Radiofrequency denervation for lumbar and cervical facet joint pain

Systematic Review

1st Update 2019

Ludwig Boltzmann Institut
Health Technology Assessment

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Commissioned by the Austrian Ministry of Health, this report systematically assessed the intervention described herein as decision support for the inclusion in the catalogue of benefits.

CONTENT INFORMATION

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Content

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List of abbreviations

CIMD ..... Clinically Important Minimum Difference
CT ..... Computer Tomography
DALYS ..... Disability-adjusted Life Year
EQ-5D ..... generic instrument to measure health-related quality of life
FDA ..... Food and Drug Administration
GPE ..... Global Perceived Effect
GRADE ..... Grading of Recommendation, Assessment, Development and Evaluation
HRQoL ..... Health-related Quality of Life
HTA ..... Health Technology Assessment
ICD ..... International Classification of Diseases
kHz ..... Kilohertz
LBI-HTA ..... Ludwig Boltzmann Institute for Health Technology Assessment
MD ..... Mean Difference
MPI ..... Multidimensional Pain Inventory
MRI ..... Magnetic Resonance Imaging
NR ..... not reported
NRCT ..... Non-Randomised Controlled Trial
NRS ..... Numeric Rating Scale
NSAR ..... Non-Steroidal Antirheumatic Drug
ODI ..... Oswestry Disability Index
OP ..... Operation
RAND-36 ..... Generic instrument to measure HRQoL
RCT ..... Randomised Controlled Trial
RF ..... Radiofrequency
RFD ..... Radiofrequency Denervation
RoB ..... Risk of Bias
ROBINS-I ..... Risk of Bias in Non-Randomised Controlled Studies
SCL-90 ..... Symptom Checklist 90
SF-36 ..... Generic instrument to measure HRQoL
US ..... United States
USD ..... United States Dollar
VAS ..... Visual Analogue Scale

Executive Summary

Introduction

Health Problem

low back pain and neck pain are among most frequently reported conditions in industrial countries

Low back pain and neck pain are among the most frequently reported pain-related diseases in industrial countries. Anatomically, chronic low back pain is localised between the costal margin and above the inferior gluteal folds, with or without referred leg pain that persists for at least 12 weeks, whereas neck pain is defined as pain located in anatomical region of the neck, with or without radiation to the head (cervicogenic headache), trunk and upper limbs. In the scope of this assessment, chronic low back pain deriving from the lumbar facet joints and chronic neck pain deriving from the cervical facet joints are the conditions of interest. Additionally, the project will focus on patients suffering from facet joint syndrome due to osteoporosis.

unspecific source of pain in most cases

Besides specific risk factors (e.g. infections and malignancies), most cases of low back pain are related to unspecific causes. For instance, smoking, obesity, physically or psychologically strenuous work, anxiety and depression have been identified as additional risk factors. In terms of neck pain, associations with degenerative changes of the lower cervical spine, musculoskeletal conditions or neurological disorders have been found.

standard therapy includes drug- and non-drug regimens

According to current guidelines, the standard therapies include conservative treatments with non-steroidal antirheumatics/antiphlogistis (NSARs) and if available, opioid analgesics, muscle relaxants or anti-depressants. In addition, several non-drug therapies are recommended (including physical and behavioural therapies).

aim of the review: RFD against pain due to cervical and lumbar facet joint syndrome

The aim of the systematic review is to evaluate the efficacy and safety of radiofrequency denervation (RFD) of the cervical and lumbar facet joints in comparison to placebo or other non-surgical treatments in patients with or without osteoporosis. This report is the 1st update of the systematic review published in 2016.

Description of Technology

RFD is a minimally invasive procedure

Radiofrequency denervation is a minimally invasive procedure, which is performed with local anaesthetic and mild sedation. After the facet joint is determined as the source of pain, it is recommended to perform a (lateral branch or medial branch) nerve block, in order to verify the localisation of the pain.

non-permanent relief of the syndrome

During the procedure, a radiofrequency generator produces an alternating electrical current (with a frequency of 250 to 500 kHz) through an insulated needle. The electric field on tip of the needle induces heat, which ultimately produces small lesions in the nerves suspecting of contributing to the pain. The technique aims to interrupt the pain signals to the brain, thus providing pain relief for 6 to 12 months. However, after that period, the nerve will eventually regenerate and the syndrome might return.

RFD devices regulated by FDA/EMA (CE-marking)

RFD is a procedure and is therefore not subject to regulation. Yet, the FDA regulates RFD devices. Currently, there are 40 items listed under the device classification code for RFD generators. Since 2015, eight lesion probes have been approved. Out of these, four products also received CE-marking (the RF Puncture Generator (Baylis Medical Company Inc.), the Coolief* Cooled

RFD can be reimbursed via the Austrian DRG-system (code AJ140)

Radiofrequency Kit (Halyard Health, Inc.) as well as the LCCS Disponsable RF Electrode and the LCCS Reusable RF Electrode (both manufactured by LCCS Products limited). Currently, radiofrequency denervation of the facet joints can be reimbursed via the Austrian DRG-system (Leistungsorientierte Krankenanstaltenfinanzierung) using the code AJ140 (percutaneous destruction of peripheral nerves).

Methods

in contrast to 1st assessment: exclusion of sacroiliac facet joint pain, inclusion of facet joint pain due to osteoporosis

The research question and the inclusion criteria of the 1st assessment were used, except that the term sacroiliac facet joint pain was excluded. Instead, an additional focus was laid on facet joint pain deriving from the cervical region and facet joint syndrome in patients with osteoporosis

A systematic literature search was carried out in several databases. Inclusion or exclusion of studies, data extraction and the quality assessment of the included studies were carried out independently by two authors. The overall judgement on the quality of evidence was done according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.

Domain effectiveness

for effectiveness and safety: RCTs and NRCTs were evaluated

In line with the 1st assessment, randomised controlled trials (RCTs) were used to assess the effectiveness of RFD for facet joint pain. Additionally, non-randomised controlled trials (NRCTs) were included.

Following key endpoints were extracted from the studies:

- Pain
- Functional status
- Global improvement
- Health-related quality of life
- Patient satisfaction
- Ability to work

Domain safety

Accordingly, randomised controlled trials (RCTs) and non-randomised controlled trials (NRCTs) were used to assess the safety of RFD for facet joint pain.

Following key endpoints for safety were extracted from the studies:

- Procedure-related complications
- Adverse events

Results

Available evidence

cervical facet joint pain: 2 RCTs ; one assessed with a high RoB

For the evaluation of cervical facet joint pain, two randomised controlled studies were identified, which used either a placebo/sham treatment or an injection with local anaesthetics as comparator. The methodological quality of the studies was assessed with the revised Cochrane risk of bias tool (RoB 2.0). Out of two studies, one was assessed with a high risk of bias.

lumbar facet joint pain: for effectiveness, 4 RCTs and 1 NRCT included

For the evaluation of the clinical effectiveness of lumbar facet joint pain, we identified five studies that were published since the release of 1st assessment. Among the four RCTs and one non-randomised controlled trial (NRCT), two studies used a placebo/sham-treatment and two studies used steroid injections as comparator. In one RCT, RFD combined with a standardised exercise program was compared to a standardised exercise program alone. The risk of bias was evaluated applying the Cochrane RoB 2.0 tool for RCTs and the ROBINS-I tool for the non-randomised trial. Four out of five studies were judged as having a high RoB.

for safety: 1 additional RCT included

An additional study (RCT) was included for the safety analysis that was comparing two different RFD techniques. The study was assessed with a high RoB.

no evidence for facet joint syndrome in patients with osteoporosis

No studies investigating radiofrequency denervation in patients with facet joint syndrome due to osteoporosis were identified through the systematic literature search; neither did any of the included studies provide data on that particular topic. Therefore, results are only presented for lumbar and cervical facet joint pain.

Clinical effectiveness

cervical facet joint pain: no statistically significant differences

Regarding cervical facet joint pain, no statistically significant differences were found in the outcomes pain intensity, functional status, global improvement and health-related quality of life and success of the treatment. Neither of the two studies reported on the outcomes ability to work or satisfaction with the treatment.

lumbar facet joint pain: inconsistent results

Regarding lumbar facet joint pain, inconsistent results were reported across the studies in terms of pain intensity, functional status and global improvement. The outcomes HRQoL and satisfaction with the treatment failed to show a significant difference between 6 weeks and 12 months. Ability to work was included in a composite measure (surgical Efficacy criteria of the spine surgery group) in one study and showed significant differences at 6 months post intervention.

Safety

cervical facet joint pain: more complications in the intervention group

Regarding cervical facet joint pain, only one study reported the outcome. In the placebo-controlled trial, a higher number of patients in the intervention group reported complications after discharge from the hospital as well as after 3 months.

lumbar facet joint pain: no adverse events or non-significant differences reported

Regarding lumbar facet joint pain, no adverse events were encountered in three studies. A single study reported non-significant differences in the number of patients experiencing post-procedural pain. One study did not report on adverse events.

Upcoming evidence

eight ongoing clinical trials; one study includes patients with osteoporosis

Eight ongoing RCTs were identified in clinical trial registries, which might provide further data on efficacy and safety of RFD for patients with cervical and lumbar facet joint syndrome in comparison to alternative treatments or placebo (sham treatment). Out of these, one study (NCT03651804) will particularly investigate the effect of radiofrequency ablation as treatment for posterior element pain from vertebral compression fractures. Amongst others, the study (with a primary completion date in March 2020) will include patients with osteoporosis.

Discussion

cervical facet joint pain: moderate to very low strength of evidence

Overall, the level of evidence for the clinical efficacy of radiofrequency denervation for the treatment of cervical facet joint pain is moderate to very low for the predefined crucial outcomes. The strength of evidence was downgraded due to methodological deficiencies and potential imprecision of the effect estimates as a result of the small sample sizes.

lumbar facet joint pain: high to low strength of evidence

Regarding the clinical efficacy of radiofrequency denervation for the treatment of lumbar facet joint pain, the level of evidence for the predefined crucial outcomes ranged from high to low. The strength of evidence was downgraded due to high risk of bias and inconsistencies between studies. In summary, there was some evidence that RFD for the treatment of lumbar facet joint pain leads to better outcomes than placebo or alternative treatments.

facet joint syndrome due to osteoporosis: no evidence found

Regarding the clinical efficacy of radiofrequency denervation for the treatment of facet joint syndrome due to osteoporosis, no evidence was found.

Interpretation of the findings

precise localisation of pain (via diagnostic block) important

heterogeneous study populations and possibility of cross-over prevented unbiased results

Firstly, the precise localisation of the pain remains to be a major issue in identifying those patients that will benefit the most from the intervention. Thereby, studies using either two diagnostic blocks and/or aimed to achieve a complete or near complete reduction of pain during this process, clearly benefited from the design. Secondly, the patient population varied significantly across the studies, especially with regard to the duration of the proceeding symptoms, which represents a well-known prediction factor for the anticipated response of the treatment. Thirdly, a cross-over after a specified time period was possible in four out of eight studies. Although the study authors might have introduced this possibility to prevent a loss-to-follow-up, any comparisons after that time point have to be considered biased and thus could not be used for the subsequent evaluation. Finally, patients suffering from facet joint pain due to trauma, malignancies or inflammatory diseases were excluded. Thus, no conclusions can be drawn on the effectiveness of RFD under these circumstances.

Conclusion

Currently not recommended

The inclusion into the hospital benefit catalogue is currently not recommended. A re-evaluation is proposed in 2023.

Zusammenfassung

Einleitung

Indikation und therapeutisches Ziel

Schmerzen im Rücken- und Nackenbereich in Bevölkerung weit verbreitet

Schmerzen im Rücken- und Nackenbereich zählen zu den häufigsten schmerzbedingten Erkrankungen in Industrieländern. Anatomisch gesehen sind chronische Schmerzen des unteren Rückens im Bereich zwischen dem unteren Rippenrand und oberhalb der unteren Gesäßfalten lokalisiert, welche mit oder ohne verwandte Beinschmerzen einhergehen können und mindestens für 12 Wochen anhalten. Nackenschmerzen werden als Schmerzen definiert, welche sich im anatomischen Bereich des Halses befinden und in den Bereich des Kopfes (zervikogener Kopfschmerz), des Rumpfes oder der oberen Gliedmaßen ausstrahlen können.

Focus des Assessments: chronische Schmerzen im Bereich der lumbalen und zervikalen Facettengelenke

Der Fokus dieses Assessments liegt auf chronischen Schmerzen des Rücken- und Nackenbereiches, welche durch Störungen der Facettengelenke der Wirbelkörper verursacht werden. Darüber hinaus konzentriert sich das Projekt auf jene OsteoporosepatientInnen, welche aufgrund von Schmerzsymptomen im Facettengelenksbereich eine Behandlung benötigen.

meist ausgelöst durch unspezifische Ursachen

Neben spezifischen Risikofaktoren (z. B. Infektionen und Tumoren) gibt es eine Reihe von unspezifische Ursachen; bei Rückenschmerzen zählen dazu Rauchen, Übergewicht, körperlich oder psychisch anstrengende Arbeit, Angstzustände und Depressionen. Als zusätzliche Risikofaktoren bei Nackenschmerzen wurden degenerative Veränderungen der unteren Halswirbelsäule, Erkrankungen des Bewegungsapparates oder neurologische Störungen identifiziert.

Behandlung umfasst medikamentöse sowie nicht-medikamentöse Therapien

Gemäß den aktuellen Richtlinien umfasst die Standardtherapie konservative Behandlungen mit nicht-steroidalen Antirheumatika/Antiphlogistika (NSARs) und, falls verfügbar, Opioid-Analgetika, Muskelrelaxantien oder Antidepressiva. Zusätzlich dazu werden mehrere nicht-medikamentöse Therapien (einschließlich körperlicher und Verhaltenstherapien) empfohlen.

Ziel des Projektes

Das Ziel dieses systematischen Reviews ist es, die Wirksamkeit und Sicherheit der Radiofrequenzdenervierung (RFD) der Facettengelenke im Nacken- und Lendenwirbelbereich im Vergleich mit Placebo oder anderen nichtoperativen Behandlungen bei Patienten mit oder ohne Osteoporose zu bewerten. Dieser Bericht ist das erste Update des 2016 veröffentlichten systematischen Reviews.

Beschreibung der Technologie

RFD ist ein minimal invasives Verfahren

Die Radiofrequenzdenervierung ist ein minimal invasives Verfahren, welches unter örtlicher Betäubung und leichter Sedierung durchgeführt wird. Es wird empfohlen, davor eine Nervenblockade (des lateralen oder medialen Astes) durchzuführen, um die Schmerzquelle bestmöglich zu identifizieren.

Resultat: nicht-permanente Schmerzunterbrechung

Während des Verfahrens erzeugt ein Hochfrequenzgenerator einen elektrischen Wechselstrom (mit einer Frequenz von 250 bis 500 kHz) entlang einer isolierte Nadel. Das elektrische Feld an der (nicht isolierten) Nadelspitze induziert Wärme, welche letztendlich Läsionen durch Gewebenekrose bzw. Lyse in jenem Nerv hervorruft, welcher als Verursacher der Schmerzweiterleitung vermutet wird. Eine Schmerzlinderung kann für eine Dauer von 6 bis 12 Monate erfolgen. Nach dieser Zeit ist die Regeneration der Nervenzellen jedoch abgeschlossen und die Syndrome können wiederkehren.

Verfahren unterliegt keiner Regulation, wohl aber die verwendeten Geräte

RFD ist ein Verfahren und unterliegt daher in den USA keiner Regulierung. Jedoch müssen die verwendeten RFD-Geräte von der FDA zugelassen werden. Derzeit sind 40 Produkte unter dem Geräteklassifizierungscode für RFD-Generatoren aufgeführt. Seit 2015 wurden acht Läsionssonden zugelassen. Von diesen Produkten erhielten vier Produkte auch die CE-Kennzeichnung (der RF-Punktionsgenerator (Baylis Medical Company Inc.), der Coolief® Cooled Radiofrequency Kit (Halyard Health, Inc.) sowie die LCCS Disponsable RF-Elektrode und die wiederverwendbare LCCS-RF-Elektrode (beide werden von LCCS Products Limited hergestellt).

Abrechnung über österr. LKF-System (Code AJ140)

Derzeit kann die Radiofrequenzdenervierung der Facettengelenke über das österreichische LKF-System (Leistungsorientierte Krankenanstaltenfinanzierung) mit dem Code AJ140 (perkutane Zerstörung peripherer Nerven) erstattet werden.

Methoden

Forschungsfrage ähnlich dem 1. Assessment: zusätzlich zervikale Facettengelenke, Iliosakralbereich nicht mehr berücksichtigt

Im aktuellen Assessment wurden die Forschungsfrage sowie die Einschlusskriterien des ersten systematischen Reviews aus dem Jahr 2016 verwendet. Jedoch wurden Schmerzen im iliosakralen Bereich nicht mehr berücksichtigt. Stattdessen wurde ein zusätzlicher Fokus auf Facettengelenksschmerz im Bereich des Nackens und auf das Facettensyndrom bei PatientInnen mit Osteoporose gelegt.

Systematische Literatursuche, Bewertung mittels GRADE

Eine systematische Literaturrecherche wurde in mehreren Datenbanken durchgeführt. Einschluss oder Ausschluss von Studien, Datenextraktion und Qualitätsbewertung der eingeschlossenen Studien wurden von zwei Autoren unabhängig voneinander durchgeführt. Die Gesamtbeurteilung der Evidenzqualität erfolgte nach dem Grading of Recommendations, Assessment, Development und Evaluation (GRADE).

Klinische Wirksamkeit

Studiendesign: RCTs sowie NRCTs berücksichtigt

Um die Wirksamkeit der RFD bei Gelenkschmerzen zu untersuchen wurden, in Übereinstimmung mit dem ersten Assessment, randomisierte kontrollierte Studien (RCTs) eingeschlossen. Zusätzlich dazu wurden nicht-randomisierte Kontrollstudien (NRCTs) analysiert.

Folgende Schlüsselendpunkte wurden aus den Studien extrahiert:

- Schmerzen
- Funktionsstatus
- Globale Verbesserung
- Gesundheitsbezogene Lebensqualität
- Patientenzufriedenheit
- Arbeitsfähigkeit

Sicherheit

Ebenso wurden randomisierte kontrollierte Studien (RCTs) und nicht-randomisierte Kontrollstudien (NRCTs) verwendet, um die Sicherheit der RFD bei Gelenkschmerzen zu untersuchen. Folgende Schlüsselendpunkte wurden dabei aus den Studien extrahiert:

- Verfahrensbedingte Komplikationen
- Unerwünschte Ereignisse

Ergebnisse

Verfügbare Evidenz

zervikales Facettengelenkssyndrom: 2 RCTs eingeschlossen; eine davon mit hohem RoB bewertet

Für die Beurteilung des zervikalen Facettengelenkschmerzes wurden zwei randomisierte kontrollierte Studien identifiziert, in denen die Intervention mit entweder Placebo (Schein-Behandlung) oder einer Injektion mit Lokalanästhetika verglichen wurden. Die methodische Qualität der Studien wurde mit dem überarbeiteten Cochrane-Instrument für das Risiko der Verzerrung (RoB 2.0) bewertet. Von zwei Studien wurde eine mit einem hohen Verzerrungsrisiko bewertet.

lumbales Facettengelenkssyndrom: 5 RCTs, ein NRCT; davon 5 mit hohem RoB bewertet

Für die Beurteilung von Gelenkschmerzen im Bereich der Lendenwirbelsäule wurden fünf Studien identifiziert, die seit der Publikation des ersten systematischen Reviews veröffentlicht wurden. Insgesamt wurden vier randomisierte Kontrollstudien (RCTs) und eine nicht randomisierten kontrollierten Studie eingeschlossen.

Von diesen verwendeten zwei Studien eine Placebo (Schein-)Behandlung und zwei Studien eine Steroid-Injektionen als Komparator. Eine randomisierte Kontrollstudie verglich den Effekt eines standardisierten Trainingsprogrammes mit einer Kombination aus RFD mit demselben standardisierten Trainingsprogramm. Das Verzerrungsrisiko wurde mit Hilfe des Cochrane RoB 2.0-Tools für RCTs und des ROBINS-I-Tools für die nicht randomisierte Studie beurteilt. Vier von fünf Studien wurden mit einem hohen Verzerrungspotential bewertet.

Eine zusätzliche randomisierte Kontrollstudie, welche zwei verschiedene RFD-Techniken miteinander verglich, wurde in die Sicherheitsanalyse miteinbezogen. Die Studie wurde mit einem hohen Verzerrungspotential bewertet.

Für die Beurteilung der Wirksamkeit und Sicherheit bei Osteoporose PatientInnen mit Facettensyndrom konnten keine Studien identifiziert werden.

Klinische Wirksamkeit

zervikales Facettengelenkssyndrom: keine statistisch signifikanten Unterschiede

Im Bereich der zervikale Facettengelenke (Nackenschmerzen) zeigte die Intervention keine statistisch signifikanten Unterschiede in den Endpunkten Schmerzintensität, Funktionsstatus, globale Verbesserung, gesundheitsbezogene Lebensqualität und Behandlungserfolg. In keiner der beiden Studien wurde über die Endpunkte Arbeitsfähigkeit oder Zufriedenheit mit der Behandlung berichtet.

lumbales Facettengelenk: inkonsistente Ergebnisse

In Bereich der lumbalen Facettengelenke (Rückenschmerzen) wurden von den eingeschlossenen Studien inkonsistente Ergebnisse für RFD in Bezug auf die Schmerzintensität, den Funktionsstatus und die globale Verbesserung berichtet. Die Endpunkte gesundheitsbezogene Lebensqualität und Zufriedenheit mit der Behandlung zeigten keinen signifikanten Unterschied im Beobachtungszeitraum zwischen 6 Wochen und 12 Monaten. Die Arbeitsfähigkeit wurde in einem zusammengesetzten Endpunkt (chirurgische Wirksamkeitskriterien der Gruppe für Wirbelsäulenchirurgie) betrachtet und zeigte 6 Monate nach der Intervention signifikante Unterschiede.

Sicherheit

zervikales Facettengelenkssyndrom: mehr Komplikationen in Interventionsgruppe

Im Bereich der zervikalen Facettengelenke (Nackenschmerzen) berichtete nur eine Studie über Komplikationen: Eine höhere Anzahl von PatientInnnen in der Interventionsgruppe berichtete Nebenwirkungen unmittelbar nach Entlassung aus dem Krankenhaus sowie nach einem dreimonatigen Beobachtungszeitraum.

lumbales Facettengelenkssyndrom: keine Nebenwirkungen bzw. nicht signifikante Unterschiede

In drei Studien, welche RFD im Bereich der lumbalen Facettengelenke (Rückenschmerzen) untersuchten, wurden keine unerwünschten Nebenwirkungen beobachtet. Eine Studie stellte nicht signifikante Unterschiede in der Anzahl der PatientInnen mit postoperativen Schmerzen fest. Eine weitere Studie berichtete nicht über diesen Endpunkt.

Laufende Studien

acht laufende Studien; eine davon inkludiert auch PatientInnen mit Osteoporose

Es wurden acht laufende RCTs in klinischen Studienregistern ermittelt, welche möglicherweise weitere Daten zur Wirksamkeit und Sicherheit von RFD für PatientInnen mit zervikalem und lumbalem Facettengelenkssyndrom im Vergleich zu alternativen Behandlungen oder Placebo (Scheinbehandlung) liefern können. In einer Studie (NCT03651804) wird insbesondere der Effekt der Radiofrequenzdenervierung als Behandlung von Schmerzen aufgrund von Wirbelkörperkompressionsfrakturen untersucht. In dieser Studie (mit einem primären Fertigstellungsdatum im März 2020) werden (unter anderen) PatientInnen mit Osteoporose eingeschlossen.

Diskussion

zervikales Facettengelenkssyndrom: moderate bis sehr niedrige Stärke der Evidenz

Insgesamt wurde die Stärke der Evidenz zur Wirksamkeit der Radiofrequenzdenervierung bei der Behandlung von zervikalen Facettengelenkschmerzen (Nackenschmerzen) für die vordefinierten entscheidenden Endpunkte als moderat bis sehr niedrig bewertet. Die Beweiskraft wurde aufgrund methodischer Mängel und möglicher Ungenauigkeiten der Effektschätzungen aufgrund der geringen Stichprobengröße der einzelnen Studien herabgestuft.

lumbales Facettengelenkssyndrom: hohe bis niedrige Stärke der Evidenz

In Bezug auf die klinische Wirksamkeit der Radiofrequenzdenervierung bei der Behandlung von Facettengelenksschmerzen in der Lendenwirbelgegend (Rückenschmerzen) wurde die Stärke der Evidenz für die vordefinierten entscheidenden Endpunkte als hoch bis niedrig bewertet. Die Beweiskraft wurde aufgrund des hohen Risikos von Verzerrungen und inkonsistenten Ergebnissen der einzelnen Studien herabgestuft. Zusammenfassend gab es einige Hinweise darauf, dass die RFD bei der Behandlung von Facettengelenksschmerzen in der Lendenwirbelsäule zu besseren Ergebnissen als Placebo oder alternative Behandlungen führt.

Facettengelenkssyndrom aufgrund von Osteoporose: keine Evidenz verfügbar

Bezüglich der klinischen Wirksamkeit der Radiofrequenzdenervierung zur Behandlung des Facettengelenksyndroms aufgrund von Osteoporose konnten keine Studien gefunden werden.

Interpretation der Ergebnisse

möglichst genaue Lokalisation der Schmerzen entscheidend

Die genaue Lokalisierung der Schmerzen scheint ein Hauptproblem bei der Ermittlung jener PatientInnen, welche am meisten von der Intervention profitieren würden, darzustellen. Studien, bei denen entweder zwei Diagnoseblöcke verwendet wurden oder welche darauf abzielten, eine möglichst vollständige Verringerung der Schmerzen während des Lokalisierungsprozesses zu erreichen, profitierten dabei eindeutig von diesem Design.

Unterschiede in der Patientenpopulation

Ein genereller Kritikpunkt der eingeschlossenen Studien waren Unterschiede in den Patientenpopulationen insbesondere im Hinblick auf die Dauer der bereits bestehenden Symptome (Schmerzen) vor der Behandlung. Es ist erwiesen, dass dieses Kriterium einen entscheidenden Faktor in Bezug auf das erwartete Ansprechen der Behandlung darstellt.

Crossover in 4 von 8 Studien möglich

Zusätzlich war in vier von acht Studien ein Crossover nach Ablauf eines bestimmten Beobachtungszeitraumes möglich. Obwohl die Studienautoren diese Option möglicherweise einführten, um die Compliance der Patienten zu erhöhen, müssen Vergleiche nach diesem Zeitpunkt als möglicherweise verzerrend betrachtet werden und könnten daher nicht für nachfolgende Analysen verwendet werden.

Schließlich wurden PatientInnen mit Facettengelenkschmerzen aufgrund von Traumata, malignen oder entzündlichen Erkrankungen ausgeschlossen. Daher können keine Rückschlüsse auf die Wirksamkeit von RFD unter diesen Umständen gezogen werden.

Empfehlung

Aufnahme derzeit nicht empfohlen

Die Aufnahme in den Leistungskatalog wird derzeit nicht empfohlen. Eine Neubewertung wird für 2023 vorgeschlagen.

Summary of 2016 assessment

systematischer Review 2016: Radiofrequenz-denervierung bei chronischen Schmerzen im Bereich des Iliosakralgelenke sowie der lumbalen Facettengelenke

In 2016, a systematic review evaluating the clinical effectiveness and safety of radiofrequency denervation (RFD) for sacroiliac and facet joint pain in patients with chronic low back pain was published by the Ludwig Boltzmann Institute for Health Technology Assessment (LBI-HTA) on request of the Austrian Federal Ministry of Health [1]. This report provides the basis for the current update. The following paragraphs summarise the scope, the results and the recommendations of the 2016 report.

Health problem and characteristics of the technology

In the scope of the assessment from 2016, chronic low back pain deriving from the facet or sacroiliac joints is the condition of interest. Radiofrequency denervation, a minimally invasive procedure, is used for the treatment of this condition.

Scope 2016

Forschungsfrage 2016

Is radiofrequency denervation of the facet joints or sacroiliac joint, in comparison to placebo or other treatments in patients with chronic facet joint pain or sacroiliac joint pain with a positive response to diagnostic block, more effective and safe concerning pain, functional status, global improvement, health-related quality of life, and complications?

The inclusion criteria for relevant studies are summarised in Table 1.

Table 1: Inclusion criteria – Assessment 2016

Population	Second-line treatment in adult patients with chronic (>3 months) low back pain (facet joint pain or sacroiliac joint pain) who had a positive response to diagnostic block ICD-10 code: M54.5 low back pain MeSH terms: low back pain, zygapophyseal joint, sacroiliac joint Patients with acute trauma, fracture, malignancy, and inflammatory disease were excluded.
Intervention	Radiofrequency (RF) denervation (synonyms: radiofrequency neurotomy, radiofrequency ablation) No limits on the temperature were applied. Both continuous and pulsed RF were included.
Control	Placebo Other treatments*

Outcomes	
Efficacy	❁ Pain ❁ Functional status ❁ Global improvement ❁ Health-related quality of life ❁ Ability to work ❁ Satisfaction with treatment
Safety	❁ Complications
Study design	Randomised controlled trials

* *In deviation from the Cochrane review, studies comparing different methods of RFD were included for safety analysis only (but not for efficacy).*

insgesamt 7 Endpunkte ausgewählt

In the 2016 report, the outcomes of pain, functional status, global improvement and health-related quality of life, as well as complications, were defined as crucial to derive a recommendation. The remaining outcomes of patient satisfaction and ability to work were defined as important, but not crucial, to derive a recommendation.

basierend auf Cochrane Review

During the scoping process, a Cochrane Review [2] dealing with radiofrequency denervation for chronic back pain, which had a broader scope, including pain from intervertebral discs and the dorsal root ganglion, was identified. Thus, the authors of the previous LBI-HTA assessment decided to use relevant parts of the Cochrane Review (dealing with facet and sacroiliac joints) as the primary source for the assessment. Additionally, a (systematic) search in Medline and PubMed using the search strategy from the Cochrane review (complemented by the search term "sacroiliac joint") was conducted, and a hand search in PubMed performed.

Results

Clinical effectiveness

klinische Wirksamkeit: 10 RCTs für Facettengelenke; 2 RCTs für Iliosakralgelenke

10 randomised controlled trials evaluating radiofrequency denervation for **facet joint pain** were included. 6 studies compared the intervention with placebo (sham treatment), while the remaining 4 trials used steroid injections as comparator.

For evaluating radiofrequency denervation for **sacroiliac joint** pain, 2 randomised controlled trials fulfilled the inclusion criteria. Both RCTs compared the intervention with placebo (sham treatment).

Evidenzstärke für RFD bei Facettengelenksschmerz niedrig bis sehr niedrig

The strength of evidence for the effectiveness of radiofrequency denervation for **facet joint pain** compared to placebo was considered low in reducing pain in the short term (≤ 1 month) and in increasing the global improvement in the intermediate term (1-6 months). Furthermore, the assessment revealed that RFD might not increase the functional status in the intermediate term, but might lead to an improvement between 6-12 months. Additionally, RFD might improve the quality of life at 3 months. These results were supported by a low level of evidence.

In comparison to steroid injections, the strength of evidence was low that RFD might reduce pain up to 12 months. A very low level of evidence supported the findings that RFD might neither improve the functional status between 6-12 months nor the quality of life up to 12 months. No evidence was available for the outcome of global improvement.

In terms of **sacroiliac joint pain**, the strength of evidence for the effectiveness of radiofrequency denervation in comparison to placebo (sham intervention) was considered low to very low. RFD might not reduce pain or improve the functional status in the short term (≤ 1 month), but up to 3 months thereafter. However, the intervention might lead to a global improvement up to 3 months. Furthermore, RFD might not increase the quality of life in the short term, but up to 3 months after the intervention. No evidence was available for any of the critical outcomes for observation periods longer than 3 months.

Evidenzstärke bei Schmerzen der Iliosakralgelenke niedrig bis sehr niedrig

Safety

In addition to the 10 studies already included in the clinical effectiveness assessment evaluating radiofrequency denervation for **facet joint pain,** 3 further RCTs comparing different RFD methods were included for safety considerations. There was very low evidence that RFD compared to placebo might not increase complications. In comparison to steroid injections, RFD does not lead to complications, but might cause superficial burns after the intervention and an initial increase in back pain.

Sicherheit: 13 RCTs für Facettengelenke; 2 RCTs für Iliosakralgelenke

Regarding the safety assessment of radiofrequency denervation **for sacroiliac joint pain**, the two aforementioned RCTs were included. There was very low evidence that RFD compared to placebo might not increase serious complications.

Evidenzstärke sehr niedrig

For both indications, the quality of evidence was downgraded due to imprecise data, study limitations, and inconsistent results across the studies.

Recommendation

The available evidence included in the 2016 report was not sufficient to prove that the assessed technology of radiofrequency denervation in adult patients with chronic (>3 months, facet joint- or sacroiliac joint) low back pain who had a positive response to diagnostic block is more effective than, and as safe as, the comparator(s) (placebo/sham intervention or conventional treatment). Therefore, the inclusion in the catalogue of benefits was not recommended, but a re-evaluation in 2019 was suggested.

Aufnahme 2016 nicht empfohlen aber Re-evaluation vorgeschlagen

UPDATE 2019

1 Scope

Scope 2019: RFD bei Schmerzen im Bereich der zervikalen und lumbalen Facettengelenke sowie bei PatientInnen mit Osteoporose

Although a re-evaluation of RFD should be performed, the scope of the present assessment is different from the previous report from 2016. As commissioned by the Austrian Ministry of Health, the present assessment should include a re-evaluation of RFD for the treatment of **lumbar facet joint pain** and an evaluation of RFD for the treatment of **cervical facet joint pain**, which was not part of the 2016 report. Furthermore, the efficacy and safety of RFD for the treatment of facet joint pain in patients suffering from osteoporosis should be evaluated. The use of RFD for sacroiliac joint pain was not further considered. Therefore, the research question of the present assessment is defined as follows:

1.1 PICO question

PICO-Frage

Is radiofrequency denervation of the cervical and lumbar facet joints, in comparison to placebo or other non-surgical treatments in patients with or without osteoporosis with chronic facet joint pain, more effective and safe concerning pain, functional status, global improvement, health-related quality of life, ability to work, and satisfaction with the treatment and complications?

1.2 Inclusion criteria

Einschlusskriterien für relevante Studien

Inclusion criteria for relevant studies are summarised in Table 1-1.

Table 1-1: Inclusion criteria

Population	Second-line treatment in adult patients with or without moderate to severe osteoporosis with chronic (>3 months) low back pain (lumbar facet joint pain) or neck pain (cervical facet joint pain) who had a positive response to a diagnostic block ICD-10 code: M54.5 low back pain, M54.2 cervical neuralgia MeSH terms: low back pain, neck pain, zygophophyseal joint, post-menopausal or age-related/senile osteoporosis Patients with acute trauma, fracture, maligancy and inflammatory disease were excluded.
Intervention	Radiofrequency (RF) denervation (synonyms: RF neurotomy, RF ablation) No limits on the temperature were applied. Both continous and pulsed RF were included. MeSH terms: denervation (includes radiofrequency neurotomy), RF ablation
Control	Placebo/sham procedures RFD Other non-surgical treatments: epidural injections of local anasthetic or steroids

Outcomes	
Efficacy	❁ Pain ❁ Functional status ❁ Global improvement ❁ HRQoL ❁ Ability to work ❁ Satisfaction with the treatment
Safety	❁ Procedure-related complications ❁ Adverse events
Study design	
Efficacy	Randomised controlled trials Non-randomised controlled trials
Safety	Randomised controlled trials Non-randomised controlled trials

2 Methods

2.1 Research questions

Description of the technology	
Element ID	**Research question**
B0001	What is radiofrequency denervation?
B0002	What is the claimed benefit of radiofrequency denervation in relation to the comparators?
B0004	Who administers radiofrequency denervation and in what context and level of care is it provided?
B0008	What kind of special premises are needed to use radiofrequency denervation?
B0009	What supplies are needed to use radiofrequency denervation?
A0020	For which indications has radiofrequency denervation received marketing authorisation or CE marking?
A0021	What is the reimbursement status of radiofrequency denervation?

Health problem and current use	
Element ID	**Research question**
A0001	For which health conditions and for what purposes is radiofrequency denervation used?
A0002	What is the disease or health condition in the scope of this assessment?
A0003	What are the known risk factors for chronic low back pain or chronic neck pain?
A0004	What is the natural course of chronic back pain or chronic neck pain?
A0005	What is the burden of disease for patients with chronic low back pain or chronic neck pain?
A0006	What are the consequences of chronic low back pain or chronic neck pain for the society?
A0024	How is chronic low back pain or chronic neck pain currently diagnosed according to published guidelines and in practice?
A0025	How is chronic low back pain or chronic neck pain currently managed according to published guidelines and in practice?
A0007	What is the target population in this assessment?
A0023	How many people belong to the target population?
A0011	How much is radiofrequency denervation of the cervical and lumbar facet joints utilised?

Clinical effectiveness	
Element ID	**Research question**
D0001	What is the expected beneficial effect of radiofrequency denervation on mortality?
D0005	How does radiofrequency denervation affect symptoms and findings (severity, frequency) of chronic low back pain or chronic neck pain?
D0006	How does radiofrequency denervation affect progression (or recurrence) of chronic low back pain or chronic neck pain?
D0016	How does the use of radiofrequency denervation affect activities of daily living?
D0012	What is the effect of radiofrequency denervation on generic health-related quality of life?
D0013	What is the effect of radiofrequency denervation on disease-specific quality of life?
D0017	Was the use of radiofrequency denervation worthwhile?

Safety	
Element ID	Research question
C0008	How safe is radiofrequency denervation in comparison to placebo or steroid injections?
C0002	Are there harms related to dosage or frequency of applying radiofrequency denervation?
C0004	How does the frequency or severity of harms change over time or in different settings?
C0005	What are the susceptible patient groups that are more likely to be harmed through the use of radiofrequency denervation?
C0007	Are radiofrequency denervation, steroid injections, injections with local anaesthetic or placebo interventions associated with user-dependent harms?

2.2 Sources

Description of the technology and health problem and current use

Informationen aus Handsuche und Literatursuche für Beschreibung des Gesundheitsproblems und der Technologie

- Publications and guidelines identified by hand search
- Background information from publications identified in database search: see Section 2.3

For the domains of clinical effectiveness and safety, a systematic literature search was conducted, as described in detail in the following chapter.

2.3 Systematic literature search

systematische Literatursuche in 4 Datenbanken

The systematic literature search was conducted on the 20th of December 2018 in the following databases:

- Medline via Ovid
- Embase
- The Cochrane Library
- CRD (DARE, NHS-EED, HTA)

After deduplication, a total of 569 citations were included. The specific search strategy employed can be found in the Appendix.

Suche nach laufenden Studien

Furthermore, to identify ongoing and unpublished studies, a search in three clinical trials registries (ClinicalTrials.gov; WHO-ICTRP; EU Clinical Trials) was conducted on the 21st of January 2019, resulting in 51 potential relevant hits.

insgesamt 569 Publikationen identifiziert

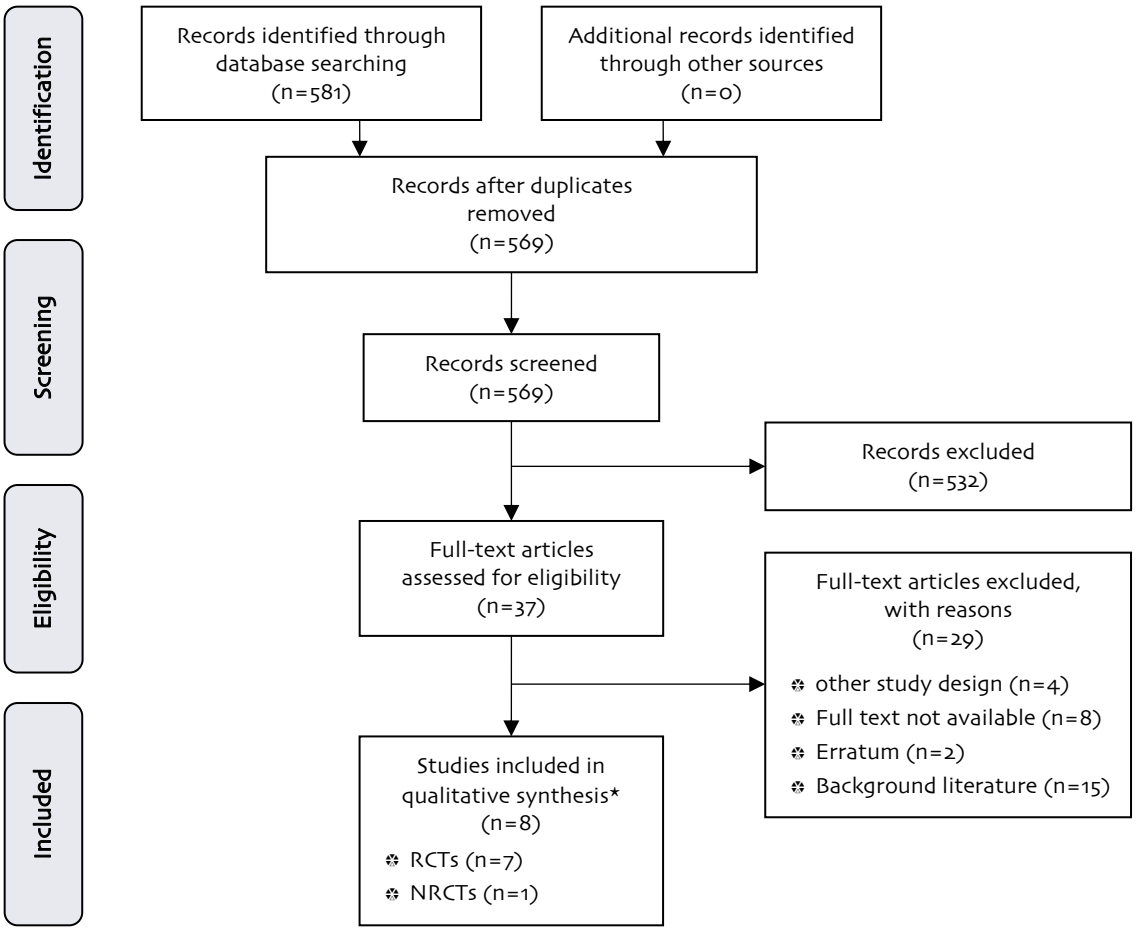
Manufacturers from the most common products (Halyard, Pajunk, Stryker, Avanos Medical and Cosman) were contacted on the 12th of December 2018. However, they did not respond to our e-mail.

No further hand search was conducted.

2.4 Flow chart of study selection

Literaturauswahl

Overall, 569 hits were identified after deduplication. All records were screened by two independent researchers. 37 records were screened in full text and 8 studies fulfilled the inclusion criteria. Of these, 2 studies for cervical facet joint pain and 6 studies for lumbar facet joint pain (published after June 2015, the literature search date of the first assessment, and which were not included in the 2016 assessment) were relevant for our assessment. No studies specifically including patients with osteoporosis were identified. The selection process is displayed in Figure 2-1.



** for effectiveness: n=7 (lumbar facet joint pain: 5; cervical facet joint pain: 2); for safety: additional 1 RCT for lumbar facet joint pain*

Figure 2-1: Flow chart of study selection (PRISMA Flow Diagram)

2.5 Analysis

Daten der einzelnen Studien extrahiert und kontrolliert

The data retrieved from the selected studies (see Chapter 2.4) were systematically extracted into a data extraction table by one researcher (EF) (see Appendix Table A-1, Table A-2, Table A-3, and Table A-4). Another researcher (SGG) checked the data for integrity and completeness.

Bewertung des Biasrisikos mittels RoB 2.0 und ROBINS-I

No further data processing (e.g., indirect comparison) was applied. The quality of the studies were systematically assessed using the revised Cochrane Risk of Bias tool (RoB 2.0) [3] for randomised controlled studies, and the Risk of Bias in non-randomised studies of intervention tool (ROBINS-I) [4] for non-randomised controlled trials (see Table A-5, Table A-6, and Table A-7 in the Appendix).

2.6 Synthesis

Bewertung der Evidenz sowie Beantwortung der Forschungsfrage mittels GRADE

Based on the data extraction tables (see Appendix), data on each selected outcome category were analysed across studies according to GRADE (Grading of Recommendations Assessment, Development and Evaluation) [5]. The research questions were answered in plain text format with reference to GRADE evidence tables that are included in the Appendix, the results of which were summarised in Table 7-1 and Table 7-2.

3 Description and technical characteristics of technology

Features of the technology and comparators

B0001 – What is radiofrequency denervation?

The use of radiofrequency denervation (RFD) for the treatment of back pain was first described in the literature in 1975 [6]. Radiofrequency denervation is a minimally invasive procedure usually performed with local anaesthetic and mild sedation. During this outpatient procedure, the patient is positioned face down and the skin is anaesthetised with a local anaesthetic such as lidocaine [7]. Before the RFD procedure is done, a (lateral branch or medial branch) nerve block is performed in order to verify that the pain is being transmitted by those nerves [8].

RFD ist minimal-invasive Intervention, die unter Lokalanästhesie durchgeführt wird

RFD is done with the following elements: a radiofrequency generator, cannulas with active tips, and a thermocoupler that serves to sense the body temperature and transmit the radiofrequency energy [6].

A radiofrequency generator produces an alternating electrical current with a frequency of 250 to 500 kHz through an insulated needle. At the tip of the needle, the electric field induces ionic movements in the tissue directly surrounding the tip. The heat from the tip of the device is used to produce a small lesion in the nerves suspected of contributing to the pain. The heat causes ionic agitation and friction, resulting in protein denaturating, cellular membrane disruptions, increased membrane permeability, and, finally, tissue necrosis or lysis. The technique aims to interrupt the pain signals to the brain in order to eliminate the pain [6, 9, 10].

Generator produziert Wechselstrom, welcher Gewebe in Nadelspitzenumgebung erwärmt und damit den Nerv gezielt schädigt

RFD procedures can be classified in low-intensity RFD (which is administered constantly for 60-90 seconds at a specific temperature), cooled RFD (which involves the use of a cannula needle that has saline running through it to cool the tip), and pulsed RFD (which is done with signal interruption every half second, creating temperatures of 42° C) [6].

unterschiedliche RFD Techniken verfügbar

Comparators include therapeutic intra-articular (steroid) injections or sham RFD. In the sham surgery, a radiofrequency needle is inserted into the same location as in RFD, but the electric current is not turned on [7].

Vergleiche der RFD mit Steroidinjektionen oder Scheinoperation

Synonyms for radiofrequency denervation are the terms radiofrequency ablation and radiofrequency neurotomy.

Synonyme auch RF-Ablation oder Neurotomie

B0002 – What is the claimed benefit of radiofrequency denervation in relation to the comparators?

When the joint is determined to be the source of pain, as indicated by radiograhic findings and supported by a positive diagnostic nerve block, prolonged pain relief may be achieved by RFD with destruction of the nerves to the affected joint. The procedure does not cure the source of pain, but destroys the pain signal to the brain by damaging the nerve, which can result in pain relief lasting from 6 months to, occasionally, greater than 12 months [7]. After this period of time, however, the nerve will regenerate and the pain may return [8].

RFD behebt nicht Schmerzursache, sondern soll Schmerzweiterleitung unterbrechen; temporärer Effekt aufgrund Regeneration des Nervengewebes

Administration, investments, personnel and tools required to use the technology and the comparator(s)

B0004 – Who administers radiofrequency denervation and in what context and level of care is it provided?

B0008 – What kind of special premises are needed to use radiofrequency denervation?

B0009 – What supplies are needed to use radiofrequency denervation?

laut Einreichern erforderlich: spezialisiertes Zentrum, erfahrenes OP-Team intraoperatives Röntgen

According to the information received by the submitting hospital, the intervention is performed at specialised centres.

The intervention is performed by an experienced operation team, including an experienced orthopaedist, an assistant physician, a nurse, an anaesthetist (in the case of sedoanalgesia), and a radiological assistant for intraoperative X-ray monitoring.

An operating room with intraoperative X-ray monitoring is needed for the intervention.

Regulatory & reimbursement status

A0020 – For which indications has radiofrequency denervation received marketing authorisation or CE marking?

FDA reguliert RFD Produkte (nicht spezifisch für die Indikation)

RFD for back pain is a procedure and is therefore not subject to regulation by the Food and Drug Administration (FDA). However, the FDA regulates RFD devices; hence, there are various devices listed in the FDA 510(k) Premarket Notification database. Currently, 40 items are listed under the device classification name 'Generator, Lesion, Radiofrequency' (Classification Product Code 'GXD') [11]. Within the past 5 years, the following generators received FDA clearance:

- Polaris RF Ablation System (Baylis Medical Company Inc.; approved 2019),
- Intracept Intraosseous Nerve Ablation System (Relievant Medsystems; approved 2017)
- Multigen^{TM} 2 RF Generator System (Stryker Corporation; approved 2017)

seit 2015 wurden 8 neue Systeme von der FDA zugelassen

Since 2015, 8 RF lesion probe devices have been approved by the FDA (Classification Product Code 'GXI'):

- Intracept Intraosseuous Nerve Ablation System (Component Intracept RF Probe) (Relievent Medsystems; approved 2018)
- Intracept Intraosseuous Nerve Ablation System Probe (Relievant Medsystems; approved 2017)
- OWL RF Insulated Cannulae (Probe) (Diros Technology, Inc.; approved 2017)
- Coolief* Cooled RF Probe (Halyard Health, Inc.; approved 2017)
- Coolief* Cooled Radiofrequency Kit (Halyard Health, Inc.; approved 2016)
- LCCS Disponsable RF Electrode, LCCS Reusable RF Electrode (LCCS Products Limited; approved 2016)

- Intracept Flexible Bi-Polar RF Probe and Easy Access Instrument Set (Relievant Medsystems; approved 2016)
- Diros OWL Sterile Single Use Trident™ RF Insulated Cannulae, Models DTR and DTRH (Diros Technology, Inc.; approved 2015)

The probes are used in conjunction with an RF generator to create RF lesions in nerves. All components have received FDA clearance as substantially equivalent to an approved predicate device.

CE marking of 4 products available

Of the above list, the RF Puncture Generator (Baylis Medical Company Inc.) and the Coolief* Cooled Radiofrequency Kit (Halyard Health, Inc.), as well as the LCCS Disponsable RF Electrode and the LCCS Reusable RF Electrode (both manufactured by LCCS Products limited), also received CE marking [12-14]. However, we were not able to identify a comprehensive list of other current CE-marked RFD systems.

A0021 – What is the reimbursement status of radiofrequency denervation?

RFD kann derzeit über Code AJ140 abgerechnet werden

Currently, radiofrequency denervation of the facet joints can be reimbursed via the Austrian DRG system (Leistungsorientierte Krankenanstaltenfinanzierung/LKF) using the code AJ140 'percutaneous destruction of peripheral nerves'.

4 Health problem and current use

Overview of the disease or health condition

A0001 – For which health conditions, and for what purposes is radiofrequency ablation/denervation used?

Radiofrequency ablation is one of several types of ablation therapy. Therefore, it can be used to treat a wide range of conditions. For example, RFA is sometimes used in oncology [15] to treat (bone, kidney, liver, lung or prostate) cancers including bone metastases [16] or precancerous lesions in the esophagus (Barrett's esophagus), in cardiology [17] to treat arrhythmias (e.g., supraventricular tachyarrhythmias), or in dermatology [18] to treat skin lesions. Finally, RFA is used in pain therapy, e.g., for the treatment of neck or low back pain (LBP).

RFD ist eine von zahlreichen Ablationstherapien, welche auch in anderen Indikationsbereichen eingesetzt wird

A0002 – What is the disease or health condition in the scope of this assessment?

In the scope of this assessment, chronic low back pain deriving from the lumbar facet joints and chronic neck pain deriving from the cervical facet joints are the conditions of interest. Low back pain is defined as pain and discomfort, localised between the costal margin and above the inferior gluteal folds, with or without referred leg pain, that persists for at least 12 weeks (European Guidelines from 2004 [19]). Accordingly, neck pain is defined as pain located in the anatomical region of the neck with or without radiation to the head (cervicogenic headache), trunk and upper limbs [20].

chronischer Rückenschmerz kann durch Veränderungen im Bereich der Facettengelenke bedingt sein

Supplementary to the previous assessment, patients suffering from facet joint syndrome due to osteoporosis will be considered. According to the information from the submitting hospital, the intervention for this particular subgroup might be more beneficial than a surgical treatment via spondylodesis (spinal fusion).

chronischer Nackenschmerz kann in andere Regionen ausstrahlen; zusätzlich Osteoporose-PatientInnen betrachtet

A0003 – What are the known risk factors of chronic back pain or chronic neck pain?

There are many possible causes for low back pain, e.g., infections, tumours, fractures, or spinal disc herniation. The majority of patients (approximately 85%) seen in the primary care, however, have non-specific low back pain, which is not attributable to a recognisable, known specific pathology or anatomical structure (e.g., infection, tumour, fracture) [10, 21]. Suspected sources of back pain include lumbar facet (zygapophyseal) joints, sacroiliac joints, and degenerated intervertebral discs [10].

zahlreiche Schmerzursachen, in der Mehrzahl der PatientInnen jedoch unspezifisch (nicht eindeutig einer Ursache zuordenbar)

Risk factors associated with back pain include smoking, obesity, age, female gender, physically strenuous work, sedentary work, psychologically strenuous work, low educational attainment, job dissatisfaction, and psychological factors such as somatisation disorder, anxiety, and depression [21].

Risikofaktoren für Rückenschmerzen u. a. Übergewicht, sitzende Tätigkeit, Stress sowie Osteoporose

Furthermore, osteoporosis has been identified as a major risk factor. The disease is characterised by low bone mass, microarchitectureal disruptions, as well as an overall skeletal fragility. The only clinical manifestations (of the otherwise asymptomatic condition) are fractures, whereas vertebral fractures and those of the hip and the femur occur most frequently [22]. If the vertebral bodies of the spine are affected, the fractures could result in a significant amount of back pain [23].

degenerative Veränderungen sind Hauptursache für Nackenschmerzen

Among the most common causes for neck pain (cervicalgia) are degenerative changes of the lower cervical spine (from C3 to C7) [24]. In addition, the symptom can arise from diverse musculoskeletal conditions (e.g., spondylosis), neurologic diseases (cervical radiculopathy) or non-spinal disorders like infections or malignancies [25].

Risikofaktoren u. a. Depressionen, soziale Konflikte, unkorrekte Körperhaltung

Several risk factors strongly associated with a first episode of neck pain, like depressed mood, high role conflict or perceived muscular tension, have been identified. Furthermore, awkward and/or sustained postures in work were most commonly reported [26]. More general risk factors include age, gender, history of neck pain, occurrence of other musculoskeletal problems, repetitive strain and poor self-rated health [27] [28].

A0004 What is the natural course of chronic back pain or chronic neck pain?

Rückenschmerzen zeigen rezidivierenden oder persistierenden Verlauf

Chronic low back pain is seen as recurring or persistent condition showing a fluctuating course over time. It is likely that patients who report LBP will continue to report LBP in the future [29]. After an initial episode of low back pain, 44-78% of the patients suffer relapses of pain [19].

Nackenschmerzen aufgrund altersbedingter Degeneration der Wirbelkörper in 50% der Erwachsenen über 40 Jahren

chronisches Syndrom in ungefähr 30% der PatientInnen

Neck pain often starts asymptomatically. Evidence of age-related chronic degeneration of the vertebral disc (spondylosis) is found in 25% of adults under 40 years of age, in 50% of adults over 40 years of age, and in 85% of adults over 60 years of age [30]. Generally, the progression is highly variable. Usually, half of the patients experience a benign form in which the episodes of neck pain resolve within one year [27]. About 50% to 80% report the recurrence of neck pain 1 to 5 years later, and approximately 30% develop chronic syndromes [31, 32]. Among the factors known to contribute to an acceleration of the symptom are a congenitally narrow vertebral canal, exposure to significant trauma, certain physical activities like soccer or rugby, and having dystonic cerebral palsy including the cervical muscles [30].

Effects of the disease or health condition on the individual and society

A0005 – What is the burden of disease for patients with chronic back pain or chronic neck pain?

PatientInnen weisen meist Komorbiditäten auf

Chronic low back pain is one of the most commonly reported pain conditions. It is often characterised by a long duration of the illness and multiple recurrent episodes of pain. Patients with low back pain often report comorbidities such as osteoarthritis, cardiovascular and cerebrovascular diseases, as well as mental disorders such as depression, anxiety disorders, and post-traumatic stress disorder. International data also show a positive correlation between low back pain and symptoms such as migraine and headache, exhaustion, and respiratory symptoms [33].

chronischer lumbaler Rückenschmerz und Nackenschmerzen sind weltweit die 4. häufigste Ursache für DALYs

In 2015, low back and neck pain ranked as the fourth leading cause of disability-adjusted life years (DALYs) globally [34]. Approximately half of all individuals will experience a clinically important episode of neck pain over the course of their lifetime, whereby more women than men are affected (5.77% vs. 3.89%), with the highest prevalence in the age group of 40-45 years [35]. More than 330 million people (4.82% of the global population) are affected by episodes of neck pain lasting more than 3 months [34].

A0006 – What are the consequences of chronic back pain or chronic neck pain for the society?

Rückenschmerzen sind eine der teuersten Erkrankungen in Industrieländern (v. a. durch Arbeitsunfähigkeit/ Frühpensionierung)

Low back pain is one of the most expensive diseases in industrialised countries. It is one of the most frequent causes for inability to work and early retirement. In Germany, low back pain is estimated to cause direct costs of € 8.4 billion per year. According to international estimates, 85% of these costs are due to productivity losses because of inability to work and the remaining 15% are spent on medical treatment [33]. In the United States, costs of low back pain have been estimated to be more than 100 billion USD per year, primarily due to lost productivity [9].

Nackenschmerzen verursachen ebenfalls enorme Kosten im Gesundheitssystem

Similarly, the economic burden of neck pain is high, including the cost of treatments, lost wages and compensation expenditures. It is second only to low back pain in workers' compensation claims in the US and accounts for 18% of all disability payments in Sweden [32].

Both conditions are among the most common medical conditions requiring medical care and affecting an individual's ability to work and manage the daily activities. In the US, the medical costs for all back-related conditions were $253 billion in 2013 (without chiropractic care, physical therapy, massage or other types of alternative care, and exclusive outpatient treatment costs [36].

Current clinical management of the disease or health condition

A0024 – How is chronic back pain or chronic neck pain currently diagnosed according to published guidelines and in practice?

Diagnose chronischer Rückenschmerz erfolgt auf Basis der Anamnese

Chronic low back pain is diagnosed by a detailed medical history (anamnesis). The medical history should include asking for the onset of symptoms, duration, localisation and causes of pain, correlation of pain with specific positions and movements, earlier pain episodes, problems in activities of daily living, as well as psychosocial risk factors. An important part of the medical history is asking for red flag symptoms, which can indicate specific causes (e.g., fracture, tumour, infection, radiculopathy/neuropathy) with potentially urgent need for action [33, 37].

potentielle spezifische Ursachen sollen durch klinische Untersuchung und Bildgebung abgeklärt werden

An additional physical examination (e.g., inspection, palpation, test of the mobility of the lumbar spine, examination of the sacroiliac joint) [33, 37] aims at distinguishing between non-specific vs. specific (physical or mental) causes (as the aforementioned red flag symptoms do). Medical imaging also aims at identifying specific causes for low back pain. However, study results question its use as a single diagnostic modality, because degenerative changes (here: osteoarthritis of facet joints detected by CT) are common in the general population and increasing with age [38]. A large population-based study failed to find an association of this CT-verified presence of degenerative osteoarthritis and low back pain [38].

During the care process, the assessment of psychosocial and somatic risk factors for pain chronification ('yellow flags'; e.g., depressiveness, pain-related cognition, passive pain behaviour, workplace-related factors, iatrogenic factors) is recommended [33].

Vielzahl an möglichen Differentialdiagnosen bei Nackenschmerzen

Due to the vast amount of differential diagnosis, the initial assessment of neck pain focuses on largely excluding serious condition 'red flags', including recent major trauma, underlying infections or cancer [25]. In patients without 'red flags' the evaluation consists of a detailed history and a physical examina-

tion (including observation, determination of the range of motions and muscle palpation), a neurologic assessment (including muscle strength, sensory, reflex and gait testing, as well as an evaluation for upper motor neuron signs), and an assessment of radicular symptoms or signs using provocative manoeuvres (Spurling's maneuver, Elvey's upper limb tension test, or manual neck distraction test). Finally, the severity of pain should be assessed [25].

A0025 – How is chronic back pain or chronic neck pain currently managed according to published guidelines and in practice?

konservative Behandlungsmethoden reichen von medikamentösen zu nicht-medikamentösen Therapien

Conservative treatment options for chronic low back pain may include drug therapies with non-steroidal antirheumatics/antiphlogistics (NSARs), and, if applicable, opioid analgesics, muscle relaxants or anti-depressants [33]. In addition, several non-drug therapies are recommended (physical activity and movement therapy, therapeutic exercise, patient education [information/training], ergonomics, multimodal, multi-, and interdisciplinary treatment/rehabilitation, self-management programmes, occupational therapy, behavioural therapy, or progressive muscle relaxation).

invasive Maßnahmen werden nicht empfohlen

According to this guideline, invasive therapeutic procedures are not recommended for the treatment of patients with non-specific low back pain [33], due to the lack of reliable data (despite numerous studies) for percutaneous procedures, and the lack of studies on the use of surgical procedures.

Einzelmaßnahmen werden als nicht ausreichend angesehen, langfristige Folgen (z. B. Krankenstände) zu verhindern

The Austrian Guideline for the management of acute and chronic non-specific low back pain, published in 2018 [37] recommends multidisciplinary treatment programmes for chronic low back pain. Single interventions, such as pharmacological treatment only, are not considered to be sufficient for alleviating pain in the long term, as well as to prevent disability and work absences [37].

Due to the diversity and complexity of possible underlying conditions, the treatment of neck pain has to be individualised and adjusted according to pain control and length of symptoms. Initially, posture modifications are recommended (e.g., adjustment of sleep positions and avoidance of sustained seated posture).

In the case of persistent pain, physical therapy, spinal manipulation and manual therapy are recommended [39]. Furthermore, pharmacological treatments with acetaminophen or non-steroidal antirheumatics/antiphlogistics (NSARs) might be effective for patients who suffer from mild to moderate pain episodes. Patients experiencing severe pain might find relief when using opioid analgesics or tramadol. Additionally, muscle relaxants could be useful [39].

Target population

A0007 – What is the target population in this assessment?

Zielpopulation: Erwachsene mit LBP und Cervicalgia >3 Monaten und entsprechender vorangehender Diagnostik

The target population in this assessment is adult patients with chronic (longer than three months) low back pain or neck pain, who had a positive response to a diagnostic block in the facet joints. Furthermore, patients with facet joint syndrome due to osteoporosis were considered. In contrast, patients with facet joint pain due to acute trauma, fractures, malignancies or inflammatory diseases were excluded.

A0023 – How many people belong to the target population?

¼ der ÖsterreicherInnen innerhalb eines Jahres betroffen; Lebenszeitprävalenz von Rückenschmerzen bis zu 84 %

According to a health survey conducted by Statistik Austria in 2014, 23% of Austrian men and 26% of Austrian women were affected by chronic low back pain or other chronic back problems in the previous 12 months. The prevalence increases with age, and more women are affected than men [40]. The lifetime prevalence of low back pain (in total) is estimated to be up to 84% [19].

In total, 1.34 million (19%) of the Austrian employees suffer from chronic neck pain. The prevalence is higher in women than in men (23% vs. 14%) and increases with age [41].

Anteil an Schmerzen im Bereich der Facetten- bzw. Iliosakralgelenke letztlich unklar

Prevalence estimates of facet joint pain are provided by the RFD studies' authors as follows: Facet-joint pain accounts for 15% to 50% [42-44] of low back pain. Against the backdrop of the high prevalence of degenerative changes detected in facet joints (63% in a sample of 188 men and women, at mean ~52 years old [38]) of the general population, the provided (high) proportion of 'facet joint pain' as a cause of low back pain can be questioned. Due to non-specific imaging and clinical testing, reliable epidemiological data seems to be missing.

The prevalence of individuals with osteoporosis among the adult population in Austria older than 50 years is estimated to be 5.5% (460,000 individuals), of which 80.4% are female [45]; however, no information about how many of them are suffering from facet joint syndrome is available.

A0011 – How much is radiofrequency denervation of the facet joints utilised?

rund 800 Behandlungen pro Jahr in Österreich

According to the information provided by one Austrian hospital, the annual frequency in this hospital is estimated to be 80 procedures of radiofrequency denervation. In 2017, 70 treatments were recorded in the submitting hospital. The number of facet joint radiofrequency denervation procedures in Austrian hospitals is estimated with 800 per year.

5 Clinical effectiveness

5.1 Outcomes

4 kritische Endpunkte: Schmerz, Funktionalität, allgemeine Verbesserung sowie die gesundheitsbezogene Lebensqualität

For both conditions (chronic neck pain and chronic low back pain), the following outcomes were defined as *crucial* to derive a recommendation:

- Pain
- Functional status
- Global improvement
- Health-related quality of life

Intensität der Schmerzen meist mittels Visual Analogue Scale (VAS) oder Numeric Rating Scale (NRS) bestimmt

Changes in **pain intensity** were measured in 4 studies [46-49] using the Visual Analogue Scale (VAS), which is a continuous scale usually ranging from 0 to 100 mm in length; ranges from 0-4 mm indicate 'no pain' while 75-100 mm indicate severe pain [50]. The clinically minimum important difference (CIMD) varies according to the severity of pain reported, and ranges between 10-14 mm [51]. Two studies [52, 53] applied the Numeric Rating Scale (NRS-11), which represents an 11-item, segmented version of the VAS.

One study [54] determined the absolute number of days with intense cervicogenic headache (resulting from neck pain with cervical facet joints involvement), and reported those patients who experienced a reduction of at least 30 days between baseline and indicated time point. In addition, the authors performed algometry measurements (pain pressure threshold measured with an algometer). The difference in the pain threshold between the non-symptomatic and the symptomatic side was calculated and the average of three single trials (performed within a few minutes) was used. The CIMD for patients with neck pain has been determined as 0.07 kg/f (right) and 0.48 kg/f (left), if measured between the C5/C6 segment [55].

Funktionalität des Rückens hauptsächlich mit Hilfe des Oswestry Disability Index (ODI) gemessen

The **functional status of the low back** was ascertained in 3 studies [47, 49, 52] using the Oswestry Disability Index (ODI). First published in 1980, the current version dates from 2000 [56]. The self-completed questionnaire contains 10 topics, each of which is scored on scale from 0 to 5, with 0 indicating 'least amount of disability' and 5 indicating 'most severe disability'. The scores of all questions are summed, multiplied by two, and given in percentages (0%-100%). Finally, the results are summarised into five broad categories ranging from minimal disability (0%-20%) to bed-bound or exaggeration of the symptoms (81%-100%). A difference between 10 points or 30% of the score is assumed to correspond to the CIMD [57].

One study [48] applied the Schober index, which is a clinical measure of flexion of the lumbar spine. During the physical examination, the patients were advised to maintain an erect position. The bilateral iliac crests were labelled at 10 cm above and 5 cm below the site where the back midline crossed. The patients were then asked to bend forward as much as possible to measure the increase in distance between the two markers. The evaluations were performed by independent observers. A change of 1 cm is considered as CIMD [58].

Bewegungstests werden für die Bestimmung der Funktionalität des Nackens verwendet

The **functional status of the neck** was measured by applying certain range of motion (active movements) tests with a baseline inclinometer in three dimensions (maximal flexion/extension, lateral flexion, and rotation). For all movements, the average of three measurements was calculated. The CIMDs are given as follows: flexion: 6.0°, extension: 4.0°, rotation right: 10.0°, rotation left: 5.0°, lateral flexion right: 3.0°, and lateral flexion left: 5.0° [55].

der unspezifische Endpunkt globale Verbesserung (Global Perceived Effect) wurde auf einer 4- oder 7-teiligen Skala gemessen

Different tools were used to study the non-specific outcome measure of **global improvement**. Five studies [46, 47, 52-54] determined the Global Perceived Effect (GPE) by asking patients to rate, numerically, how much their condition has improved or deteriorated from the predefined time point, either a 4-point scale (complete relief of pain, more than 50% relief, no effect, increase in pain) [47] or a 7-point scale from either 1-7 (fully recovered to worse than ever) [52] or from -3 (much worse) to +3 (much better) [46] was used. The CMID on the 7-point scale is considered to be 1.26 points (18% difference) [59].

eine chinesische Studie verwendete die Surgical Efficacy Criteria (Chinese Medical Association)

A single study [48] applied the Surgical Efficacy Criteria of the Spine Surgery Group of the Orthopedic Branch of Chinese Medical Association, which is divided into four categories: excellent (the patient's pain disappeared, the lumbar range of motion was restored, and the patient returned to normal life), good (the patient's pain was eliminated, the lumbar range of motion was partly restored, and the patient returned to normal work and life), eligible (the patient's pain was partly relieved, the lumbar range of motion was partly restored, and the patient was unable to return to normal work and life), and poor (treatment had no effect or the symptoms were aggravated and the related signs did not improve).

die Lebensqualität wurde mittels mehrerer Fragebögen erhoben

Health-related quality of life was assessed by calculating the mean health scores comprising the generic 36-item questionnaire compiled from the Rand Health Insurance Long Form Health Status Scale (RAND-36), the West Haven-Yale Multidimensional Pain Inventory (MPI) in the Dutch language (MPI-DLV) and the Dutch version of the Symptom Checklist-90 (SCL-90) [46] or by using the EQ-5D-3L [52].

The Rand Health Insurance Long Form Health Status Scale (RAND-36) investigates the HRQoL in the dimensions of physical function, social function, role physical limitations, role emotional limitations, mental health, vitality, bodily pain, and general health. The answers are then transformed into a 0-100 scale, whereby a higher score is indicative of less disability. The CMID is considered to be 4 arbitrary units [60]. The West Haven-Yale MPI assesses the adaptation to chronic pain and is composed of 52 items. The outcome is given on a 7-point scale [61]. (No information regarding the CMID was found.) The SCL-90 consists of 90 items investigating 9 primary symptom dimensions (e.g., somatisation, depression, interpersonal sensitivity) and 3 global distress parameters. (No information about the CMID was found.) The EQ-5D-3L is a standardized instrument for measuring the generic health status. It is composed of 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). The respondents rate their level of severity on a 3-level scale. The CMID is considered to be 0.10 arbitrary units [62].

wichtige, jedoch nicht entscheidende Endpunkte: Patientenzufriedenheit und Arbeitsfähigkeit

The outcomes of

- Patient satisfaction and
- Ability to work

were defined as important, but not crucial, to derive a recommendation.

5.2 Included studies

Cervical facet joint pain: study and patient characteristics

zwei RCTs für die Evaluation von RFD bei zervikalen Facettengelenksschmerzen mit insg. 42 PatientInnen eingeschlossen; 21 erhielten RFD

Two randomised controlled studies [46, 54] were included for evaluating RFD in patients with cervical facet joint pain. One study [54] compared the intervention with a placebo/sham treatment, while the other study [46] used injections with local anaesthetics as a comparator.

These studies were conducted in the Netherlands [46] and in Norway [54]. Neither of the two studies, which were published in 2004 [54] and 2006 [46], provided information about potential funding sources. The sample sizes were 12 and 30 patients, with an equal amount of individuals (n=21) in the intervention and control groups.

Studien unterschiedlich in Bezug auf die Dauer bestehender Kopfschmerzen

Both trials used the criteria of Sjaastad for diagnosing cervicogenic headache. In the placebo-controlled trial, the patients had to suffer from cervicogenic headache for more than 1 year. Furthermore, the participants had to have experienced an insufficient effect of appropriate prophylactic headache medication. Additionally, any cerebral CT or MRI or cervical MRI had to be without significant pathology [54]. In the steroid injection study, the headache had to be persistent for more than 2 years, including significant pain periods (VAS score of more than 50 mm) of at least 2 days a week [46].

Alter der PatientInnen zwischen 45 und 53 Jahre; mindestens 50 % Frauen

The mean age of patients ranged between 45 and 53 years. In both studies, patients in the control group were slightly older (1.6 years and 8.0 years, respectively). The percentage of females was 73% [46] and 50% [54]. The follow-up periods were 12 months [46] and 24 months [54], respectively.

Loss to follow-up ranged from 8.3% [54] to 30% [46].

The study characteristics and the results of the included studies are displayed in Table A-1.

Cervical facet joint pain: quality assessment

1 von 2 RCTs mit hohem Biasrisiko

The study of Stovner et al. [54] has been judged as having a low risk of bias. In contrast, the study of Haspeslagh [46] was evaluated to have a high risk of bias due to potential deviations from intended interventions and due to missing outcome data.

The results of the quality assessment of the included studies are displayed in Table A-5 and in the evidence profile in Table A-8.

Lumbar facet joint pain: study and patient characteristics

5 Studien für die Evaluation von RFD im Bereich der lumbalen Facettengelenke eingeschlossen: 4 RCTs + 1 NRCT

In the course of the literature search for this update, 5 studies investigating the effect of radiofrequency denervation for lumbar facet joint pain, and which have been published since the first assessment in 2016, were identified. 4 of these were randomised controlled trials [47, 48, 52, 53], while 1 study was designed as a non-randomised controlled study [49]. 2 studies [47, 53] used a sham procedure as a comparator; 2 studies compared the intervention with a steroid injection [48, 49]. In one clinical trial, RFD in combination with a standardised exercise programme was compared to the standard exercise programme alone [52].

zwischen 60 und 251 StudienteilnehmerInnen insg. 571 PatientInnen, davon erhielten 285 RFD

2 trials were conducted in the Netherlands, and the remaining 3 studies in China, Egypt and Turkey. All of the studies were published between 2016 and 2018. The sample sizes of the trials ranged from 60 to 120 participants, with a total number of 180 patients in the placebo-controlled studies, as well as in the steroid injection controlled studies. The only exception was the exercise-controlled trial with a total number of 251 patients. The total study population comprised 571 participants, of which 285 received RFD.

unterschiedliche Einschlusskriterien v. a. in Bezug auf die Schmerzdauer

Patients were included into the studies if the low back pain lasted for more than 3 months [49, 53], 6 months [48], or more than 12 months [47]. No definition regarding the duration of the symptoms was given in 1 study [52]. In 4 studies, the participants had to experience a failure of any previously received conservative treatment [47, 49, 52, 53]. Only normal radiological findings were accepted in the study of Yasar et al. [49], while radiographic findings indicating deviations from asymptomatic statement were tolerated by Zhou and colleagues [48]. Furthermore, the studies differed as either 1 positive diagnostic block [48, 49, 52, 53] or 2 diagnostic blocks (on different occasions) [47] had to be performed to localise the cause of the pain. The reduction of pain after the block had to reach 50% [52] to 80% [48], near complete pain reduction [47], or at least 2 points on the NRS. No information regarding the amount of reduction after the diagnostic block was given in 1 trial [49].

in 4 Studien PatientInnen zwischen 55 und 65 Jahre alt; in einer Studie jünger (43-47 Jahre); Beobachtungszeitraum 6-36 Monate; loss to follow-up: 0 % bis 29 %

The mean age of patients ranged from 55 to 65 years in 4 trials. A single study investigated younger patients (43 to 47 years) [49]. The percentage of female participants was above 50% in 3 studies [47, 52, 53]. In the remaining 2 (steroid-injection) studies, the percentages of females were 45% [49] and 26% [48]. Patient follow-up ranged from 6 months to mostly 12 months; 1 study used a maximum observational period of 36 months [47].

Loss to follow-up ranged from 0% [47, 48, 53] to 29% [52]. 1 trial did not report on drop-outs [49].

The study characteristics and the results of the included studies are displayed in Table A-2, Table A-3, and Table A-4.

Lumbar facet joint pain: quality assessment

4 Studien mit hohem Biasrisiko; eine plazebokontrollierte Studie mit niedrigem Biasrisiko

One placebo-controlled trial [47] was judged to have a low risk of bias on a single study level, while the other placebo-controlled trial [53] was considered as having a high risk of bias due to the possibility of a crossover for the sham group after a minimum period of 3 months. The study investigating the effect of RFD in combination with a standard exercise programme [52] was assessed as having a high risk of bias due to the non-blinding of patients and caregivers, bias due to missing data, and putative bias in the measurement of the outcome due to the non-blinding of the patients (i.e., overestimation of effects due to self-reported outcomes of patients).

The steroid injection studies were assessed as having a high risk of bias either due to potential confounding [49], or due to potential deviation from the intended interventions, and in the measurement of the outcome [48].

The results of the quality assessment of included studies are displayed in Table A-6 and Table A-7, and in the evidence profile in Table A-9.

Facet joint syndrome in patients with osteoporosis

No studies investigating radiofrequency denervation in patients with facet joint syndrome due to osteoporosis were identified through the systematic literature search; neither did any of the included studies provide data on that particular topic. Therefore, results are only presented for lumbar and cervical facet joint pain.

keine Literatur zu Facettengelenks-syndrome aufgrund von Osteoporose

5.3 Results

Mortality

D0001 – What is the expected beneficial effect of radiofrequency denervation on mortality?

Mortality is not a relevant outcome for assessing the clinical effectiveness of radiofrequency denervation, since neither the disease nor the intervention is life-threatening. Therefore, none of the included studies reported this outcome.

Mortalität: für die vorliegende Fragestellung kein relevanter Endpunkt

Morbidity (Pain)

D0005 – How does radiofrequency denervation affect symptoms and findings (severity, frequency) of chronic neck pain or chronic low back pain?

The 2 outcomes, pain intensity and global improvement, were available to answer this question.

Cervical facet joint pain

*Improvement in **pain intensity** was reported in both studies [46, 54]:*

After 8 weeks, the percentage of patients reporting an improvement in pain intensity differed by 1.7% in favour of the intervention (43.9% vs. 42.4%). However, the result was not statistically significant (p=0.87) [46]. Additional measurements were performed at 16 weeks (23.9% vs. 50.1%; p=0.17), 6 months (28.5% vs. 49.4%; p=0.38) and at 12 months (16.8% vs. 49.9%; p=0.34), but since cross-over at 16 weeks to other therapies was optional, the data provided no further evidence.

im Vergleich zu Steroid-Injektionen kein signifikanter Unterschied 8 Wochen nach Intervention

In the placebo-controlled trial, 66.7% of the patients (4 out of 6) in the intervention group reported a reduction of at least 30 days with intense headache compared to 33.3% of the patients (2 out of 6) in the control group at 3 months of follow-up. Between 12 and 24 months, fewer patients of the intervention group experienced a reduction of intense headache days compared to patients of the control group (20% vs. 50%-60%) [54]. The statistical significance of these results was not provided by the authors.

nach 3 Monaten wirksamer als Plazebo in der Reduktion von Tagen mit intensivem Kopfschmerz

*Changes in the **global improvement** were reported in two studies [46, 54]:*

The outcome was assessed using the Global Perceived Effect (GPE) and/or successful VAS in one study [46]. At 8 weeks, 80% of the patients in the intervention group and 66.7% of the patients in the control group reported a global improvement. In addition, the outcome was assessed at 16 weeks (66.7% vs. 53.3%) and 12 months (53.3% vs. 46.7%), but failed to show a statistically

kein signifikanter Unterschied im Endpunkt allgemeine Verbesserung

significant effect. The second study [54] reported the outcome at 3 months (50% vs. 33.3%), 12 months (40% vs. 0%) and 24 months (60% vs. 16.7%). However, the statistically significance of the result was not reported.

Lumbar facet joint pain

*Improvement in **pain intensity** was reported in all 5 studies [47-49, 52, 53]:*

kein signifikanter Unterschied in einer von 2 Studien im Vergleich mit Plazebo

Applying the NRS, one placebo-controlled trial [53] reported a similar reduction in pain intensity (MD: -1.9; p=0.66) in both groups 1 month after treatment. (No detailed results for other time points were provided. However, the authors stated that no statistically significant differences between groups occurred.) Comparing patients who received RFD with patients of the sham control group, the second study reported a VAS reduction of at least 50% throughout the entire follow-up period [47]: At 3 months, 75% of patients in the intervention group compared to 57.7% of patients in the control group indicated a reduction in pain intensity. Further measurements were performed at 6 months (60% vs. 20%), 12 months (45% vs. 7.5%), 24 months (17.5% vs. 2.5%) and 36 months (12.5% vs. 2.5%). (The statistical significance of the difference between the 2 groups was not provided by the authors.)

signifikant niedrigere Schmerzintensitäten in einer von 2 Studien im Vergleich mit Steroid-injektionen

In one steroid-injection controlled study [48], significantly lower VAS scores were reported in patients of the intervention group compared to patients of the control group (p<0.01). At 1 week, the mean VAS score in the intervention group was 1.4 compared to 1.9 in the control group. At 1 month, the scores in the respective groups were 1.4 and 3.6. After 6 months, the mean VAS scores were 1.7 and 5.8, respectively. In the second steroid-injection trial [49], the mean VAS scores in the intervention and control groups were measured at 3 months (2.5 vs. 3.3), 6 months (2.3 vs. 3.3), 9 months (2.7 vs. 2.5) and 12 months (3.0 vs. 3.0). (The statistical significance of the difference between the 2 groups was not provided by the authors.)

RFD als add-on Therapie zeigt keinen Effekt

If RFD was used in combination with a standardised exercise programme [52], measurements of the pain intensity in both groups were performed at 3 weeks (5.17 vs. 5.92, p=0.18), 6 weeks (5.19 vs. 5.92; p=0.02), 3 months (5.19 vs. 5.90; p=0.55), 6 months (4.61 vs. 4.84; p=0.91), 9 months (4.66 vs. 4.73; p=0.53), and 12 months (4.49 vs. 4.44; p=0.13) by applying the NRS. No significant differences in the mean pain intensity scores between the intervention and control groups were found throughout the follow-up period.

*Differences in the **global improvement** were extracted from 4 studies [47, 48, 52, 53]:*

signifikanter Unterschied nach 6 Monaten bei Anwendung der Surgical Efficacy Criteria

In order to assess this outcome, the Surgical Efficacy Criteria of the Spine Surgery Group were applied in 1 injection-controlled trial [48]. At 6 months, 62.5% of the patients receiving RFD and 12.5% of the patients in the respective control group were evaluated as experiencing an 'excellent' improvement. Accordingly, 27.5% vs. 30%, were rated as having made 'good' improvements, while 7.5% vs. 5.0% were categorized as experiencing 'eligible' improvements, compared to 2.5% vs. 52.5% who were rated as having a 'poor' global improvement. The differences between the two groups were reported as statistically significant (p<0.01).

Three studies assessed the outcome applying the Global Perceived Effect scale (GPE). Van Tilburg and colleagues [53] reported a mean difference of -0.1 and -0.2 between patients of the intervention group and patients of the control group at 1 and 2 months, respectively. The differences were not statistically significant. Moussa et al. [47] documented the percentage of patients reporting an improvement of more than 50%. The outcome was assessed at 3 months (65% vs. 50.0%), 6 months (52.5% vs. 15%), 12 months (37.5% vs. 2.5%), 24 months (10% vs. 2.5%), and 36 months (7.5% vs. 0%). However, the statistical significance of the difference between the 2 groups was not provided by the authors. In the third study [52], the outcome was given as number of patients improving by 1-2 scores and assessed at 3 weeks (RR=5.41; 95% CI: 2.29-10.34; p>0.001), 6 weeks (RR=2.71; 95% CI: 1.37-4.68; p=0.005), 3 months (RR=1.35; 95% CI: 0.81-2.05; p=0.24), 6 months (RR=1.04; 95% CI: 0.64-1.12; p=0.85), 9 months (RR=0.81; 95% CI: 0.48-0.57; p=0.35) and 12 months (RR=0.90; 95% CI: 0.55-1.33; p=0.65). Thus, a statistically significant difference in favour of the intervention was found between 3-6 weeks post RFD.

RFD als add-on Therapie zeigt allgemeine Verbesserung der Patienten nach 3-6 Wochen; kein signifikanter Unterschied im Vergleich mit Plazebo

D0006 – How does radiofrequency denervation affect progression (or recurrence) of chronic neck pain or chronic low back pain?

Cervical facet joint pain

Long-term data on pain improvement was reported in 1 of 2 studies [54]:

Follow-up data (24 months) was provided by 1 study comparing RFD with placebo in 12 patients [54]. No difference in the outcome (reduction of at least 30 days of intense headache) was detected between 12 and 24 months; the percentage of participants reporting a reduction remained at 20% in the intervention group compared to a percentage of 66.7% in the respective control group, suggesting no long-term effect of the treatment.

kein Langzeiteffekt nach 12 Monaten beobachtbar

Lumbar facet joint pain

Long-term data on pain improvement was reported in 1 of 5 studies [47]:

At 24 months, 17.5% of the patients treated with RFD reported a reduction in pain intensity of at least 50%, compared with 2.5% of patients in the placebo group. At 36 months, the percentages were 12.5% vs. 2.5%, respectively, suggesting that more participants benefit from intervention in the long term. (However, the statistical significance of the difference between the two groups was not provided by the authors.)

möglicher Langzeiteffekt im lumbalen Bereich

Functional status & ability to work

D0016 – How does the use of radiofrequency denervation affect activities of daily living?

The two outcomes of functional status and ability to work were available to answer this question.

Cervical facet joint pain

*Differences in the **functional status** were reported in 1 of 2 studies [54]:*

The placebo-controlled study determined changes from baseline to 3 different time points after the intervention by several range of motion tests and by algometry. Regarding the neck flexion/extension at 3 months, 14% of the patients in the intervention group reported a change, compared to 20% of the

kein signifikanter Unterschied in der Funktionalität

patients in the control group (p=0.9). At 12 months, 6% vs. 6% (p=not applicable) reported changes, and after 24 months, 14% vs. 8% (p=0.7) observed differences. Regarding the neck lateral flexion at 3 months, mean scores of 10° vs. 4° (p=0.6) were reported. Additional measurements at 12 months (6° vs. 5°; p=0.6) and 24 months (-2° vs. 7°; p=0.6) were performed. Regarding the neck rotation movement, differences of 0° vs. 4° were observed 3 months after the intervention (p=not applicable). At 12 months, the respective values were 9° vs. -14° (p=0.3), and at 24 months the scores were reported as -8° vs. -6° (p=0.9). Changes in the algometry measurements were documented at 3 months (-24 vs. -19; p=0.9), 12 months (-88 vs. -42; p=0.1), and 24 months (0 vs. -35; p=0.5). However, the differences were not statistically significant.

Daten zur Arbeitsfähigkeit wurden nicht gesammelt

None of the included RCTs for cervical facet joint pain reported the outcome '**ability to work**'.

Lumbar facet joint pain

Changes in the functional status were reported in 4 of 5 studies [47-49, 52]:

im Vergleich zu Plazebo ein hoher Unterschied in der Funktionalität zwischen 6 und 12 Monaten beobachtbar

Differences in the functional status were reported by 1 placebo-controlled trial [47] using the ODI. The mean differences between the intervention and control groups were highest between 6 months and 12 months of follow-up (30 and 35.7, respectively), while at 24 months the difference declined to 9.1. The smallest variations were observed at 3 months and 36 months post intervention (4.5 and 5.3, respectively). (The statistical significance of the difference between the two groups was not provided by the authors.)

keine erhöhte Wirksamkeit als add-on Therapie Erhöhte Funktionalität zwischen 1 und 6 bzw. 9 Monaten im Vergleich zu Steroid-injektionen

In 1 steroid-controlled trial [48], significant differences between intervention and control group were found between 1 month (9.0 vs. 8.9; p<0.05) and 6 months (8.8 vs. 6.2; p<0.01), indicating an increased flexibility of the lumbar spine in patients of the intervention group as measured with the Schober index. In the second trial [49], the functional status of the participants was measured using the ODI. At 3 months (18.9 vs. 24.1), 6 months (14.9 vs. 24.8), and 9 months (10.4 vs. 12.2), a lower scoring (indicating less disability) was reported by patients of the intervention group, while after 12 months, patients of the control group seemed to be less compromised (17.2 vs. 12.1). (However, the authors did not report on the statistically significance of the findings.)

The study comparing RFD plus exercise with exercise alone [52] measured the mean functional score, applying the ODI at 3 months (26.03 vs. 28.67), 6 months (25.38 vs. 27.15), 9 months (25.74 vs. 24.52), and 12 months (24.59 vs. 25.04). However, the analysis revealed no statistically significant differences between both groups throughout the entire observational period.

ein höherer Prozentsatz der RFD-behandelten PatientInnen kann zur normalen Arbeit zurückkehren

The Surgical Efficacy Criteria were used for assessing the outcome "**ability to work**" in 1 study [48].

A higher percentage of patients in the intervention group were able to return to normal work, compared to patients of the control group (90% vs. 42.5%). Accordingly, fewer patients of the intervention group were unable to return to normal work (10% vs. 57.5%). The differences between the groups were statistically significant.

Health-related quality of life

D0012 – What is the effect of radiofrequency denervation on generic health-related quality of life?

Cervical facet joint pain

This outcome was reported by 1 study [46].

However, the authors provided no absolute numbers. They nonetheless stated that no statistically significant difference between the mean health scores of the intervention and the control groups were found throughout the follow-up period.

kein Unterschied in der Lebensqualität bei RFD vs. Steroidinjektionen bei zervikalen Facettengelenks-schmerzen

Lumbar facet joint pain

This outcome was assessed by 1 study [52] using the EQ-5D-3L questionnaire.

The mean utility score was reported at 3 weeks (0.69 vs. 0.64; p=0.08), 6 weeks (0.69 vs. 0.67; p=0.32), 3 months (0.68 vs. 0.69; p=0.85), 6 months (0.73 vs. 0.71; p=0.42), 9 months (0.72 vs. 0.75; p=0.11), and 12 months (0.73 vs. 0.73; p=0.37). However, all analysed time points failed to show a statistically significant difference.

kein Unterschied in der Lebensqualität bei RFD als add-on bei lumbalen Facettengelenks-schmerzen

D0013 – What is the effect of radiofrequency denervation on disease-specific quality of life?

None of the studies reported on disease-specific quality of life.

keine Daten zur krankheitsbedingten Lebensqualität vorhanden

Patient satisfaction

D0017 – Was the use of radiofrequency denervation worthwhile?

Cervical facet joint pain

To answer this research question, the outcome 'satisfaction with treatment' was used, but none of the RCTs reported this outcome.

Daten zur Zufriedenheit mit der Behandlung wurden nicht erhoben

Lumbar facet joint pain

2 studies [52, 53] assessed this outcome using the Global Perceived Effect scale.

In the placebo-controlled trial [53], the satisfaction with the treatment was reported, with a mean score of 3.4 in the intervention group compared to a score of 3.5 in the control group. Similar results were observed at 2 months (3.4 vs. 3.7). The authors reported no statistically significant differences between the 2 groups throughout the entire follow-up period, yet provided no further details. Juch et al. [52] reported the mean patient satisfaction at 3 months (2.95 vs. 3.26; p=0.34), 6 months (2.96 vs. 3.06; p=0.94), 9 months (2.88 vs. 3.13; p=0.91), and 12 months (2.88 vs. 3.01; p=0.32). Thus, no statistically significant difference between intervention and control was found until the end of the 12-month follow-up period.

kein signifikanter Unterschied zwischen den Studiengruppen gefunden

6 Safety

6.1 Outcomes

The following outcomes were defined as *crucial* to derive a recommendation:

- Procedure-related complications
- Adverse events.

These outcomes were summarised as 'complications' in the following chapter and in tables, as they are not reported separately within the included studies. The outcome 'complications' therefore includes direct intervention-related side effects, as well as any other negative consequences observed in the follow-up period.

als entscheidende Endpunkte werden prozedurbezogene Komplikationen und Nebenwirkungen der Therapie betrachtet, welche unter "Komplikationen" zusammengefasst werden

6.2 Included studies

Cervical facet joint pain

Both RCTs already included for the efficacy analysis were also used to evaluate safety [46, 54].

zervikale Facettengelenke: zwei RCTs inkludiert

The study characteristics and the results of the included studies are displayed in Table A-1. The results of the quality assessment of the included studies are summarised in Table 7-1, and in the evidence profile in Table A-8.

Lumbar facet joint pain

In addition to the 5 studies that had already been included in the clinical effectiveness assessment, we included 1 RCT with a total of 55 participants that compared thermal radiofrequency denervation (26 patients) with pulsed dose radiofrequency denervation (29 patients) [63]. The trial was conducted in the United States and published in 2016. The patients were included if they suffered at least 6 months from low back pain and did not response to any conservative treatment. Furthermore, they had to show a positive response (>80% pain relief) to 2 diagnostic blocks.

lumbale Facettengelenke: 5 RCTs sowie 1 NRCT

The mean age of the participants was 51 years; 76% were female. The follow-up was 48 hours (2 days), during which 10.3% of the thermal radiofrequency denervation group and 19.2% of the pulsed dose radiofrequency denervation group were lost.

The study was judged to have a high risk of bias due to possible bias on account of missing data.

hohes Biasrisiko der zusätzlich eingeschlossenen Studie

The study characteristics and the results of the included studies are displayed in Table A-2, Table A-3, and Table A-4. The results of the quality assessment of the included studies are displayed in Table A-6, Table A-7, and Table A-9.

Facet joint syndrome in patients with osteoporosis

keine Studien zu Osteoporose oder Facettengelenks-syndrome

No studies that include patients with osteoporosis and facet joint syndrome were identified through the systematic literature search.

Therefore, results for safety are only presented for lumbar and cervical facet joint pain.

6.3 Results

Patient safety

C0008 – How safe is radiofrequency denervation in comparison to placebo or steroid injections?

Cervical facet joint pain

Komplikationen in 6 Patienten der Interventiongruppe vs. 3 Patienten der Kontrollgruppe

Complications were reported in 1 placebo-controlled trial [54]:

At discharge from the hospital, 6 out of 6 (100%) patients who received RFD reported adverse events, in comparison to 3 out of 6 (50%) patients in the control group. At three months, 50% of the patients in the intervention group reported complications, compared to 33.3% of the patients in the respective control group.

Lumbar facet joint pain

einzige Komplikation bei RFD im Bereich der lumbalen Facettengelenke: Schmerzen nach der Intervention

No complications were reported in 4 trials [48, 49, 52, 53]. In 1 trial with methylprednisolone injection as the control group, 4 patients of the control group suffered from pain after the injection [49]. The same complication (post-procedural pain) was documented in 38% of those patients receiving a thermal radiofrequency denervation, and in 15% receiving a pulsed dose radiofrequency denervation (p=0.1) [63].

C0002 – Are the harms related to dosage or frequency of applying radiofrequency denervation?

kein signifikanter Unterschied beobachtbar

A higher percentage reported post-procedural pain in the thermal ablation group compared to the patient group that received a pulsed dose radiofrequency denervation (38% vs. 15%). However, the result was not statistically significant [63].

C0004 – How does the frequency or severity of harms change over time or in different settings?

Veränderungen unbekannt

No evidence was found to answer that research question.

C0005 – What are the susceptible patient groups that are more likely to be harmed through the use of radiofrequency denervation?

vulnerable Gruppen unbekannt

No evidence was found to answer that research question.

C0007 – Are radiofrequency denervation, steroid injections, injections with local anaesthetic or placebo interventions associated with user-dependent harms?

anwenderinnenbedingte Komplikationen unbekannt

No evidence was found to answer that research question.

7 Quality of evidence

RoB for individual randomised controlled studies was assessed with the revised Cochrane risk of bias tool for randomised trials (RoB 2.0) [3]. Non-randomised controlled trials were evaluated using the risk of bias in non-randomised studies of interventions (ROBINS-I) [4]. The RoB assessments for the included studies are presented in Table A-5, Table A-6, and Table A-7 in the Appendix.

Einschätzung des Biasrisikos mittels RoB 2.0 und ROBINS-I

Regarding the 2 RCTs included for **cervical facet joint pain**, one was graded with a *high* [46] RoB due to the non-blinding of patients and due to missing outcome data, and the second was graded with *low* RoB [54].

Hauptgründe: fehlende Verblindung und unvollständige Daten

Regarding the 5 RCTs included for **lumbar facet joint pain**, 4 were also graded with a *high* RoB [48, 52, 53, 63] mainly due to the non-blinding of patients and caregivers, high loss to FU, and incomplete reporting or measurement of outcomes. The non-randomised controlled trial [49] was graded with a serious RoB due to possible confounding.

No studies investigating RFD in **patients with osteoporosis and facet joint syndrome** were identified. Therefore, no evidence was available to perform a GRADE-analysis.

Quality of evidence according to GRADE

The strength of evidence was rated according to GRADE (Grading of Recommendations Assessment, Development and Evaluation) [49] for each endpoint individually. Each study was rated by 2 independent researchers. In case of disagreement a third researcher was involved to solve the difference. A more detailed list of criteria applied can be found in the recommendations of the GRADE Working Group [49].

Qualität der Evidenz mittels GRADE bewertet

GRADE uses four categories to rank the strength of evidence:

- **High** = We are very confident that the true effect lies close to that of the estimate of the effect.
- **Moderate** = We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- **Low** = Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
- **Very low** = Evidence either is unavailable or does not permit a conclusion.

The ranking according to the GRADE scheme for the research question can be found in the summary of findings table below (Table 7-1 and Table 7-2), and in the evidence profile in the Appendix (Table A-8 and Table A-9).

Overall, the strength of evidence for the effectiveness and safety of radiofrequency denervation for **cervical facet joint pain in comparison to injections with local anaesthetics or placebo (sham intervention)** is moderate to very low.

zervikalen Facettengelenksdenervation: mittlere bis sehr niedrige Evidenz

There is **moderate evidence** that RFD compared to placebo

- might not reduce the pain intensity at 24 months,
- might not increase the functional status at 24 months,
- might increase the global improvement at 24 months,
- might increase complications at 3 months.

There is **low evidence** that RFD compared to injections

- might not increase the pain intensity at 2 months,
- might not improve the quality of life from 2-12 months.

There is **very low evidence** that RFD compared to placebo or injections

- might increase the global improvement at 12 months.

bei lumbaler Facettengelenksdenervation hohe bis niedrige Evidenz vorhanden

Overall, the strength of evidence for the effectiveness and safety of radiofrequency denervation for **lumbar facet joint pain in comparison to steroid injections or placebo (sham intervention)** ranges from high to low.

There is **high evidence** that RFD compared to placebo,

- might reduce the pain intensity at 36 months,
- might increase the functional status at 36 months,
- might increase the global improvement at 36 months.

There is **moderate evidence** that RFD compared to steroid injections or placebo

- might reduce the pain intensity at 12 months.

There is **moderate evidence** that RFD compared with steroid injections

- might increase the functional status at 6 months,
- might not increase the global improvement at 6 months
- might not improve the quality of life up to 12 months.

There is **moderate evidence** that RFD compared with placebo

- might not increase the global improvement at 2 months.

There is **low evidence** that RFD compared to steroid injections or placebo

- might reduce the pain intensity at 6 months,
- might increase the functional status at 12 months,
- might increase the global improvement at 12 months,
- might increase complications from 6-36 months.

Table 7-1: Summary of findings table of radiofrequency denervation compared to alternative treatment for patients with chronic neck pain

Outcome	Absolute effects (explanation)	Relative effect (95% CI)	Number of participants (studies)	Quality	Comments
Pain intensity (VAS) at 2 months follow-up	IG: 43.9 (22.0) vs. 42.4 (28.6); p=0.87	-	30 (1 RCT) [46]	⊕⊕◯◯ LOW [a,b]	a higher score indicates more pain
Pain intensity (reduction of at least 30 days with intense headache) at 24 months follow-up	IG: 1/5 (20.0%) vs. CG: 3/5 (60.0%)	-	10 (1 RCT) ([54])	⊕⊕⊕◯ MODERATE [b]	-
Functional status at 24 months follow-up	No significant differences between IG and CG.	-	10 (1 RCT) [54]	⊕⊕⊕◯ MODERATE [b]	-
Global improvement (GPE) at 12 months follow-up	IG: 40%-53.3% vs. CG: 0%-46.7%	-	41 (2 RCTs) [46, 54]	⊕◯◯◯ VERY LOW [a,b,c]	-
Global improvement (GPE) at 24 months follow-up	IG: 3/5 (60%) vs. 1/6 (16.7%)	-	11 (1RCT) [54]	⊕⊕⊕◯ MODERATE [b]	-
HRQoL 2- 12 months of follow-up	No significant differences in the mean health scores between IG and CG.	-	30 (1 RCT) [46]	⊕⊕◯◯ LOW [a,b]	-
Ability to work – not reported	-	-	-	-	-
Satisfaction with the treatment – not reported	-	-	-	-	-
Complications at 3 months	IG: 3/6 (50%) vs. CG: 2/6 (33.3%)	-	12 (1RCT) [54]	⊕⊕⊕◯ MODERATE [b]	-

Abbreviations: *VAS (Visual Analogue Scale) ranging from 0 indicating 'no pain' to 100 indicating 'severe pain';*
GPE (Global Perceived Effect) measured with a 7-point scale ranging from 'much worse' to 'much better'

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect.

Comments:

[a] *High RoB*

[b] *Imprecision due to small sample size*

[c] *Inconsistency (comparator either sham procedure or steroid injections/TENS)*

Table 7-2: Summary of findings table of radiofrequency denervation compared to alternative treatment for patients with chronic back pain

Outcome	Absolute effects	Relative effect (95% CI)	Number of participants (studies)	Quality	Comments
Pain intensity (NRS) at 12 months follow-up	No significant differences between IG and CG.	-	311 (2 RCTs) [52, 53]	⊕⊕⊕◯ MODERATE [a]	
Pain intensity (VAS) at 6 months follow-up	IG: 1.7-6.0 vs. CG: 2.1-5.8	-	200 (2 RCTs) [47, 48]	⊕⊕◯◯ LOW [b,c]	A higher score incidates more pain.
Pain intensity (VAS) at 36 months follow-up (mean change)	IG: 2.2 vs. CG: 0.4	-	80 (1 RCT) [47]	⊕⊕⊕⊕ HIGH	A higher score incidates more pain.
Functional status (ODI) at 12 months follow-up	IG: 24.59-31.6 vs. CG: 5.9-25.04	-	331 (2 RCTs) [47, 52]	⊕⊕◯◯ LOW [b,c]	A lower score indicates less disability.
Functional status (ODI) at 36 months follow-up (mean change)	IG: 8.2 vs.2.9(p=0.007)	-	80 (1 RCT) [47]	⊕⊕⊕⊕ HIGH	A lower score indicates less disability.
Functional status (Schober Index) at 6 months follow-up	IG: 8.8 vs. CG: 6.2 (p<0.01)	-	80 (1 RCT) [48]	⊕⊕⊕◯ MODERATE [b]	A lower number indicates a reduced functional status.
Global improvement (GPE) at 2 months follow-up	IG: 3.4 (1.0)vs. CG: 3.6 (1.1)	-	60 (1 RCT) [53]	⊕⊕⊕◯ MODERATE [b]	A lower score indicates a global improvement.
Global improvement (success in GPE) 12 months follow-up	IG: 37.5%-42.7% vs. CG: 2.5%-39.2%	-	331 (2 RCTs) [47, 52]	⊕⊕◯◯ LOW [b,c]	
Global improvement (success in GPE) 36 months follow-up	IG: 7.5% vs. CG: 0%	-	80 (1 RCT) [47]	⊕⊕⊕⊕ HIGH	
Global improvement (Surgical Efficacy Criteria) at 6 months follow-up	Statistically significant differences between IG and CG (p<0.01).	-	80 (1 RCT) [48]	⊕⊕⊕◯ MODERATE [b]	
HRQoL (EQ-5D-3L Questionnaire) 3 weeks-12 months of follow-up	No significant differences between IG and CG.		251 (1 RCT) [52]	⊕⊕⊕◯ MODERATE [b]	
Ability to work (Surgical Efficacy Criteria) at 6 months of follow-up	Excellent: IG: 25 (62.5%) vs. CG: 5 (12.5%) Good: IG: 11 (27.5%) vs. CG: 12 (30%) Eligible: IG: 3 (7.5%) vs. CG: 2 (5.0%) Poor: IG: 1 (2.5%) vs. CG: 21 (52.5%)	-	80 (1 RCT) [48]	⊕⊕⊕◯ MODERATE [b]	
Satisfaction (GPE) at 2 months of follow-up	IG: 3.4 (1.0) vs. CG: 3.7 (1.3)	-	60 (1 RCT) [53]	⊕⊕⊕◯ MODERATE [b]	
Satisfaction (GPE) at 12 months of follow-up	IG: 2.88 (2.60-3.16) vs. CG: 3.01 (2.73-3.29); p=0.32	-	251 (1 RCT) [52]	⊕⊕⊕◯ MODERATE [b]	A lower score indicates a higher satisafction.
Complications; follow-up: 6-36 months (range)	IG: 10 vs. CG: 8	-	586 (4 RCT+ 1 observational study) [47-49, 52, 53]	⊕⊕◯◯ LOW [c,f]	

Abbreviations: *NRS: Numeric Rating Scale ranging from 0 to 10; VAS: Visual Analogue Scale ranging from 0 to 100; ODI: Oswestry Disability Index ranging from 0 to 100; GPE: Global Perceived Effect Scale ranging from 1 to 7*

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect.

Comments:

[a] *High RoB in 2 of 2 studies*

[b] *High RoB*

[c] *Inconsistency due to different comparators*

[d] *Significant vs. non-significant differences between studies and time points*

[e] *High RoB due to deviations from intended interventions and bias in the measurement of the outcome*

[f] *High RoB in 5 of 5 studies*

8 Discussion

klinische Wirksamkeit und Sicherheit von RFD im Bereich der zervikalen und lumbalen Facettengelenke untersucht

Pain originating from the neck or the low back belongs to most commonly reported conditions worldwide and is characterised by a long duration of the illness and recurrent episodes. The non-surgical intervention radiofrequency denervation of the facet joints is a non-permanent technique, which is used to suspend/resolve the symptoms based on previous localisation of pain. The aims of the project were to assess the clinical efficacy and safety of radio-frequency denervation of the cervical and lumbar facet joint pain, compared to alternative non-surgical methods or placebo in patients with or without osteoporosis.

keine Studien RFD bei Osteoporose PatientInnen vorhanden

No studies investigating the clinical efficacy and safety of radiofrequency denervation in patients with facet joint syndrome and osteoporosis were identified by the systematic search. Therefore, only results in people without osteoporosis are discussed.

2 RCTs zur zervikalen Facettengelenks-denervation evaluiert

Evidenz zu 21 RFD PatientInnen

For assessing the clinical efficacy and safety of radiofrequency denervation for **cervical facet joint pain**, 2 RCTs met the inclusion criteria with a total of 42 patients (21 of whom received RFD). No statistically significant differences were found in the outcomes of pain intensity, functional status, global improvement, health-related quality of life, and success of the treatment. Neither of the 2 studies reported on the outcomes of ability to work or satisfaction with the treatment. Yet, a higher number of patients in the intervention group reported complications after discharge from the hospital as well as after 3 months, among which increased neck pain was mentioned most frequently.

6 Studien (5 RCTs + 1 NRCT) zur lumbalen Facettengelenks-denervation bewertet

Evidenz zu 385 RFD PatientInnen

inkonsistente Ergebnisse

For assessing the clinical efficacy of radiofrequency denervation for **lumbar facet joint pain**, 4 RCTs and 1 non-randomised controlled trial (NRCT) met the inclusion criteria, with 571 patients in total (of which 285 patients received RFD). For assessing safety, 1 further RCT comparing thermal RFD with pulsed dose RFD was included as well. Thus, the study population for evaluating safety included 666 patients (of which 351 received RFD). In regard of pain intensity, functional status and global improvement, inconsistent results were reported across the studies. The outcomes of HRQoL and satisfaction with the treatment failed to show a significant difference between 6 weeks and 12 months. Ability to work was included in a composite measure (surgical efficacy criteria of the spine surgery group) in 1 study and showed significant differences at 6 months post intervention. In terms of safety, no adverse events were encountered in 3 studies. A single study reported non-statistically significant differences in the number of patients experiencing post-procedural pain. 1 study did not report on adverse events.

Interpretation of findings

mittlere bis sehr niedrige Stärke der Evidenz bei zervikalen Facettengelenks-denervationen aufgrund von hohem Biasrisiko sowie der Möglichkeit des Crossover

Overall, the level of evidence for the clinical efficacy of radiofrequency denervation for the treatment of **cervical facet joint** pain is moderate to very low for the defined crucial outcomes. The RCT that investigated RFD compared to an injection with local anaesthetics was assessed with a high RoB due to missing data and deviations from intended intervention. The participants had the possibility to receive a second treatment after 8 weeks (repetition of the initial treatment) and a third treatment (TENS) after 16 weeks in both groups, and thus were non-blinded to the intervention received. Furthermore, all relevant efficacy outcome parameters (pain intensity, functional status,

global improvement and health-related quality of life) did rely on patient self-reporting, which is likely to be influenced by the knowledge of having or having not received the intervention of interest.

geringer Stichprobenumfang der eingeschlossenen Studien

Furthermore, the strength of evidence was downgraded due to the small sample size of both included trials, which were not adequately powered to detect even considerable differences (e.g., success of the treatment after 8 weeks). In summary, there is no robust evidence that radiofrequency denervation of **cervical facet joints** leads to better outcomes than an alternative treatment with local injections or placebo.

With regard to RFD for **lumbar facet joint** pain, 6 studies (5 RCTs and 1 NRCT) had been published since the last assessment in 2016 and were considered within the present update.

hohe bis niedrige Evidenzstärke bei lumbaler Facettengelenksdenervation

The level of evidence regarding the clinical efficacy of radiofrequency denervation for the treatment of **lumbar facet joint** pain in these newly identified studies ranges from high to low. The reasons for downgrading were high risk of bias in the majority of the included trials, and inconsistencies between studies depending on the comparator used (placebo/sham treatment vs. steroid injections).

ausschlaggebend für Erfolg: präzise Lokalisation des Schmerzes

There is some evidence that radiofrequency denervation of **lumbar facet joints** leads to better outcomes than alternative treatments or placebo. In the following, different aspects that might have influenced these results are presented. The precise localisation of the source of the pain is a major issue in identifying those patients who will benefit the most from the intervention of interest. If, however, this premise is not fulfilled, patients enrolled in the study are not suffering from the conditions for which they were treated (i.e., facet joint-related pain). In turn, the anticipated effect will be diluted and the direction of the effect estimate would be biased towards zero. In this regard, the preference of 2 diagnostic blocks performed at different time points have been shown to be advantageous compared to only 1. Similarly, the degree of the pain relief achieved thereby is important in reducing the amount of false positives. For this reason, it seems not surprising that those 2 studies that used either 2 diagnostic blocks [47] and/or aimed to achieve a complete or near complete reduction of pain for inclusion [47, 48] were successful in observing/reporting significant differences between the groups in the outcomes of pain intensity, functional status, and global improvement.

General discussion points

divergierende Studienpopulationen verhindern generelle Aussagen zur Wirksamkeit

The patient population varied significantly between studies, especially with regard to the duration of the preceding. Patients were included if they suffered from chronic facet pain for a period of 3 months up to 24 months. This variation could have a major impact on the investigated outcomes, as the duration of pain prior to treatment is a known prediction factor of the anticipated response [64].

Ausschluss bestimmter Patientengruppen

In terms of age, it was noticeable that older patients (> 70 years) were not included in the study populations, although this subgroup would more commonly suffer from facet-related pain [65]. Furthermore, patients suffering from joint pain due to trauma, malignancies or inflammatory diseases were excluded, as were patients experiencing degenerative disorders. Thus, no conclusion can be drawn on the effectiveness of RFD under these circumstances.

A major point of concern was the possibility of a crossover after a specified period in 3 of 8 included studies [46, 52, 53]. Therefore, any comparisons between groups obtained after that time point have to be considered as biased [66]. Although the study authors might have introduced this possibility to prevent a loss-to-follow-up due to unresponsiveness, most of the studies encountered a high percentage of drop-outs. Some authors [52, 54] solved this problem by removing patients lost to follow-up from the dataset. However, this approach leads to an overestimation of the treatment response and should therefore be avoided [64].

Möglichkeit zusätzlicher Behandlungen verhindert Aussagen zur Effektivität der Therapie

Due to the non-permanent nature of the intervention, prolonged follow-up periods (>12 months) for investigating the effect of RFD as a primary endpoint seemed to be not meaningful. On the other hand, it would be worthwhile analysing potential co-/post-treatments, as an achieved pain reduction might increase the commitment of patients in physical therapies, etc.

Langzeitbeobachtung erscheinen in Hinblick auf zeitlich beschränkten Therapieeffekt nicht sinnvoll

Upcoming evidence

The search in clinical trial registries resulted in 51 relevant hits, of which 8 ongoing RCTs might provide further data on the efficacy and safety of cervical (Table A-12) and lumbar radiofrequency denervation (Table A-13), in comparison to alternative treatments or placebo (sham treatment). Out of these, 1 study (NCT03651804) will particularly investigate the effect of radiofrequency ablation as treatment for posterior element pain from vertebral compression fractures. Amongst others, the study (with a primary completion date in March 2020) will include patients with osteoporosis.

Ausblick: 8 laufende RCTs, davon eine Studie mit Osteoporose-PatientInnen

Limitations of the present report

First of all, we decided to exclusively include studies with a high level of evidence (RCTs and NRCTs), as such high evidence is available.

Secondly, possibly not all appropriate studies could have been identified, although different terms in the systematic literature search were used and the manufacturers were contacted for additional studies, but did not respond to our request.

Limitationen: nur RCTs eingeschlossen; möglicherweise geeignete Studien übersehen

Finally, the efficacy outcomes were measured with different scores across studies. As a result, in most cases, only a single study was evaluated in the GRADE analysis for a particular outcome at a particular time point, thereby reducing the explanatory power of the strength of evidence.

unterschiedliche Messinstrumente bei gleichem Endpunkt verringern Aussagekraft

9 Recommendation

In Table 9-1 the scheme for recommendations is displayed and the according choice is highlighted.

Table 9-1: Evidence-based recommendations

	The **inclusion** in the catalogue of benefits is **recommended**.
	The **inclusion** in the catalogue of benefits is **recommended with restrictions**.
X	The inclusion in the catalogue of benefits is ***currently*** **not recommended.**
	The **inclusion in** the catalogue of benefits is **not recommended.**

Reasoning:

The current evidence is not sufficient to prove that the assessed technology of **radiofrequency denervation of the cervical facet joints** in patients with **chronic neck pain** is more effective and equally safe in comparison to placebo or other non-surgical treatments concerning pain, functional status, global improvement, health-related quality of life, ability to work, satisfaction with the treatment and complications.

The additional evidence since the 2016 assessment is not sufficient to prove that the assessed technology of **radiofrequency denervation of the lumbar facet joints** in patients with **chronic low back pain** is more effective and equally safe in comparison to placebo or other non-surgical treatments concerning pain, functional status, global improvement, health-related quality of life, ability to work, satisfaction with the treatment, and complications.

For patients suffering from **facet joint syndrome due to osteoporosis**, no evidence was found and therefore no recommendation can be given.

New study results will potentially influence the effect estimate considerably. The re-evaluation is recommended in 2023.

10 References

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Appendix

Evidence tables of individual studies included for clinical effectiveness and safety

Table A-1: Cervical facet joints: Results from randomised controlled trials

Author, year	Haspeslagh, 2006 [46]	Stovner, 2004 [54]
Country	Netherlands	Norway
Sponsor	Not reported	Not reported
Study design	RCT	RCT
Number of pts	30 (15 vs. 15)	12 (6 vs. 6)
Intervention	Step_1: Percutaneous facet denervation of the facet joints C3-C6: RF-lesion of the medial ranches of the posterior primary rami; local anaesthetic solution (Lidocaine 2%), 60 sec lesion at 67°C; Step_2: If after 8 weeks the headache was not relieved sufficiently: Diagnostic cervical segmental nerve blocks at the levels that were most likely to conduct an excess of afferent stimuli were performed (at least 2); if there was an reduction of ≥ 50% of the VAS, an RF lesion adjacent to the relevant dorsal root ganglion (DRG) was performed Step_3: If no positive diagnostic block or after the RF lesion of the DRG and 8 weeks after Step_1 no sufficient headache relief: Transcutaneous Electrical Nerve Stimulation (TENS)	Cervical RF medial branch neurotomies performed on facet joints C2-C6: fluoroscopic control, after injection of local anaesthetic, 3-4 lesions at 85°C for 60 sec
Comparator	Step_1: Blocking the greater occipital nerve (GON): injection with local anaesthetics (Bupivacaine 0.5%) Step_2: If no sufficient headache relief after 8 weeks, repetition of treatment Step_3: If still no sufficient pain relief after 16 weeks: TENS	Sham procedure: Exactly same operation, except that after local anaesthesia, no lesions were given after positioning of the needles.
Inclusion criteria	Patients with cervicogenic headache according to the diagnostic criteria of Sjaastad: 20-65 years of age; chronic cervicogenic headache > 2 years; initial visual analogue scale (VAS) score of > 50 mm during a pain period; significant pain during at least two days per week	25-65 years of age, severe complaints lasting > 1 year inhibiting participation in work or social life, insufficient effect of appropriate prophylactic headache medication, cerebral CT or MRI and cervical MRI without significant pathology Striclty unilateral headache without side-shift At least 2 of the following: Reduced range of motion in the neck, precipitation of typical headache by palpation or pressure exerted against muscle insertions in the occiput or the neck, precipitation of typical headache by neck movements or positions, irradiation of pain to ipsilateral shoulder or arm

Author, year	Haspeslagh, 2006 [46]	Stovner, 2004 [54]
Exclusion criteria	Patients with previous surgical procedures of the cervical spine; coagualiton disturbances; patients who are pregnant; patients with multilevel severe degenerative changes at their cervical X-ray; diagnosed with post-whiplash syndrome	Cervical spinal stenosis or disc herniation, previous neck surgery, malignant disease, rheumatic or other disease necessitating intake of analgesics, other clinically significant disease, clinically significant concomitant headache disorder, ongoing or pending litigation for compensation after trauma
Mean age of patients, yrs, (SD)	47.5 (11.0) vs. 49.1 (12.8)	44.5 (34-52) vs. 52.5 (41-64) (median age and range)
Sex (% female)	11/15 (73%) v.s 11/15 (73%)	3/6 (50%) vs. 3/6 (50%)
Duration of pain, yrs	9.7 vs.6.6	5.0 (2-10) vs. 6.0 (2-50) (years from diagnosis to inclusion, median and range)
Follow-up (months)	12	24
Loss to follow-up, n (%)	4 (26.7%) vs. 5 (33.3%)	1 (16.7%) vs. 0 (0%)
Primary endpoint	Percentage of success at 8 weeks (time point 1)	Days with intense pain (defined as the number of days per 2 weeks with pain intensity 2 (moderate) or 3 (severe) which would reflect the number of days where headache interfered with the function of the patient; a meaningful clinical response was defined as a reduction of at least 30% of days with significant headache)
Outcomes		
Efficacy		
Pain intensity, mean (SD)	Percentage VAS improving[a] 8 weeks: 43.9 (22.0) vs. 42.4 (28.6); p=0.87 16 weeks: 45.4 (23.9) vs. 24.1 (50.1); p=0.17 6 months: 41.7 (28.5) vs. 28.0 (49.4); p=0.38 12 months: 44.4 (16.8) vs. 30.7 (49.9); p=0.34	Reduction of at least 30 days with intense headache between baseline and indicated time point (pain diary) 3 months: 4/6 (RF) vs. 2/6 (Sham) 12 months: 1/5 (RF) vs. 3/6 (Sham) 24 months: 1/5 (RF) vs. 3/5 (Sham)
Functional status	Not reported	Change from baseline (range) in % 3 months: Neck flexion/extension: 14 vs. 20 (p=0.9) Neck lateral flexion: 10 vs. 4 (p=0.6) Neck rotation: 0 vs. 4 (NA) Algometry: -24 vs. -19 (p=0.9) 12 months: Neck flexion/extension: 6 vs. 6 (NA) Neck lateral flexion: 6 vs. 5 (p=0.6) Neck rotation: 9 vs. -14 (p=0.3) Algometry: -88 vs. -42 (p=0.1) 24 months: Neck flexion/extension: 14 vs. 8 (p=0.7) Neck lateral flexion: -2 vs. 7 (p=0.6) Neck rotation: -8 vs.-6 (p=0.9) Algometry: 0 vs. -35 (p=0.5)

Author, year	Haspeslagh, 2006 [46]	Stovner, 2004 [54]
Global improvement	Global Perceived Effect (GPE) and/or successful VAS (mean VAS reduction of > 20 mm OR 2 points OR 50%): n with success (%) 8 weeks: 12 (80%) vs. 10 (66.7%); (not statistically significant) 16 weeks: 10 (66.7%) vs. 8 (53.3%); (not statistically significant) 12 months: 8 (53.3%) vs. 7 (46.7); (not statistically significant)	Improved to markedly improved Global Impression of Effect 3 months: 3/6 (RF) vs. 2/6 (Sham) 12 months: 2/5 (RF) vs. 0/6 (Sham) 24 months: 3/5 (RF) vs. 1/6 (Sham)
Health-related quality of life	Mean health scores (detailed results not available): No statistically significant difference between the mean health scores of both groups at different moments	Not reported
Ability to work	Not reported	Not reported
Success of the treatment	Global Perceived Effect (GPE) and/or successful VAS (mean VAS reduction of > 20 mm OR 2 points OR 50%): n with success (%) 8 weeks: 12 (80%) vs. 10 (66.7%); (not statistically significant) 16 weeks: 10 (66.7%) vs. 8 (53.3%); (not statistically significant) 12 months: 8 (53.3%) vs. 7 (46.7); (not statistically significant)	Meaningful clinical response (reduction of at least 30% of days with significant headache) 3 months: 4/6 (RF) vs. 1/6 (Sham) 12 months: 1/5 (RF) vs. 3/6 (Sham) 24 months: 1/5 (RF) vs. 3/5 (Sham)
Satisfaction with treatment	Not reported	Not reported
Safety		
Complications, n (%)	Not reported	At discharge from the hospital (1-2 days after the procedure): Increased neck pain (4/6 RF group vs. 1/6 Sham group) Slightly increased neck pain (1/6 RF vs. 1/6 Sham) Headache & nausea (1/6 RF vs. 0/6 Sham) Dizziness (0/6 RF vs. 1/6 Sham) 3 months: Worsening of the neck pain (1/6 RF vs. 0/6 Sham) Neck tenderness (1/6 RF vs. 0/6 Sham) Sensory loss in small neck area (1/6 RF vs. 0/6 Sham) Fasciculations in right cheek (0/6 RF vs. 1/6 Sham) Acute form of rheumatoid arthritis (0/6 RF vs. 1/6 Sham)

Abbreviations: *VAS (Visual Analogue Scale) ranging from 0 to 100; ODI (Oswestry Disability Index) ranging from 0 indicating no restrictions in daily activities to 100 indicating most restrictions in daily activities; GPE (Global Perceived Effect) ranging from -3 indicating much worse to +3 indicating no complaints anymore; HRQoL (Health-related Quality of Life*

Comments:

[a] *Sufficient relief of pain was indicated by a mean VAS reduction of more than 20%.*

Table A-2: Lumbar facet joints: Radiofrequency denervation vs. other methods: Results from randomised controlled trials

Author, year	Juch, 2017 [52] (Footnote: 3 RCTS)	Moussa, 2016 [47]	Van Tilburg, 2016 [53]	Zhou, 2016 [48]
Country	Netherlands	Egypt	Netherlands	China
Sponsor	Funded by grants from the Netherlands Organisation for Health Research and Development, the Dutch Society for Anesthesiology and the Dutch health insurance companies	No funding was received.	No benefits in any form have been received from a commercial party related directly or indirectly to the subject of this article.	Not reported
Study design	RCT	RCT	RCT	RCT
Number of pts	251 (facet joint trial [1 RCT] of in total 681 patients in 3 RCTs): 125 vs. 126[b]	120 (3 groups à 40 patients)	60 (30 vs. 30)	80 (40 vs. 40)
Intervention	Standardised exercise programme (8-12 hours) over a 3-month period; within 1 week after first exercise: radiofrequency denervation after injection of 2% lidocaine, RFD lesion was made at 90°C for 90 sec; co-interventions or recurring RFD allowed after 3-month period; over-the-counter medication was allowed; psychological care was provided when needed	Percutaneous RF denervation of the medial dorsal branch; lesion created at 85°C for 90 sec.; lesions were performed at L3-4, L4-5 and L5-S1 bilaterally[d]	Percutaneous radiofrequency heat lesion at 80°C at 60 sec. (total of three steps) into the medial branches of the primary dorsal ramus after introduction of 2% lidocaine; additionally, patients were treated with graded activity physiotherapy	Percutaneaous radiofrquency thermocoagulation denervation on the lumbar facet joint (at 80°C for 90 sec. after injection of 2% lidocaine)
Comparator	A 8- to 12-hour standardised exercise programme during a 3-month intervention period	Percutaneous radiofrequency coagulation of the facet joint capsule (each capsule received two lesions) Sham control group (did not receive radiofrequency lesioning)	Sham procedure: Same procedure as interventions group except without the radiofrequency heat lesion; a crossover of the sham group was provided after > 3 months, if no significant pain relief (decrease of NRS ≥ 2) was obtained; additionally, patients were treated with graded activity physiotherapy	Injection of betamethasone and 2% lidocaine into the lumbar facet joint
Inclusion criteria	Pain considered to be related to facet joint, 18-70 years of age, no improvement in symptoms after conservative treatment, 1 positive diagnostic anesthetic block (2% lidocaine) prior to randomisation (positive, if the participant reported ≥ 50% pain reduction within 30-90 minutes after the block)	Patients complaining of continuous CLBP with or without radiating into the upper leg lasting for ≥ 1 year without improvement after 3 months of conservative treatment (analgesics and physiotherapy); clinical manifestations suggesting a facet origin of pain; initial VAS score of ≥ 7;	Patients with a history of LBP > 3 months; failure of conservative care (rest, analgesics and physiotherapy); decrease in the Numerical Rating Scale for pain of ≥ 2 on a 0 to 10 point scale after a test injection at the medial branch of the primary dorsal ramus with local anaesthesia Inclusion criteria based on the New Zealand LBP Guide	Patients with a history of lumbar facet joint-related low back pain ≥ 6 months Symptoms: Pain of the lower waist, hips and buttocks, spastic pain of the lower limbs, stiffness of the waist, no paresthesia Signs: Stiffness of adjacent lumbar muscles, pain aggravated by extension, no signs of nerve damage or nerve root traction Diagnostic block: Positive findings after test injection with 2% lidocaine, pain allevation by 80%

Author, year	Juch, 2017 [52] (Footnote: 3 RCTS)	Moussa, 2016 [47]	Van Tilburg, 2016 [53]	Zhou, 2016 [48]
Inclusion criteria *(continuation)*		positive diagnostic test blockade: achieving complete or near complete reduction of pain on the VAS 30 min after injection of local anesthetic (on two different occations); ≥ 18 years		Radiographic findings: Deviation of the spinous processes from the midline, asymmetrical bilateral facet joints or lateral bending and asymmetrical shadows of psoas major, CT- or MRI-proven lumbar facet joint osteoarthritis, narrowing of facet joint, sclerosis or hypertrophy, loss of articular cartilage or periarticular hyperostosis
Exclusion criteria	Pregnancy, severe psychological problems, involvement in work-related conflicts or claims, BMI > 35, anticoagulant drug therapy or coagulopathy	Surgical causes of LBP; patients who did not experience complete or near complete reduction of LBP after the test block; prior lumbar surgery; associated major comorbidities; prior RF treatment for LBP; presence of radicular syndromes; infection at the injection site; pregnancy; allergic reaction to the local anesthetic; patients with possible work compensation litigations; mental handicap or psychiatric condition precluding adequate communication; scoring ≥ 50 in the Zung Self-Rating Depression Scale.	Exclusion criteria based on the New Zealand LBP Guide	Lumbar disc herniation, lumbar spinal stenosis, spondylolisthesis, specific and unspecific inflammations and tumors, allergies to local anesthetics, pregnancy or lactating, symptomatic radiculopathies, uncontrolled medical illnesses and any conditions that could interfere with the interpretation of the outcome assessments
Mean age of patients, yrs, (SD)	52.98 (11.48) vs. 52.60 (10.79)	56.5 (NA) vs. 58.1 (NA) vs. 55.9 (NA)	65 vs. 58 (median age)	56.5 (8.7) vs. 54.6 (7.5)
Number of females (%)	65 (55.6%) vs. 60 (51.7%)	31 (77.5%) vs. 29 (72.5%) vs. 27 (67.5%)	16 (3.3%) vs. 18 (60.0%)	17 (42.4%) vs. 19 (47.5%)
Duration of symptoms, months (SD)	Time since first experience with low back pain: Median (range) 146 (49.8-267.7) vs. 100.3 (36.5-186.3)	Not reported	Duration of low back pain: n (%) <6 months: 4 (13.3%) vs. 5 (16.7%) 6-12 months: 2 (6.7%) vs. 6 (20%) 12-60 months: 10 (33.3%) vs. 10 (33.3%) >60 months: 13 (43.3%) vs. 6 (20%) Unknown: 1 (3.3%) vs. 3 (10%)	24.5 (9.7) vs. 26.4 (10.2)
Follow-up (months)	12	36	12	6
Loss to follow-up, n (%)	72 (29%)	No dropouts till the evaluation at 6 months post-procedure; 8%, 13% and 20% of patients were lost to follow-up at 1, 2 and 3 years follow-up, respectively, without comparatively significant differences between groups (p=0.492)	0 (0%)	0 (0%)

Author, year	Juch, 2017 [52] (Footnote: 3 RCTS)	Moussa, 2016 [47]	Van Tilburg, 2016 [53]	Zhou, 2016 [48]
Primary outcome	Pain intensity: Measured on an 11-point numerical rating scale (NRS; a score of 0 indicates no pain; 10 indicates worst pain imaginable) 3 months after the intervention	A predefined mulitdimensional combined outcome measure (COM) at 1-year follow-up comprising a balance between changes in VAS, changes in daily physical activities (using the Oswestry disability index, version 1.0) and analgesics consumption	Decrease in pain using the NRS-11	Half-year efficacy after the treatment based on the Surgical Efficacy Criteria (1994) of the Spine Surgery Group Orthopedic Branch of Chinese Medical Association (graded as Excellent, Good, Eligible, Poor)
Outcomes				
Efficacy				
Pain intensity	11-point numeric rating scale (NRS): Mean pain intensity score (95% CI)[c] 3 weeks: 5.17 (4.73-5.61) vs. 5.92 (5.58-6.26); p=0.18 6 weeks: 5.19 (4.76-5.61) vs. 5.90 (5.53-6.26); p=0.20 3 months: 5.01 (4.59-5.43) vs. 5.44 (5.03-5.85); p=0.55 6 months: 4.61 (4.18-5.04) vs. 4.84 (4.38-5.30); p=0.91[a] 9 months: 4.66 (4.20-5.00) vs. 4.73 (4.24-5-22); p=0.53[a] 12 months: 4.49 (4.00-4.97) vs. 4.44 (3.94-4.94); p=0.13[a]	Mean change in VAS of the back: 3 months: 6.0 vs. 6.3 vs. 5.4; p=0.481 6 months: 6.0 vs. 6.1 vs. 2.1; p=0.061 12 months: 5.8 vs. 6.0 vs. 0.7; p=0.036 24 months: 2.3 vs. 5.9 vs. 0.5; p=0.026 36 months: 2.2 vs. 5.9 vs. 0.4; p=0.011 VAS reduction in the back > 50% n (%): 3 months: 30 (75) vs. 28 (70) vs. 23 (57.5); p=0.884 6 months: 24 (60) v.s 26 (65) vs. 8 (20); p=0.037 12 months: 18 (45) vs. 23 (57.5) vs. 3 (7.5); p=0.026 24 months: 7 (17.5) vs. 20 (50) vs. 1 (2.5); p=0.017 36 months: 5 (12.5) vs. 19 (47.5) vs. 1 (2.5); p=0.012	Numercal rating scale (0 to 10): NRS (SD) 1 month: 5.3 (1.8) vs. 5.5 (1.9); p=0.66 (No detailed results for other time points available. However, the authors stated that no statistically significant differences between the groups occured with the passage of time.)	VAS scores: 1 week: 1.4 vs. 1.9 1 month: 1.4 vs. 3.6 6 months: 1.7 vs. 5.8 The VAS scores of the patients in the denervation group at each time point was signifcantly lower than the control (p<0.01).
Functional status	Measured by Oswestry Disability Index (ODI): Mean Functioning Score (95% CI)[c] 3 months: 26.03 (23.01-29.06) vs. 28.67 (26.06-31.84); p=0.17 6 months: 25.38 (22.45-28.30) vs. 27.15 (24.07-30.23); p=0.74[a] 9 months: 25.74 (22.74-28.73) vs. 24.52 (21.49-27.54); p=0.21[a] 12 months: 24.59 (21.39-27.79) vs. 25.04 (21.77-28.31); p=0.42[a]	Measured by Oswestry Disability Index (ODI): Mean Change 3 months: 44.3 vs. 40.6 vs. 39.8; p=0.994 6 months: 40.3 vs. 38.1 vs. 10.3; p=0.042 12 months: 31.6 vs. 33.9 vs. 5.9; p=0.037 24 months: 12.3 vs. 29.5 vs. 3.2; p=0.018 36 months: 8.2 vs. 29.2 vs. 2.9; p=0.007	Not reported	Schober index assessment: 1 week: 9.0 vs. 8.9; p>0.05 1 month: 8.6 vs. 7.3; p<0.05 6 months: 8.8 vs. 6.2; p<0.01
Global improvement	Global Perceived Recovery using GPE scale (a score of 1-2 indicates success)[c]: 3 weeks: 32/108 vs. 5/101; RR: 5.41 (2.29-10.34); p<0.001) 6 weeks: 35/119 vs. 11/118; RR: 2.71 (1.37-4.68); p=0.005	More than 50% improvement in LBP on GPE (n,%): 3 months: 26 (65) vs. 25 (62.5) vs. 20 (50); p=0.892 6 months: 21 (52.5) vs. 23 (57.5) vs. 6 (15); p=0.048	Global Perceived Effect scale GPE Recovery (SD) 1 month: 3.3 (1.0) vs. 3.4 (1.2) 2 months: 3.4 (1.0) vs. 3.6 (1.1) (No statistically significant difference was found.)	Surgical Efficacy Criteria of the Spine Surgery Group, Orthopedic Branch of Chinese Medical Association:

Author, year	Juch, 2017 [52] (Footnote: 3 RCTS)	Moussa, 2016 [47]	Van Tilburg, 2016 [53]	Zhou, 2016 [48]
Global improvement *(continuation)*	3 months: 43/119 vs. 27/114; RR=1.35 (0.81-2.05); p=0.24 6 months: 46/113 vs. 39/108; RR=1. 04 (0.64-1.12); p=0.85[a] 9 months: 41/106 vs. 42/105; RR=0.81 (0.48-0.57); p=0.35[a] 12 months: 44/103 vs. 40/102; RR=0.90 (0.55-1.33); p=0.65[a]	12 months: 15 (37.5) vs. 20 (50) vs. 1 (2.5); p=0.027 24 months: 4 (10) vs. 18 (45) vs. 1 (2.5); p=0.015 36 months: 3 (7.5) vs. 17 (42.5) vs. 0 (0); p=0.009		6 months: n(%) Excellent: 25 (62.5%) vs. 5 (12.5%) Good: 11 (27.5%) vs. 12 (30%) Eligible: 3 (7.5%) vs. 2 (5.0%) Poor: 1 (2.5%) vs. 21 (52.5%)
Health-related quality of life	Measured by EQ-5D-3L Questionnaire: Mean Utility Score[c] 3 weeks: 0.69 vs. 0.64 (p=0.08) 6 weeks: 0.69 vs. 0.67 (p=0.32) 3 months: 0.68 vs. 0.69 (p=0.85) 6 months: 0.73 vs. 0.71 (p=0.42)[a] 9 months: 0.72 vs. 0.75 (p=0.11)[a] 12 months: 0.73 vs. 0.73 (p=0.37)[a]	Not reported	Not reported	Not reported
Ability to work	Not reported	Not reported	Not reported	Included in the Surgical Efficacy Criteria of the Spine Surgery Group, Orthopedic Branch of Chinese Medical Association: 6 months: n(%) Excellent: 25 (62.5%) vs. 5 (12.5%) Good: 11 (27.5%) vs. 12 (30%) Eligible: 3 (7.5%) vs. 2 (5.0%) Poor: 1 (2.5%) vs. 21 (52.5%)
Satisfaction with treatment	Assessed with Global Perceived Effect scale (GPE): Mean patient satisfaction (95% CI)[c] 3 months: 2.95 (2.70-3.20) vs. 3.26 (3.00-3.52); p=0.34 6 months: 2.96 (2.74-3.17) vs. 3.06 (2.81-3.31); p=0.94[a] 9 months: 2.88 (2.63-3.12) vs. 3.13 (2.83-3.42); p=0.91[a] 12 months: 2.88 (2.60-3.16) vs. 3.01 (2.73-3.29); p=0.32[a]	Not reported	Global Perceived Effect scale: GPE Satisfaction (SD) 1 month: 3.4 (1.0) vs. 3.5 (1.2) 2 months: 3.4 (1.0) vs. 3.7 (1.3) (no statistically significant difference with the passage of time in satisfaction between the groups)	Not reported
Safety				
Complications, n (%)	No treatment-related adverse events were reported during the 1-year follow-up.	Not reported	No serious adverse events were encountered.	Patients in both groups did not develop complications such as nerve root injury or back skin anesthesia during and after treatment

Abbreviations: *NRS (Numeric Rating Scale) ranging from 0 indicating no pain to 10 indicating worst pain imaginable; VAS (Visual Analogue Scale) ranging from 0 to 100; ODI (Oswestry Disability Index) ranging from 0 indicating no restrictions in daily activities to 100 indicating most restrictions in daily activities; GPE (Global Perceived Effect) ranging from 1 indicating fully recovered to 7 indicating worse than ever; HRQoL (Health-related Quality of Life; EQ-5D-L (3-level EuroQoL 5D Health Questionnaire ranging from 0 indicating worst imaginable health state to 1 indicating best imaginable health state*

Comments:

[a] *Additional treatments/co-interventions possible*

[b] *Twelve patients in control group received RFD within first 3 months*

[c] *Intention-to-treat analysis*

[d] *Intervention of interest was RFD of the facet joint capsule.*

Table A-3: Lumbar facet joints: Radiofrequency denervation vs. other RFD method: Results from randomised controlled trials

Author, year	Arsanious, 2016 [63]
Country	United States
Sponsor	No compensation from any companies associated with the procedures or study
Study design	RCT
Number of pts	55 (26 vs. 29)
Intervention	Thermal radiofrequency ablation (RFA): Local anaesthetic with 1% lidocaine, a 21 G 100 mm needle with 5 mm active tip, if optimally positioned, 0.25% bupivacaine was infiltrated, 120 sec. pause, followed by RFA at 80°C for 90 sec
Comparator	Pulsed dose radiofrequency (PDRF): Local anaesthetic with 1% lidocaine, a 21 G 100 mm needle with 5 mmactive tip, if optimally positioned, 0.25% bupivacaine was infiltrated, PDRF at 42°C/2 Hz/240 pulses, followed by thermal RFA at 80°C for 90 sec.
Inclusion criteria	Patients with diagnosed back pain from facet joint disease, pain for ≥ 6 months, average pain level of ≥ 4 on a numerical pain scale (NPS)#, pain not alleviated with conservative therapy; positive response to 2 diagnostic medial branch blocks (> 80% pain relief for at least 2 hours with lidocaine and > 4 hours with bupivacaine)
Exclusion criteria	Participation in other trials; patients with poorly controlled systematic diseases including cardiovascular, hepatic, renal, hematologic, and/or neurologic conditions, severe depression, coagulopathies, and/or were on anticoagulants; or who had other significant sources of chronic pain, complex regional pain syndrome, fibromyalgia, rheumatoid arthritis or chronic fatigue syndrome; patients consuming > 2 alcoholic drinks and patients with recreational drug use;
Mean age of patients, yrs, (SD)	52.4 (8.5) vs. 50.1 (12.1)
Female (%)	77% vs. 75%
Mean duration of symptoms, months (SD)	Not reported
Follow-up (months)	2 days (first 48 hours following the procedure)
Loss to follow-up, n (%)	5 (19.2%) vs. 3 (10.3%)
Primary outcome	Effects on postprocedural pain and the requirement of oral analgesic medication usage in the first 48 hours following the procedure

Author, year	Arsanious, 2016 [63]
Outcomes	
Efficacy	
Pain intensity	Pain levels: Numeric pain scale: NPS (SD) Day 1 (morning): 4.43 (2.9) vs. 2.38 (2.4); p=0.01 Day1 (afternoon): 4.80 (3.2) vs. 3.08 (2.8); p=0.06 Day 2 (morning): 3.86 (2.8) vs. 2.31 (2.7); p=0.06 Day 2 (afternoon): 3.90 (2.7) vs. 2.60 (2.4); p=0.09
Functional status	Not reported
Global improvement	Not reported
Health-related quality of life	Not reported
Ability to work	Not reported
Satisfaction with treatment	Not reported
Safety	
Complications, n (%)	Post-procedural pain (patients using pain medication): 38% vs. 15%; p=0.1

Abbreviations: *NRS (Numeric Rating Scale) ranging from 0 indicating no pain to 10 indicating severe unbearable pain*

Table A-4: Lumbar facet joints: Radiofrequency denervation vs. other treatment: Results from non-randomised controlled trials

Author, year	Yasar, 2018 [49]
Country	Turkey
Sponsor	None
Study design	Non-randomised controlled trial
Number of pts	100 (50 vs. 50)
Intervention	Pulsed radiofrequency denervation at 42°C for 120 sec.
Comparator	Injection of 0.25% bupicacaine + 40 mg methylprednisolone acetate (steroid) into each level
Inclusion criteria	Lower back pain and sciatalgia with normal neurological examination; bilateral pain on facet articulations, in addition to lower back pain and sciatalgia, no gain from usual treatment methods, ≥ 3 months of duration for lower back pain and sciatalgia; normal radiological findings, except stonisis of the joint space and degeneration of the joint; benefited from diagnostic block with local anesthetic agent infiltration to the facets
Exclusion criteria	Not reported
Mean age of patients, yrs, (SD)	47.4 (11.1) vs. 43.1 (8.35)

Author, year	Yasar, 2018 [49]
Female (%)	10 (20%) vs. 16 (32%)
Mean duration of symptoms, months (SD)	Not reported
Follow-up (months)	12
Loss to follow-up, n (%)	Not reported
Primary outcome	Pain intensitiy measured with the Visual Analogue Scale (VAS) and functional disability measured with the Oswestry Disability Index (ODI)
Outcomes	
Efficacy	
Pain intensity	VAS Score: mean (SD) 3 months: 2.5 (1) vs. 3.3 (1) 6 months: 2.3 (1.4) vs. 3.3 (0.9) 9 months: 2.7 (0.9) vs. 2.5 (1) 12 months: 3.0 (1.1) vs. 3.0 (1.5)
Functional status	Oswestry Disability Index (ODI): Mean (SD) 3 months: 18.9 (5.7) vs. 24.1 (8.7) 6 months: 14.9 (7) vs. 24.8 (9.5) 9 months: 10.4 (2.8) vs. 12.2 (3.8) 12 months: 17.2 (6.4) vs. 12.1 (4.4)
Global improvement	Not reported
Health-related quality of life	Not reported
Ability to work	Not reported
Satisfaction with treatment	Not reported
Safety	
Complications, n (%)	No complications were reported; pain after injection occurred in 4 patients.

Abbreviations: *VAS (Visual Analogue Scale) ranging from 0 to 100; ODI (Oswestry Disability Index) ranging from 0 to 100*

Risk of bias tables and GRADE evidence profile

Internal validity of the included studies was judged by two independent researchers. In case of disagreement a third researcher was involved to solve the differences. A more detailed description of the criteria used to assess the internal validity of the individual study designs can be found in the Internal Manual of the LBI-HTA [53] and in the Guidelines of EUnetHTA [53].

Table A-5: Risk of bias – Cervical facet joints (randomised studies), RoB 2.0 see [53]

Trial	Bias arising from the randomisation process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of the oucome	Bias in selection of the reported result	Risk of bias – study level
Haspeslagh, 2006 [46]	Some concerns[1]	High[2]	High[3]	Low	Low	High
Stovner, 2004 [54]	Low	Low	Low	Low	Low	Low

[1] *No information available*
[2] *Patients aware of their respective treatment*
[3] *Loss to follow-up (26.7% vs. 33.3%)*

Table A-6: Risk of bias – Lumbar facet joints (randomised studies), RoB 2.0 see [53]

Trial	Bias arising from the randomisation process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of the oucome	Bias in selection of the reported result	Risk of bias – study level
Juch, 2017 [52][1]	Low	High[2]	High[3]	High[4]	Low	High
Moussa, 2016 [47]	Low	Low	Low	Low	Low	Low
Van Tilburg, 2016 [53]	Some concerns[5]	High[6]	Low	Low	Some concerns[7]	High
Zhou, 2016 [48]	Low	High[8]	Low	High[9]	Low	HIgh
RF vs. other method of RF (for safety only)						
Arsanious, 2016 [63]	Low	Low	High[10]	Low	Low	High

Comments:

[1] *Evaluation of facet joint study only*
[2] *Non-blinding of patients and caregivers*
[3] *29% lost to follow-up*
[4] *Participants and caregivers were not blinded.*
[5] *No random sequence generated*
[6] *A crossover for the sham group was provided after a minimum period of 3 months if no significant pain relief was obtained.*
[7] *Multiple analyses of the data*
[8] *Patients and caregivers not blinded*
[9] *Non-blinded outcome assessors were aware of the intervention.*
[10] *8 patients were lost to FU: IG: 5 (19.2%) vs. CG: 3 (10.3%)*

Table A-7: Risk of bias of non – randomised studies comparing RF denervation versus steroid injection, ROBINS-I see [3]

Study reference/ID	Bias due to confounding	Bias selection of participants into the study	Bias in classification of interventione	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported results	Overall bias	Comments
Yasar, 2018 [49]	Serious[1]	Low	Low	Low	Low	Moderate[2]	Low	Serious	…

[1] *The only demographic characteristics of the patient population described and compared between the two study groups were age, gender, length and weight.*

[2] *Outcome was influenced by knowledge of intervention and outcome assessors were aware of intervention.*

Table A-8: Evidence profile: efficacy and safety of Radiofrequency denervation for patients with chronic neck pain

Quality assessment							Number of patients		Absolute effect (SD)	Certainty	Importance
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Impression	Other considerations	RFD	Alternative treatments			
Efficacy											
Pain intensity (VAS) at 2 months follow-up											
1	RCT [46]	Serious [a]	Not s erious	Not serious	Serious [b]	None	15	15	IG: 43.9 (22.0) vs. CG: 42.4 (28.6)	⊕⊕◯◯ LOW	CRITICAL
Pain intensity (Reduction of at least 30 days with intense headache) at 24 months follow-up											
1	RCT [54]	Not serious	Not serious	Not serious	Serious [b]	None	5	5	IG: 1 (20%) vs. CG: 3 (60%)	⊕⊕⊕◯ MODERATE	CRITICAL
Functional status at 24 months of follow-up											
1	RCT [54]	Not serious	Not serious	Not serious	Serious [b]	None	5	5	No significant differences between IG and CG.	⊕⊕⊕◯ MODERATE	CRITICAL
Global improvement (GPE) at 12 months follow-up											
2	RCTs [46, 54]	Serious [a]	Serious [c]	Not serious	Serious [b]	None	20	21	IG: 40%-53.3% vs. CG: 0%-46.7%	⊕◯◯◯ VERY LOW	CRITICAL
Global improvement (GPE) at 24 months follow-up											
1	RCT [54]	Not serious	Not serious	Not serious	Serious [b]	None	5	6	IG: 3 (60%) vs. CG: 1 (16.7%)	⊕⊕⊕◯ MODERATE	CRITICAL
HRQoL 2-12 months of follow-up											
1	RCT [46]	Serious [a]	Not serious	Not serious	Serious [b]	None	15	15	No significant differences between the IG and CG.	⊕⊕◯◯ LOW	CRITICAL

Quality assessment							Number of patients		Absolute effect (SD)	Certainty	Importance
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Impression	Other considerations	RFD	Alternative treatments			
Ability to work – not reported											
-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Satisfaction with the treatment – not reported											
-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Safety											
Complications 2 days to 3 months follow-up											
1	RCT [54]	Not serious	Not serious	Not serious	Serious [b]	None	6	6	IG: 9 (150%) vs. DG: 5 (83.3%)	⊕⊕⊕◯ MODERATE	CRITICAL

Abbreviations: *VAS (Visual Analogue Scale) ranging from 0 to 100; GPE (Global Perceived Effect) ranging from 1 to 7; HRQoL (Health-related Quality of Life)*

Comments:

a High RoB

b Imprecision due to small sample size

c Inconsistency (comparator either sham procedure or steroid injections/TENS)

Table A-9: Evidence profile: efficacy and safety of Radiofrequency denervation for patients with chronic back pain

Quality assessment							Number of patients		Absolute effect	Certainty	Importance
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Impression	Other considerations	RFD	Alternative treatments			
Efficacy											
Pain intensity (NRS) at 12 months follow-up											
2 [52, 53]	RCTs	Serious [a]	Not serious	Not serious	Not serious	None	155	156	No significant differences between IG and CG.	⊕⊕⊕◯ Moderate	CRITICAL
Pain intensity (VAS) at 6 months follow-up											
2 [47, 48]	RCTs	Serious [b]	Serious [c]	Not serious	Not serious	None	80	80	IG: 1.7-6.0 vs. CG: 2.1-5.8	⊕⊕◯◯ Low	CRITICAL
Pain intensity (VAS) at 36 months follow-up											
1 [47]	RCT	Not serious	Not serious	Not serious	Not serious	None	40	40	IG: 2.2 vs. CG: 0.4	⊕⊕⊕⊕ High	CRITICAL
Functional status (ODI) at 12 months follow-up											
2 [47, 52]	RCTs	Serious [b]	Serious [c]	Not serious	Not serious	None	165	166	IG: 24.59-31.6 vs. CG: 5.9-25.04	⊕⊕◯◯ LOW	CRITICAL
Functional status (ODI) at 36 months follow-up											
1 [47]	RCT	Not serious	Not serious	Not serious	Not serious	None	40	40	IG: 8.2 vs. CG: 2.9	⊕⊕⊕⊕ HIGH	CRITICAL
Functional status (Schober Index) at 6 months follow-up											
1 [48]	RCT	Serious [d]	Not serious	Not serious	Not serious	None	40	40	IG: 8.8 vs. CG: 6.2 (p<0.01)	⊕⊕⊕◯ MODERATE	CRITICAL
Global improvement (GPE) at 2 months follow-up											
1 [53]	RCT	Serious [d]	Not serious	Not serious	Not serious	None	30	30	IG: 3.4 vs. CG: 3.6 (p>0.05)	⊕⊕⊕◯ MODERATE	CRITICAL
Global improvement (success* in GPE) at 12 months follow-up											
2 [47, 52]	RCTs	Serious [b]	Serious [c]	Not serious	Not serious	None	165	166	IG: 37.5%-42.7% vs. CG: 2.5%-29.3%	⊕⊕◯◯ LOW	CRITICAL
Global improvement (success* in GPE) at 36 months follow-up											
1 [47]	RCT	Not serious	Not serious	Not serious	Not serious	None	40	40	IG: 7.5% vs. CG: 0%	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							Number of patients		Absolute effect	Certainty	Importance
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Impression	Other considerations	RFD	Alternative treatments			
Global improvement (Surgical Efficacy Criteria) at 6 months follow-up											
1 [48]	RCTs	Serious [d]	Not serious	Not serious	Not serious	None	40	40	Statistically significant differences between IG and CG.	⊕⊕⊕◯ MODERATE	CRITICAL
HRQoL (EQ5D-3L) 3 weeks-12 months follow-up											
1 [52]	RCT	Serious [d]	Not serious	Not serious	Not serious	None	125	126	No significant differences between the mean health scores of IG and CG at different time points.	⊕⊕⊕◯ MODERATE	CRITICAL
Ability to work (Surgical Efficacy Criteria) at 6 months follow-up											
1 [48]	RCT	Serious [d]	Not serious	Not serious	Not serious	None	40	40	Excellent: IG: 62.5% vs. CG: 2.5% Good: IG: 27.5% vs. CG: 30% Eligible: IG: 7.5% vs. C: 5.0% Poor: 2.5% vs. CG: 52.5%	⊕⊕⊕◯ MODERATE	IMPORTANT
Satisfaction with the treatment (GPE) at 2 months follow-up											
1 [53]	RCT	Serious [d]	Not serious	Not serious	Not serious	None	30	30	IG: 3.4 (1.0) vs. CG: 3.7 (1.3)	⊕⊕⊕◯ MODERATE	IMPORTANT
Satisfaction with the treatment (GPE) at 12 months follow-up											
1 [52]	RCT	Serious [d]	Not serious	Not serious	Not serious	None	125	126	IG: 2.88 (2.60-3.16) vs. CG: 3.01 (2.73-3.29); p=0.32	⊕⊕⊕◯ MODERATE	IMPORTANT
Complications 6-36 months follow-up											
5 [48, 49, 52, 53, 63]	RCTs(4) + observational trials (1)	Serious [e]	Serious [i]	Not s erious	Not serious	None	311	275	IG: 10 vs. CG: 8	⊕⊕◯◯ LOW	CRITICAL

Abbreviations: *NRS (Numeric Rating Scale) ranging from 0 to 10; VAS (Visual Analogue Scale) ranging from 0 to 100; ODI (Oswestry Disability Index) ranging from 0 to 100; GPE (Global Perceived Effect) ranging from 1 to 7; HRQoL (Health-related Quality of Life)*

Comments:

[a] *High RoB in 2 of 2 studies*

[b] *High RoB in 1 of 2 studies*

[c] *Inconsistency (comparator either sham procedure or steroid injections/TENS)*

[d] *High RoB*

[e] *High RoB in 5 of 5 studies*

[f] *Inconclusive results*

Applicability table

Table A-10: Summary table characterising the applicability of a body of studies (RFD for cervical facet joint pain)

Domain	Description of applicability of evidence
Population	The total number of patients was 42. The participants had to experiencing cervicogenic headache for at least 1 or 2 years. The mean age of the patients ranged from 44.5 to 52.5 years. The percentages of female participants were 50% and 73%, respectively.
Intervention	Both RCTs applied a percutaneous RF denervation of the facet joints C2/C3-C6 (67°C-85°C for 60 sec).
Comparators	One RCT compared RFD with an injection of local anaesthetics, the other with a placebo/sham treatment.
Outcomes	All outcomes defined as crucial were reported by at least one study (functional status, health-related quality of life and complications). Both studies reported on the outcomes of pain intensity (percentage VAS improving and reduction of at least 30 days with intense headache between baseline and indicated time point), global improvement, and success of the treatment (Global Perceived Effect and/or successful VAS and meaningful clinical response of a reduction of at least 30% of days with significant headache). Neither of the two studies reported data on the important outcome ability to work.
Setting	The trials were conducted in the Netherlands and in Norway, and published in 2004 and 2006, respectively.

Table A-11: Summary table characterising the applicability of a body of studies (RFD for lumbar facet joint pain)

Domain	Description of applicability of evidence
Population	The patient population (n=666) varied considerably between the studies. The participants had to suffer from chronic low back pain from at least 3 months to 12 months. The mean age ranged from 43-65 years. 20% to 77.5% of the particpants were female.
Intervention	All studies applied percutaneous RF denervation of the facet joints at 80°C-90°C for 60-90 sec., except for one study, which performed the intervention at 42°C for 120 sec. One study investigated RFD in conjunction with a 3-month exercise programme.
Comparators	In 4 studies, RFD was either compared to placebo/sham treatment or to steroid injections. One study used a 3-month exercise programme as a comparator. In 2 studies, conventional RFD was compared with either percutaneous RF coagulation of the facet joint capsule or pulsed dose radiofrequency (PDRF).
Outcomes	All outcomes defined as crucial for a decision were reported in the included trials. All trials reported on the pain intensity (generally measured by VAS or NRS); 4 studies documented the functional status and the global improvement of the participant. A single study examined the health-related quality of life of the patient. 5 studies reported on complications. The important outcome of ability to work was documented by 1 study within a composite measure. 2 studies provided data regarding the satisfaction with treatment.
Setting	The trials were conducted in the Netherlands, Turkey, Egypt, China and the United States, and published between 2016 and 2018.

List of ongoing randomised controlled trials

Table A-12: List of ongoing randomised controlled trials of RFD for cervical facet joint pain

Identifier/ Trial name	Patient population	Intervention	Comparison	Primary Outcome	Primary completion date	Sponsor
NCT03066960 Radiofrequency Neurotomy for Chronic Facet Joint-Related Neck Pain	18-80 years, stable neck pain > 12 months, with or without unilateral headache	RF neurotomy	Sham treatment	Change in neck function; change in pain intensity after 6 months	December 2022	Oslo University Hospital, St. Olavs Hospital

Table A-13: List of ongoing randomised controlled trials of RFD for lumbar facet joint pain

Identifier/ Trial name	Patient population	Intervention	Comparison	Primary Outcome	Primary completion date	Sponsor
NCT03614793 A Prospective Trial of Cooled Radiofrequency Ablation of Medial Branch Nerves vs. Facet Joint Injection of Corticosteroid for the Treatment of Lumbar Facet Syndrome	>40 years of age, axial back pain for at least 3 months, no response to conventional treatment MRfFUS ablation	Cooled RF ablation of medial branch nerves	Facet joint injection of corticosteroids	Proportion of patients with a successful response	August 2023	University of Utah
NCT03168802 MRgFUS and RFA for Treatment of Facet-joint Osteoarthritis Low Back Pain	20-79 years of age, suffering from lumbar vertebral facet joint syndrome	MRgFUS ablation	RF ablation	Pain score change	March 2019	Taipei Medical University Hospital
NCT02478437 A Trial of Cooled RFA of Medial Branch Nerves for the Treatment of Lumbar Facet Syndrome	18-79 years, patients with lumbar facet syndrome pain for at least 6 months	Conventional RFA	Cooled RFA	Percent of participants who reported ≥50% improvement of pain	August 2018	Northwestern University, American Pain Society
NCT02942147 Conventional Radiofrequency, Pulse Radiofrequency, and TENS for Lumbar Facet Joint Pain	18 years or older, chronic low back pain for at least 3 months	TENS	Conventional or Pulse Radiofrequency	Change in Visual Analogue Scale	September 2015	Ege University (Turkey)
NCT03651804 Radiofrequency Ablation: Treatment for Posterior Element Pain from Vertebral Compression Fractures	18-90 years, single level vertebral compression fracture, osteo-porotic vertebral compression fracture, cancer-related patho-logic 'compres-sion' not 'end-plate' fracture	RFA	Usual care for fractures	Change in Visual Analogue Scale	March 2020	University of California, Davis Medical Center
NCT02148003 Effect of the Temperature Used in Thermal Radiofrequency Ablation	18 years or older, low back pain ≥ 3 months	RFA at 90 degrees Celsius	RFA at 80 degrees Celsius	Change of pain relief	February 2021	The Cleveland Clinic
ISRCTN17868852 Percutaneous Radiofrequency treatment for FACET joint pain	18 years and older, suggestive facet joint pain on lumbar level	RFD	Sham treatment	Pain reduction (NRD)	March 2015	Lievensberg Hospital, Netherlands

Literature search strategies

Search strategy for Cochrane

Search Name: RF Denervation of facet joints	
Search Date: 20.12.2018	
#1	(facet joint*) (Word variations have been searched)
#2	MeSH descriptor: [Zygapophyseal Joint] explode all trees
#3	#1 OR #2 (Word variations have been searched)
#4	MeSH descriptor: [Denervation] explode all trees
#5	(denervat*) (Word variations have been searched)
#6	#6 MeSH descriptor: [Ablation Techniques] explode all trees
#7	(ablat*) (Word variations have been searched)
#8	(neurotom*) (Word variations have been searched)
#9	#4 OR #5 OR #6 OR #7 OR #8 (Word variations have been searched)
#10	MeSH descriptor: [Radio Waves] explode all trees
#11	MeSH descriptor: [Pulsed Radiofrequency Treatment] explode all trees
#12	(radiofrequenc*) (Word variations have been searched)
#13	#13 (RF):ti,ab,kw
#14	MeSH descriptor: [Electrocoagulation] explode all trees
#15	(electrocoag*) (Word variations have been searched)
#16	(electro-coag*) (Word variations have been searched)
#17	(thermocoag*) (Word variations have been searched)
#18	(thermo-coag*) (Word variations have been searched)
#19	#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 (Word variations have been searched)
#20	#9 AND #19 (Word variations have been searched)
#21	#3 AND #20
#22	((facet* or zygapophyseal or zygapophysial) NEAR ((radiofrequenc* or radio-frequenc* or RF) NEAR (denervat* or ablat* or neurotom*))) (Word variations have been searched)
#23	#21 OR #22
Total: 94 Hits	

Search strategy for CRD

Search Name: RF Denervation of facet joints	
Search Date: 20.12.2018	
#1	MeSH DESCRIPTOR Zygapophyseal Joint EXPLODE ALL TREES
#2	(facet*)
#3	MeSH DESCRIPTOR Denervation EXPLODE ALL TREES
#4	MeSH DESCRIPTOR Radio Waves EXPLODE ALL TREES
#5	(denervat*)
#6	MeSH DESCRIPTOR Ablation Techniques EXPLODE ALL TREES
#7	(ablat*)
#8	(neurotom*)
#9	#1 OR #2
#10	#3 OR #4 OR #5 OR #6 OR #7 OR #8
#11	#9 AND #10
#12	(((facet* or zygapophyseal or zygapophysial) NEAR ((radiofrequenc* or radio-frequenc* or RF) NEAR (denervat* or ablat* or neurotom*))))
#13	#11 OR #12
Total: 28 Hits	

Search strategy for Embase

Search Date: 20.12.2018	
No.	Query Results
#1	'facet joint'/exp
#2	'facet joint syndrome'/exp
#3	'facet joint osteoarthritis'/exp
#4	'facet joint degeneration'/exp
#5	'facet joint pain'/exp
#6	'facet joint*':ti,ab,de
#7	'zygapophyseal joint'/exp
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
#9	'radiofrequency denervation'/exp
#10	'radiofrequency ablation'/exp
#11	radiofrequency neurotomy'/exp
#12	((radiofrequenc* OR 'radio frequenc*' OR rf) NEAR/5 (denervat* OR ablat* OR neurotom*)):ti,ab,de
#13	#9 OR #10 OR #11 OR #12
#14	#8 AND #13
#15	((facet* OR zygapophyseal OR zygapophysial) NEAR/5 (radiofrequenc* OR 'radio frequenc*' OR rf) NEAR/5 (denervat* OR ablat* OR neurotom*)):ti,ab,de
#16	#14 OR #15
Total: 475 Hits	

Search strategy for Medline

Search Date: 20.12.2018	
No.	Query Results
#1	facet joint*.mp.
#2	exp Zygapophyseal Joint/
#3	1 or 2
#4	exp DENERVATION/
#5	denervat*.mp.
#6	de-nervat*.mp.
#7	exp ABLATION TECHNIQUES/
#8	ablat*.mp.
#9	neurotom*.mp.
#10	4 or 5 or 6 or 7 or 8 or 9
#11	Radio Waves/
#12	exp Pulsed Radiofrequency Treatment/
#13	radiofrequenc*.mp.
#14	radio-frequenc*.mp.
#15	RF.ti,ab.
#16	exp ELECTROCOAGULATION/
#17	electrocoag*.mp.
#18	electro-coag*.mp.
#19	thermocoag*.mp.
#20	thermo-coag*.mp.
#21	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
#22	10 and 21
#23	3 and 22
#24	((facet* or zygapophys#al) adj5 ((radiofrequenc* or radio-frequenc* or RF) adj5 (denervat* or ablat* or neurotom*))).mp.
#25	23 or 24
#26	remove duplicates from 25
Total: 300 Hits	

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Health Technology Assessment