinator (registered nurse) made group assignment (unclear methods).	Probably no; *Reason:* patients and healthcare providers were not blinded to assignment. Data collector and outcome assessor was blinded but with high risk of obtaining knowledge of assignment; blinding of data analysts not reported.	Probably no; *Reason:* Loss to follow-up was frequent in intervention and control group. Imputation method following MCAR was used (inadequate).	Probably no; *Reason:* According to protocol, no cervical flexor endurance and pain were to be collected.	Unclear; *Reason:* Insufficient information how much of usual care training was applied in intervention group.	**HIGH** - unclear randomization procedure (and allocation concealment) - Insufficient blinding - difference intervention and control not entirely clear
Peolsson, 2019	Definitely yes; *Reason:* computerized randomization list created by statistician.	Definitely yes; *Reason:* list was handled by an independent researcher who put the results into opaque envelopes for	Probably no; *Reason:* patients and healthcare providers were not blinded to assignment. Data collector and outcome assessor were blinded; blinding of data analysts not reported.	Probably no; *Reason:* Loss to follow-up was frequent(>25%) in intervention and control group. Unclear imputation methods or analyses used.	Definitely no; *Reason:* According to protocol, 25 outcome measures; not all reported (e.g. work ability index)	Unclear; *Reason:* possible dilution of effect by pragmatic approach to control group (also allowed physiotherapy)	**Some concerns** - Insufficient blinding - Frequent loss to follow-up - Dilution of effect by pragmatic approach to control group

		further distribution					

Table of excluded studies

Reference	Reason for exclusion
Bono CM, Leonard DA, Cha TD, Schwab JH, Wood KB, Harris MB, Schoenfeld AJ. The effect of short (2-weeks) versus long (6-weeks) post-operative restrictions following lumbar discectomy: a prospective randomized control trial. Eur Spine J. 2017 Mar;26(3):905-912. doi: 10.1007/s00586-016-4821-9. Epub 2016 Nov 2. PMID: 27807771.	Wrong population (lumbar discectomy)
Camara R, Ajayi OO, Asgarzadie F. Are External Cervical Orthoses Necessary after Anterior Cervical Discectomy and Fusion: A Review of the Literature. Cureus. 2016 Jul 14;8(7):e688. doi: 10.7759/cureus.688. PMID: 27555986; PMCID: PMC4980205.	Wrong study design
Cheng CH, Tsai LC, Chung HC, Hsu WL, Wang SF, Wang JL, Lai DM, Chien A. Exercise training for non-operative and post-operative patient with cervical radiculopathy: a literature review. J Phys Ther Sci. 2015 Sep;27(9):3011-8. doi: 10.1589/jpts.27.3011. Epub 2015 Sep 30. PMID: 26504347; PMCID: PMC4616148.	Wrong population
Lantz JM, Abedi A, Tran F, Cahill R, Kulig K, Michener LA, Hah RJ, Wang JC, Buser Z. The Impact of Physical Therapy Following Cervical Spine Surgery for Degenerative Spine Disorders: A Systematic Review. Clin Spine Surg. 2021 Oct 1;34(8):291-307. doi: 10.1097/BSD.0000000000001108. PMID: 33323701.	Includes study of Peolsson (2019) which is included.
Morris S, Morris TP, McGregor AH, Doré CJ, Jamrozik K. Function after spinal treatment, exercise, and rehabilitation: cost-effectiveness analysis based on a randomized controlled trial. Spine (Phila Pa 1976). 2011 Oct 1;36(21):1807-14. doi: 10.1097/BRS.0b013e31821cba1f. PMID: 21505377.	Wrong intervention
Ozkara GO, Ozgen M, Ozkara E, Armagan O, Arslantas A, Atasoy MA. Effectiveness of physical therapy and rehabilitation programs starting immediately after lumbar disc surgery. Turk Neurosurg. 2015;25(3):372-9. doi: 10.5137/1019-5149.JTN.8440-13.0. PMID: 26037176.	Wrong population (lumbar discectomy)
Svensson J, Hermansen A, Wibault J, Löfgren H, Dedering Å, Öberg B, Zsigmond P, Peolsson A. Neck-Related Headache in Patients With Cervical Disc Disease After Surgery and Physiotherapy: A 1-Year Follow-up of a Prospective Randomized Study. Spine (Phila Pa 1976). 2020 Jul 15;45(14):952-959. doi: 10.1097/BRS.0000000000003430. PMID: 32609465.	Secondary analysis of Peolsson (2019), same study population
Wibault J, Öberg B, Dedering Å, Löfgren H, Zsigmond P, Persson L, Andell M, R Jonsson M, Peolsson A. Neck-Related Physical Function, Self-Efficacy, and Coping Strategies in Patients With Cervical Radiculopathy: A Randomized Clinical Trial of Postoperative Physiotherapy. J Manipulative Physiol Ther. 2017 Jun;40(5):330-339. doi: 10.1016/j.jmpt.2017.02.012. Epub 2017 May 9. PMID: 28495026.	Precursor of Peolsson (2019), same study population
Wibault J, Öberg B, Dedering Å, Löfgren H, Zsigmond P, Peolsson A. Structured postoperative physiotherapy in patients with cervical radiculopathy: 6-month outcomes of a randomized clinical trial. J Neurosurg Spine. 2018 Jan;28(1):1-9. doi: 10.3171/2017.5.SPINE16736. Epub 2017 Nov 3. PMID: 29087809.	Precursor of Peolsson (2019), same study population

Literature search strategy

Algemene informatie

Cluster/richtlijn: Cervicaal Radiculair Syndroom	
Uitgangsvraag/modules: Wat is het advies post-operatief ten aanzien van belastbaarheid van de nek?	
Database(s): Ovid/Medline, Embase.com	Datum: 17-08-2022
Periode: 1990 - heden	Talen: Engels, Nederlands
Literatuurspecialist: Miriam van der Maten	
BMI-zoekblokken: voor verschillende opdrachten wordt (deels) gebruik gemaakt van de zoekblokken van BMI-Online https://blocks.bmi-online.nl/ Bij gebruikmaking van een volledig zoekblok zal naar de betreffende link op de website worden verwezen.	
Toelichting: Voor deze vraag is gezocht op de elementen: • Patiënten die chirurgie voor CRS hebben ondergaan • Postoperatieve situatie • Fysieke belastbaarheid • In eerste instantie is er naar SR en RCT gezocht, wanneer er ook naar vergelijkend of ander type onderzoek moet worden gezocht, graag contact opnemen.	
Te gebruiken voor richtlijnen tekst: *Nederlands* In de databases Embase.com en Ovid/Medline is op 17 augustus 2022 met relevante zoektermen gezocht naar systematische reviews en RCT over het advies post-operatief ten aanzien van belastbaarheid van de nek. De literatuurzoekactie leverde 382 unieke treffers op. *Engels* On the 17th of August 2022, relevant search terms were used to search for systematic reviews and RCT about the advice regarding postoperative activity of the neck in the databases Embase.com and Ovid/Medline. The search resulted in 382 unique hits.	

5 ***Zoekopbrengst***

	EMBASE	OVID/MEDLINE	Ontdubbeld
SRs	102	104	147
RCT	109	206	235
Totaal	211	310	382

Zoekstrategie

Embase.com

No.	Query	Results
#12	#8 AND #10 NOT #11 **= RCT**	109
#11	#8 AND #9 **= SR**	102
#10	'randomized controlled trial'/exp OR random*:ti,ab OR (((pragmatic OR practical) NEAR/1 'clinical trial*'):ti,ab) OR ((('non inferiority' OR noninferiority OR superiority OR equivalence) NEAR/3 trial*):ti,ab) OR rct:ti,ab,kw	1839814
#9	'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly*:ti,ab OR 'meta analy*':ti,ab OR metanaly*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review* OR overview*)):ti,ab) OR ((systemic* NEAR/1 review*):ti,ab) OR (((systemati* OR literature OR database* OR 'data base*') NEAR/10 search*):ti,ab) OR (((structured OR comprehensive* OR systemic*) NEAR/3 search*):ti,ab) OR ((((literature NEAR/3 review*):ti,ab) AND (search*:ti,ab OR database*:ti,ab OR 'data base*':ti,ab)) OR (('data extraction':ti,ab OR 'data source*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review* OR overview* OR synthes*)):ti) OR ((((critical* OR rapid*) NEAR/3 (review* OR overview* OR synthes*)):ab) AND (search*:ab OR database*:ab OR 'data base*':ab)) OR metasynthes*:ti,ab OR 'meta synthes*':ti,ab	733409
#8	#5 AND #6 AND #7 AND ([english]/lim OR [dutch]/lim) AND [1990-2022]/py NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp)	929
#7	'head movement'/exp OR 'exercise'/exp OR 'physical activity, capacity and performance'/exp OR 'physical activity'/exp OR 'physical inactivity'/exp OR ((activit* NEAR/3 (limitat* OR restrict*)):ti,ab,kw) OR 'restriction protocol*':ti,ab,kw OR physical:ti,ab,kw OR exercise*:ti,ab,kw OR move*:ti,ab,kw OR restriction*:ti,ab,kw OR limitation*:ti,ab,kw OR advice:ti,ab,kw OR recommend*:ti,ab,kw OR	4487162

	distress:ti,ab,kw OR 'daily life activity'/exp OR ((daily NEAR/5 activit*):ti,ab,kw)	
#6	'aftercare'/exp OR followup:ti,ab,kw OR 'follow up':ti,ab,kw OR 'perioperative period'/exp OR 'postoperative complication'/exp OR 'postoperative period'/exp OR postoperati*:ti,ab,kw OR 'post-operat*':ti,ab,kw OR postsurg*:ti,ab,kw OR 'post-surg*':ti,ab,kw OR 'perioperat*':ti,ab,kw	3826926
#5	#3 OR #4	11699
#4	((anterior NEAR/2 cervical NEAR/2 (foraminotomy OR microforaminotomy)):ti,ab,kw) OR 'anterior cervical discectomy'/exp OR 'anterior cervical discectomy and fusion'/exp OR cadf:ti,ab,kw OR cadp:ti,ab,kw OR acdf:ti,ab,kw OR ((anterior NEAR/2 cervical NEAR/2 (dis*ectom* OR 'disc fusion' OR microdiscectom*)):ti,ab,kw) OR 'foraminotomy'/exp OR 'degenerative cervical disc':ti,ab,kw	6547
#3	#1 AND #2	6466
#2	'surgery'/exp OR 'surgery'/lnk OR surgical:ti,ab,kw OR surger*:ti,ab,kw OR operation*:ti,ab,kw OR operative:ti,ab,kw	7143152
#1	'cervicobrachial neuralgia'/exp/mj OR cervicobrachialgia:ti,ab,kw OR ((radiculalgia:ti,ab,kw OR radiculitis:ti,ab,kw OR radiculitides:ti,ab,kw OR radiculopath*:ti,ab,kw OR polyradiculopath*:ti,ab,kw OR neuralgia:ti,ab,kw OR 'herniated disc*':ti,ab,kw OR hernia:ti,ab,kw OR ((radicular NEAR/3 (pain* OR neuralgia* OR symptom*)):ti,ab,kw) OR (('nerve root' NEAR/3 (pain* OR inflammation* OR disorder* OR compression* OR avulsion* OR impingement)):ti,ab,kw)) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw)) OR (('radicular pain'/exp/mj OR 'radiculopathy'/exp/mj) AND ('cervical spine'/exp OR 'neck'/exp OR cervical:ti,ab,kw OR cervico*:ti,ab,kw OR neck:ti,ab,kw))	10847

Ovid/Medline

#	Searches	Results
15	13 or 14	310
14	(10 and 12) not 13 **= RCT**	206
13	10 and 11 **= SR**	104
12	exp randomized controlled trial/ or randomized controlled trials as topic/ or random*.ti,ab. or rct?.ti,ab. or ((pragmatic or practical) adj "clinical trial*").ti,ab,kf. or ((non-inferiority or noninferiority or superiority or equivalence) adj3 trial*).ti,ab,kf.	1538278
11	meta-analysis/ or meta-analysis as topic/ or (metaanaly* or meta-analy* or metanaly*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati* or scoping or umbrella or "structured literature") adj3 (review* or overview*)).ti,ab,kf. or (systemic* adj1 review*).ti,ab,kf. or ((systemati* or literature or database* or data-base*) adj10 search*).ti,ab,kf. or ((structured or comprehensive* or systemic*) adj3 search*).ti,ab,kf. or ((literature adj3 review*) and (search* or database* or data-base*)).ti,ab,kf. or (("data extraction" or "data source*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review* or overview* or synthes*)).ti. or (((critical* or rapid*) adj3 (review* or overview* or synthes*)) and (search* or database* or data-base*)).ab. or (metasynthes* or meta-synthes*).ti,ab,kf.	612107
10	limit 9 to ((english language or dutch) and yr="1990 -Current")	1233
9	8 not (comment/ or editorial/ or letter/ or ((exp animals/ or exp models, animal/) not humans/))	1327
8	5 and 6 and 7	1341
7	exp Head Movements/ or exp Exercise Therapy/ or exp Exercise/ or exp Physical Exertion/ or (activit* adj3 (limitat* or restrict*)).ti,ab,kf. or 'restriction protocol*'.ti,ab,kf. or physical.ti,ab,kf. or exercise*.ti,ab,kf. or move*.ti,ab,kf. or restriction*.ti,ab,kf. or limitation*.ti,ab,kf. or advice.ti,ab,kf. or recommend*.ti,ab,kf. or distress.ti,ab,kf. or exp "Activities of Daily Living"/ or (daily adj5 activit*).ti,ab,kf.	3105747
6	exp Aftercare/ or exp Postoperative Complications/ or exp Perioperative Care/ or exp Pain, Postoperative/ or followup.ti,ab,kf. or 'follow up'.ti,ab,kf. or postoperati*.ti,ab,kf. or 'post-operat*'.ti,ab,kf. or postsurg*.ti,ab,kf. or 'post-surg*'.ti,ab,kf. or 'perioperat*'.ti,ab,kf.	2357368
5	3 or 4	12098
4	(anterior adj2 cervical adj2 (foraminotomy or Microforaminotomy)).ti,ab,kf. or exp Diskectomy/ or CADF.ti,ab,kf. or CADP.ti,ab,kf. or ACDF.ti,ab,kf. or (anterior adj2 cervical adj2 (dis*ectom* or 'disc fusion' or microdiscectom*)).ti,ab,kf.	8900
3	1 and 2	4160
2	exp Surgical Procedures, Operative/ or exp Specialties, Surgical/ or su.fs. or (surgical or surger* or operation* or operative).ti,ab,kf. or exp Decompression, Surgical/ or decompress*.ti,ab,kf.	5244759
1	((exp Radiculopathy/ or radiculalgia.ti,ab,kf. or radiculitis.ti,ab,kf. or radiculitides.ti,ab,kf. or radiculopath*.ti,ab,kf. or polyradiculopath*.ti,ab,kf. or neuralgia.ti,ab,kf. or 'herniated disc*'.ti,ab,kf. or hernia.ti,ab,kf. or (radicular adj3 (pain* or neuralgia* or symptom*)).ti,ab,kf. or ('nerve root' adj3 (pain* or inflammation* or disorder* or compression* or avulsion* or impingement)).ti,ab,kf.) and (exp Cervical Vertebrae/ or exp Neck/ or cervical.ti,ab,kf. or cervico*.ti,ab,kf. or neck.ti,ab,kf.)) or cervicobrachialgia.ti,ab,kf.	6629

Kennislacunes

Module 1 Diagnostiek

Op basis van deze module stelt de werkgroep dat verscheidene facetten nog onvoldoende onderzocht zijn. Bewijs met een hoge bewijskracht ontbreekt momenteel nog voor de huidige PICO. Er liggen kennislacunes bij de diagnostische accuratesse van neurologisch onderzoek. Daarnaast liggen er ook uitdagingen omtrent implementatie.

- Wat is de diagnostische accuratesse van neurologisch onderzoek?
- Wat is de meest valide manier van het uitvoeren van de Spurling's test?
- Hoe kan de bekendheid onder clinici m.b.t. het uitvoeren en interpreteren van de fysieke testen geoptimaliseerd worden?

Module 2.1 Fysiotherapie

Wat is het effect van een halfharde nekkraag/cervicale tractie/oefentherapie/neuromobilisatie/manuele therapie vergeleken met een afwachtend beleid en/of anderen vormen van fysiotherapie bij patiënten met cervicaal radiculair syndroom?

P: Patients with cervical radiculopathy
I: Physiotherapy
C: C1. Usual care/ watchful waiting/ placebo or sham (passive control)
C2. Other forms of physiotherapy (active control)
O: Pain, disability, function, quality of life, return to work, psychosocial outcomes, drug consumption, adverse effects

Op het gebied van predictie

- Zijn hier predicties voor te maken?
- Zijn er baseline factoren aan te wijzen die voorspellen welk type patiënt goed reageert op fysio/manuele therapie?

Module 2.2 Epidurale corticosteroïde-injecties

Op basis van deze module stelt de werkgroep dat verscheidene facetten nog onvoldoende onderzocht zijn. Bewijs met een hoge bewijskracht ontbreekt momenteel nog voor de huidige PICO. Daarnaast ligt er ook nog kennislacune bij de toedieningswijze.

Onderzoeksvraag 1 *Wat is de effectiviteit van epidurale corticosteroïde-injecties in vergelijking met de conservatieve therapie bij patiënten met CRS?*

P Patiënten met (subacute, < 3 maanden) CRS
I: epidurale *corticosteroïde*-injecties
C: Conservatieve behandeling (combinatie van fysiotherapie en pijnmedicatie)
O: Pijn, patiënttevredenheid, complicaties, medicijngebruik, functioneren, kwaliteit van leven

Onderzoeksvraag 2 *Wat is het verschil in effectiviteit tussen interlaminaire en transforaminale epidurale corticosteroïden bij patiënten met CRS?*

P: Patiënten met (subacute, < 3 maanden) CRS
I: Interlaminaire toediening van epidurale corticosteroïden
C: Transforaminale toediening van epidurale corticosteroïden
O: Pijn, patiënttevredenheid, complicaties, medicijngebruik, functioneren, kwaliteit van leven

Onderzoeksvraag 3 *Wat is het verschil in effectiviteit tussen epidurale steroidinjecties in vergelijking met epidurale injecties met alleen (lokaal) anesthaeticum bij patiënten met een CRS?*

P Patiënten met (subacute, < 3 maanden bestaand) CRS
I: epidurale cortico*steroïd*-injecties (ECSI)
C: Epidurale injecties met alleen (lokaal) anestheticum
O: Pijn, patiënttevredenheid, complicaties, medicijngebruik, functioneren, kwaliteit van leven

Module 2.3 Pulsed Radiofrequency (PRF)

Op basis van deze module stelt de werkgroep dat verscheidene facetten nog onvoldoende onderzocht zijn. Bewijs met een hoge bewijskracht ontbreekt momenteel nog voor de huidige PICO. Daarnaast liggen er ook nog kennislacunes bij de effectiviteit van de gecombineerde PRF-behandeling met steroïden, bij patiënten met een subacute CRS (≤3 maanden) en bij herhaalde PRF-behandeling.

Onderzoeksvraag 1 Wat is de effectiviteit van PRF-behandeling in vergelijking met de conservatieve therapie bij patiënten met CRS?

P Patiënten met CRS
I: PRF-behandeling
C: Conservatieve behandeling (combinatie van fysiotherapie en pijnmedicatie)
O: Pijn, patiënttevredenheid, complicaties, medicijngebruik, functioneren, kwaliteit van leven, voorkomen nekchirurgie

Onderzoeksvraag 2 Wat is de effectiviteit van PRF-behandeling in vergelijking met de conservatieve therapie bij patiënten met een subacuut CRS (≤3 maanden)?

P Patiënten met subacute CRS (≤3 maanden)
I: PRF-behandeling
C: Conservatieve behandeling (combinatie van fysiotherapie en pijnmedicatie)
O: Pijn, patiënttevredenheid, complicaties, medicijngebruik, functioneren, kwaliteit van leven, voorkomen nekchirurgie

Onderzoeksvraag 3 Wat is het verschil in effectiviteit tussen PRF-behandeling zonder en met steroïden bij patiënten met CRS?

P: Patiënten met CRS
I: PRF-behandeling met steroïden
C: PRF-behandeling zonder steroïden
O: Pijn, patiënttevredenheid, complicaties, medicijngebruik, functioneren, kwaliteit van leven, voorkomen chirurgie

Onderzoeksvraag 4 Wat is de effectiviteit van een tweede PRF-behandeling op hetzelfde niveau in vergelijking met het toepassen van één behandeling?

P: Patiënten met CRS
I: Tweede PRF-behandeling
C: Eén PRF-behandeling
O: Pijn, patiënttevredenheid, complicaties, medicijngebruik, functioneren, kwaliteit van leven, voorkomen chirurgie

Module 3.1. Chirurgische decompressie van de zenuwwortel

Er is betere kwaliteit onderzoek nodig om het klinisch effect en de kosten-effectiviteit van chirurgie op het cervicaal radiculair syndroom te beoordelen. Reeds is in Nederland een RCT uitgevoerd op dit gebied, echter bleek dit studiedesign niet haalbaar. Daarom lijkt een observationele studie (comparative effectiveness study) of een registerstudie de werkgroep passender.

Voorstel onderzoeksvraag: *Wat is de (kosten)effectiviteit van chirurgische anterieure decompressie in vergelijking met conservatieve behandeling bij patiënten met een cervicaal radiculair syndroom?*

P: Patiënten met een cervicaal radiculair syndroom
I: Chirurgische decompressie van de zenuwwortel (anterieure microforaminotomie, ACD, ACDF, ACDP)
C: Conservatieve behandeling (bijv. fysiotherapie, halskraag, PRF, corticosteroïden);
O: Patiënttevredenheid, (arm)pijn, kwaliteit van leven, werkhervatting, tintelingen, functioneren, complicaties, her-operatie, ziekte op aangrenzend segmentniveau, kosten-effectiviteit (€/QALY)

Aanvullend kan onderzoek gedaan worden naar ouderen in slechtere conditie en/of obesitas. Op dit vlak ontbreekt momenteel wetenschappelijk onderzoek.

Submodule 3.1.1 Timing chirurgische behandeling

Er is betere kwaliteit onderzoek nodig om het de timing van chirurgie bij patiënten met een cervicaal radiculair syndroom vast te stellen. *Voorstel onderzoeksvraag:* Wat is het optimale moment na aanvang van klachten voor een chirurgische interventie?

P: Patiënten met cervicaal radiculair syndroom
I: Lange termijn (> 2 maanden)
C: Korte termijn (< 2 maanden)
O: Patiënttevredenheid, (arm)pijn, kwaliteit van leven, werkhervatting, tintelingen, functioneren, complicaties, her-operatie, ziekte op aangrenzend segmentniveau, kosten-effectiviteit (€/QALY)

Module 3.2 ACDF: met of zónder plaat

De klinische en radiologische consequentie van het wel/niet toevoegen van een plaat aan een cage plaatsing na een anterieure discectomie vanwege een CRS is op basis van de huidige literatuur onvoldoende bekend.

Momenteel is nog onduidelijk vanaf hoeveel niveaus een aanvullende plaat bij een anterieure discectomie en fusie van meerwaarde is bij patiënten met een cervicaal radiculair syndroom. Indien er een multilevel ACDF wordt verricht, wordt vaak ook het sagittale profiel geoptimaliseerd waarbij de plaat van aanvullende waarde kan zijn. Ook is er bekend dat een plaat zorgt voor een kleinere kans op subsidence, waardoor dit in het geval van optimaliseren van de sagittale balans voordelig zou kunnen zijn.

Onderzoeksvraag: *Vanaf hoeveel niveaus bij een ACDF is een aanvullende plaat effectief?*

P: Patients with radiculopathy (regardless acute or chronic, developmental degenerative or non-degenerative)
I: Cage with plate ≥2 level
C: Cage without plate ≥2 level
O: Pain, patient satisfaction complications, return to work, medication use, quality of life, functioning, neck stability

Daarnaast is het onbekend wat het toevoegen van een plaat bij een ACDF doet op patient tevredenheid, return to work, gebruikt van pijnmedicatie, kwaliteit van leven, functioneren en nekstabiliteit.

Onderzoeksvraag: *Wat doet een aanvullende plaat bij een ACDF op tevredenheid, return to work, gebruikt van pijnmedicatie, kwaliteit van leven, functioneren en nekstabiliteit?*

P: Patients with radiculopathy (regardless acute or chronic, developmental degenerative or non-degenerative)
I: Cage with plate
C: Cage without plate
O: Patient satisfaction, return to work, medication use, quality of life, functioning, neck stability

Module 3.3. Anterieure Cervicale Discectomie met Prothese (ACDP)

Op basis van deze module stelt de werkgroep dat verscheidene facetten nog onvoldoende onderzocht zijn. Bewijs met een hoge bewijskracht ontbreekt momenteel nog voor de huidige PICO. Daarnaast liggen er ook nog kennislacunes bij operatietechnieken om een discusprothese te implanteren.

Onderzoeksvraag 1: Wat is de invloed van de operatietechniek op het ontstaan van heterotope ossificatie?

Onderzoeksvraag 2: Bestaat er een subcategorie patiënten bij wie het implanteren van een discusprothese wel klinisch voordeel biedt?

Module 3.4. Anterieure (micro)foraminotomie

Op dit onderwerp zijn er nog een legio aan kennislacunes. Het belangrijkst voor nu is om onderstaande PICO te beantwoorden:

P: Patients with CRS
I: Anterior microforaminotomy
C: Anterior discectomy
O: Pain, disability, Odom criteria, re-operations, complications, adjacent level disease, disc height, work status, QOL, use of pain medication, patient satisfaction

Module 4 Dorsale behandelingen

Om meer inzicht te krijgen in de (kosten)effectiviteit van beide benaderingen en om lange termijn resultaten te kunnen beoordelen, is vervolg onderzoek nodig bij het bepalen van de plaats van de dorsale foraminotomie in vergelijking met de anterieure discectomie bij patiënten met een cervicaal radiculair syndroom. Tevens bestaat er onvoldoende kennis over de vergelijking van beide benaderingen bij multilevel pathologie.

Voorstel onderzoeksvraag 1: Wat is de (kosten)effectiviteit van dorsale foraminotomie in vergelijking met de anterieure discectomie bij patiënten met een cervicaal radiculair syndroom op de lange termijn?

P: CRS-patiënten die in aanmerking komen voor chirurgische behandeling
I: Dorsale foraminotomie
C: Anterieure discectomie
O: Reoperaties, adjacent segment disease, nekpijn, kosten-effectiviteit

Voorstel onderzoeksvraag 2:

P: Patiënten met multi-level CRS die in aanmerking komen voor chirurgische behandeling
I: multilevel Dorsal foraminotomy (excluding laminectomy)
C: multilevel Anterior discectomy

O: Pain, disability, reoperations, complications (including dysphagia), adjacent segment disease (ASD), work status, quality of life, use of pain medication, patient satisfaction

Module 5 AI gebaseerde predictiemodellen

Het is onvoldoende onderzocht of predictiemodellen kunnen leiden tot een betere voorspelling van Klinische uitkomsten bij patiënten met CRS ide een operatie ondergaan. Voorstel onderzoeksvraag: *Welk AI-model voorspelt klinische uitkomsten en complicaties (aangrenzende segmentziekte/aanhoudend opioïdengebruik) bij patiënten met CRS en wat is bij externe validatie de voorspellende waarde van dit model?*

P: Patiënten met CRS die een ACDF-operatie ondergaan
I: Predictiemodel gebaseerd op machine learning/deep learning-principes
C: Model gebaseerd op klinisch oordeel of klassieke statistische methoden (bijv. regressieanalyse)
O: Voorspellende waarde (bijv: AUC, C-stats) voor het voorspellen van complicaties of klinische uitkomsten

Module 7 Postoperatief beleid

Alle conclusies hebben geen of zeer lage GRADE. Daarom blijft bestaande onderzoeksvraag een kennislacune: *Wat is het advies postoperatief ten aanzien van belastbaarheid van de nek voor patiënten met CRS? (met betrekking tot kwaliteit van leven, global perceived effect, pijn, disability, arbeidshervatting en degeneratie van aanliggend segment)?*

P: patiënten met CRSs
I1: gestructureerd postoperatief oefenprogramma.
I2: postoperatief dragen van een nekkraag met mobiliteitsrestricties
C: usual care
O: kwaliteit van leven, global perceived effect, pijn, disability, arbeidshervatting en degeneratie van aanliggend segment