Doctor, why does my hand hurt? The nature, course and treatment of pain in hand osteoarthritis

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CHAPTER 6

SURGICAL DENERVATION AS A TREATMENT STRATEGY FOR PAIN IN HAND OSTEOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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ABSTRACT

Objective

Surgical denervation has been proposed as a treatment for pain in hand osteoarthritis (OA). This review aimed to summarize the available evidence and to propose a research agenda.

Methods

A systematic literature search was performed up to September 2022. Two investigators independently identified studies that reported on denervation for OA of the proximal interphalangeal, distal interphalangeal, metacarpophalangeal or carpometacarpal joints. Quality of studies was assessed and study characteristics, patient characteristics, details of the surgical technique and outcomes of the surgery were extracted.

Results

Of 169 references, 17 articles reporting on 384 denervations in 351 patients were selected. Sixteen case series reported positive outcomes with respect to pain, function and patient satisfaction. One non-randomized clinical trial reported no difference in outcome when comparing denervation of the first CMC I joint to trapeziectomy. Adverse events were frequent, with sensory abnormalities occurring the most, followed by the need for revision surgery. All studies had significant risk of bias.

Conclusion

Surgical denervation for pain in hand OA shows some promise, but the available evidence does not allow any conclusions of efficacy and higher quality research is needed. Techniques should be harmonized and more data regarding how denervation compares to current usual care, other denervation methods or placebo in terms of outcomes and adverse events are needed.

Key messages

What is already known on this topic

Pain is a core symptom of hand osteoarthritis, which often cannot be fully alleviated with current treatment options. Surgical denervation has been proposed as a treatment option.

What this study adds

Surgical denervation may yield favorable outcomes, but evidence on surgical denervation is still insufficient to make a recommendation.

How this study might affect research, practice or policy

Future research should focus on 1) the innervation of the joints 2) the best technique for surgical denervation 3) high quality RCTs investigating efficacy of surgical denervation vs sham or 4) comparing surgical denervation to alternative treatments and 5) the safety of surgical denervation.

INTRODUCTION

Hand osteoarthritis (OA) is a common disease which causes loss of function, structural damage to the joints and, most importantly, pain (1, 2). As there are currently no disease-modifying treatments, therapy is aimed at symptom control. Current guidelines of the European Alliance of Associations for Rheumatology (EULAR) and American College of Rheumatology (ACR) recommend non-pharmacological treatment first (e.g. education, training, braces) (3, 4). Topical or systemic treatments with NSAIDs are recommended for pain alleviation, with a preference for topical treatment due to the considerable toxicity of oral NSAIDs for elderly patients. For patients with structural abnormalities and inadequate pain control, surgery consisting of trapeziectomy with or without interposition and/or suspension arthroplasty (CMCJ-I), arthrodesis or arthroplasty (PIPJ and DIPJ) is recommended as the last resort. The recommended therapies can also be combined (3, 4).

Alternatively, treatment can target the nerves, disturbing the transmission of pain signals through nerves innervating the joint. An example is radiofrequency ablation, which is conditionally recommended by the ACR guidelines for knee OA (3). Surgical denervation, that is, the surgical dissection of nerves, can theoretically achieve the same goal as ablation. It was originally described in the hip and later developed for the hand and wrist (5-7), and has been proposed as an alternative surgical intervention (5, 8-10). Currently, surgical denervation is increasingly being performed to treat pain in hand OA, although precise numbers are unclear.

Surgical denervation aims to dissect the nerves innervating the painful joint, thereby disabling the pain signaling without impairing joint function. Surgical denervation does not seem to be associated with a loss of function or strength, and it does not preclude further surgeries if required, which is advantageous compared to other surgical options (9, 10). However, some downsides have to be taken into consideration. For the denervation to be effective, anatomical knowledge of the joints of the hand and their innervation is essential. The nerves currently known to innervate the hands are summarized in appendix 1 (11-15). The innervation of the joints in the hands is still subject to debate and more nerve branches than the currently treated with surgical denervation may contribute to the innervation of specific joints (11). Furthermore, the occurrence of adverse effects has been reported, including wound infection, necrosis of skin flaps, or sensory abnormalities (9, 10).

It is currently unclear whether the advantages of surgical denervation outweigh the disadvantages. We performed a systemic literature search, aiming to summarize available evidence on the efficacy and safety of denervation as a treatment for hand OA compared to other treatments, and to set a research agenda.

METHODS

Search strategy

A systematic literature search was conducted in PubMed, Ovid and Cochrane databases from their inception up to 21 September 2022, with additional references collected from the identified publications and other systematic literature reviews. The search strategies consisted of terms for "hand", "osteoarthritis" and "denervation" and can be found in appendix 1.

Eligible study types were randomized clinical trials, case control studies, cohort studies, case reports and case series. Studies on OA in other joints (including wrist) or other causes of hand pain were excluded. Studies regarding interventions other than surgical denervation were similarly excluded. Reviews, comments and editorials, as well as abstracts without a full publication, were considered ineligible for review, but have been used to gather more suitable articles from the references.

Studies of surgical denervation (intervention) in adults with hand OA (population) were included. Hand OA comprised OA or degenerative arthritis of the DIPJ, PIPJ, CMCJ-I or MCPJ. The comparator could be any other treatment for hand OA, or none, in the case of case studies. No requirements were set for the outcome measures.

Study selection, data extraction and risk of bias assessment

Two reviewers (CvdM and AC) independently screened titles and abstracts to determine eligibility for inclusion. Screening results were compared and discussed in case of disagreement. Relevant data on study characteristics, interventions (denervated joint, nerves dissected, incisions used, postoperative care), study population (sample size, diagnostic criteria, demographics and baseline characteristics) and outcomes (pain and function scores after surgery, patient satisfaction, follow-up time, strength, adverse events) was extracted (CvdM) and summarized as average and/or range. The risk of bias was assessed (CvdM and SEST). For case series the Joanna Briggs institute (JBI) checklist for case series was used, judging studies based on inclusion, diagnosis and classification of condition, reporting of demographic, clinical and outcome information, and statistical analysis (16). The ROBINS-I was used for comparative studies, judging on confounding, selection bias, classification and adherence to intervention, missing data, outcome measurements and selective reporting (17).

Some of the JBI checklist items required further specification. The following definitions have been used. For the measurement of the severity of the condition to be standard and reliable, it was required to be identical for all patients and be reproducible. The use of any validated clinical or radiological system was deemed valid. For diagnosis, a validated radiological or clinical system was similarly required. Consecutive and complete inclusion of patients was judged on whether this was explicitly stated in the paper. Clear reporting of the demographics of the patients was defined as clear presentation of at least age and sex.

The risk of bias assessments were performed independently by the two reviewers, after which the outcomes were compared. In case of disagreement, the item was discussed to reach consensus. In case no consensus was reached, it was discussed with a third reviewer (MK).

The level of evidence of the individual studies was rated according to the Oxford Centre for Evidence-Based Medicine levels of evidence by CvdM (18).

No review protocol was registered.

RESULTS

Searching Pubmed, Ovid and Cochrane databases yielded 212 records. After deduplication, 169 publications remained. Screening of titles and abstracts resulted in 27 records. After full text screening, another thirteen were excluded (1 due to an unclear patient group, 12 due to type of publications). References from retrieved publications included three suitable records, leading to a total of seventeen records included.

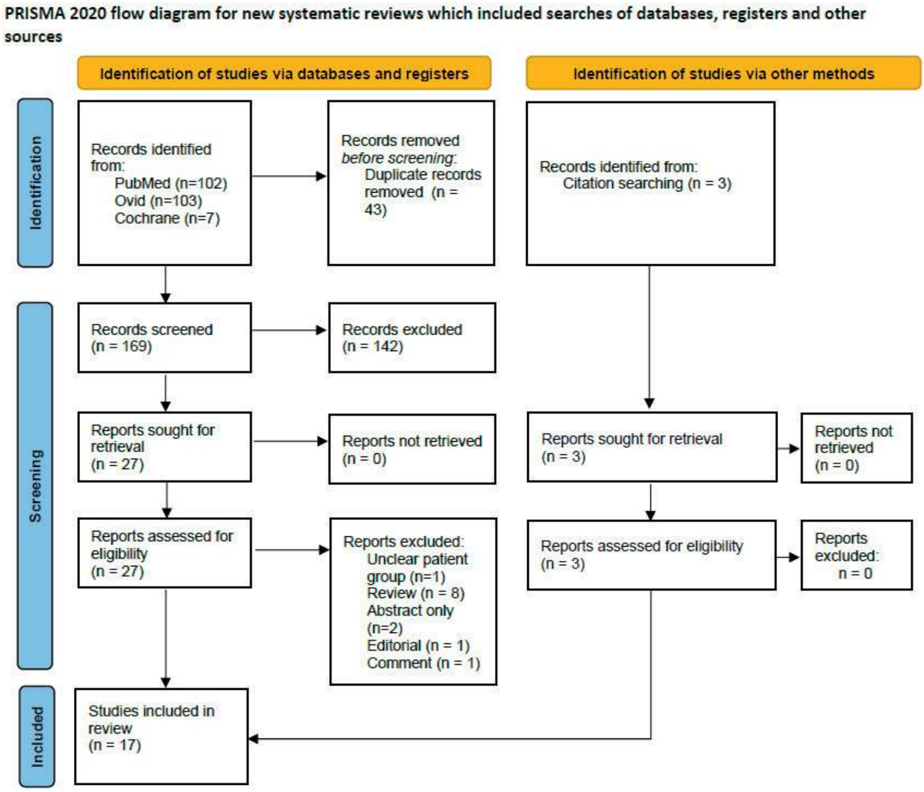

Figure 1. Flowchart of literature search

Study characteristics

The included studies consisted of sixteen case series and one non-randomized comparative clinical trial. Studies are summarized in table 1. Most publications (n=11) described CMCJ-I denervation. MCPJ (n=1), DIPJ (n=1) and PIPJ (n=3) denervation were less frequent. One case series described a mixture of MCPJ, DIPJ and PIPJ denervation. A total of 384 denervations were performed in 351 patients. Twelve of these patients were described in two publications (Suresh et al. (19) and Tuffaha et al. (20)). Furthermore, overlap between the patient groups in the two publications by Ehrl et al. (21, 22) could not be excluded.

In seven of the case series, OA was diagnosed based on clinical presentation. In two a clinical diagnosis confirmed by radiography was used, in four only radiography was used. Amongst these four, the Eaton-Littler criteria were used in two, the Dell criteria in one, and no criteria were specified in one. The method of diagnosing OA was not specified in four publications. Inclusion and/or exclusion criteria were specified in twelve publications and often included failure on conservative treatment, some description of radiological damage, response to nerve block or mobility of the joint. Previous joint surgery was used as an exclusion criterion in the majority of studies.

The non-randomized trial described a comparison of trapeziectomy to CMCJ-I denervation. Ten participants were included in the trapeziectomy arm, 35 were included in the denervation arm. Diagnosis was clinical. Inclusion criteria consisted of thumb base OA requiring surgery, with no prior surgery.

For details, see table 1.

Methodological quality of included studies

Table 2 describes the methodological quality of the sixteen case-series. Most had clear inclusion criteria, but only in a few, presence and severity of hand OA were measured in a reliable and standard way, with the assessment often not described or based on clinical judgement. Clinical assessment and radiographic staging, or a combination, were most frequently used. Radiographs were scored using either the Dell (n=1), Eaton-Littler (n=3) or unspecified (n=2) criteria. Seven reports stated inclusion had been complete, with five stating it had been consecutive. Demographic and clinical characteristics, as well as outcomes, were often presented clearly, although often few characteristics were given. None of the studies reported the demographic information of the study center (geographic location, setting of the center). Finally, in eleven of the case series, the statistical analysis was either absent (n=6) or inappropriate (n=5). All reviewed case series therefore had severe methodological shortcomings.

The clinical trial by Salibi et al. (23) had serious risk of bias in multiple domains: It was an open label study, a substantial proportion of participants switched interventions from denervation to trapeziectomy and were subsequently removed from the analysis, and confounding was not taken into account in the analysis. For an overview, see table A2 in appendix 3.

Surgical techniques

The studies used a variety of techniques, summarised in table 3.

CMCJ-I denervation

Most studies used a single incision, either a Wagner approach (figure A1), a transverse incision (figure A2), or a radial S-shaped incision (figure A3). Two groups (Donato et al. (24) and Lorea (25)) used two incisions: a palmar and a dorsal transverse incision (figure

A4 and figure A5). Giesen et al (26) added a third incision in the fourth extensor compartment (figure A6).

Which nerves were dissected differed between studies. One study did not specify the dissected nerves and one only stated that all branches leading to the joint capsule were dissected (23, 27). The other nine studies all reported dissecting of branches from the radial nerve (extending from the radial sensory nerve or the superficial branch of the radial nerve), the medial nerve (from the thenar, palmar or palmar cutaneous branches) and the lateral antebrachial cutaneous nerve (from the Cruveilhier branch, or without further specification of smaller branches). Giesen et al (26). additionally dissected the posterior interosseous nerve, Donato et al. (24) and Lorea (25) a small part of the dorsal articular nerve of the first interosseous space.

Four groups added additional procedures during the surgery: Dellon et al. (27) injected the nerve endings with lidocaine and removed volar osteophytes, Ehrl et al. (21, 22) performed synovectomy and excised osteophytes, followed by saline irrigation of the joint. Arenas-Prat (28) performed periosteal resection of the first metacarpal and Suresh et al. (19) report anesthesia with lidocaine of articular branches.

PIPJ denervation

Several incision techniques were used. A Brunner incision was used in all four studies investigating PIPJ denervation (figure A7). Amongst the four, only Servasier et al. (29) also used other approaches: A double lateral (figure A8) or straight incision on the dorsal aspect of the joint (figure A9).

Again, the specific nerves that were dissected varied. Servasier et al. (29) stated they dissected all joint afferents, Madsen et al. (30) dissected the articular branches of the radial, ulnar and dorsal digital nerves, Jiménez et al. (31) dissected the palmar articular nerve, and the articular branches of the common and dorsal digital nerves, and Braga-Silva et al. (32) dissected the branches from the palmar digital nerves.

DIPJ denervation

A skin flap extending from the eponichium to the joint was used in both studies on DIPJ denervation (figure A10). Both described dissecting the articular branches of the digital nerves, with Arenas-Prat (33) specifying the volar and dorsal digital nerves.

MCPJ denervation

MCPJ denervation was done using two incisions in both studies describing it: a volar Brunner (figure A11) or Chevron incision (figure A12) and a dorsal linear incision (figure

A13). Both groups dissected articular branches of the digital nerves (dorsal and volar for Arenas-Prat (34), radial and ulnar by Madsen et al. (30)). Arenas-Prat et al. further dissected the branches from the deep branch of the ulnar nerve. Madsen et al. dissected the branches from the digital branch of the radial sensory nerve and the dorsal sensory branch of the ulnar nerve.

Postoperative care

When described, most recovery plans were comparable: Gentle return to activities as pain allows, with the main difference between studies being the time before return to activities (0-3 weeks).

Patient characteristics and outcomes

Baseline characteristics

The studies encompassed a patient group with average age from 55-65 years (range 30 to 87 years) (table 4). The study by Jiménez et al. (31) stood out, having a population with a lower median age (52 years). The percentage of female participants was around 60-75% in most studies, with a very high percentage (98%) in the study by Servasier et al. (29), and a very low percentage (36%) in the study by Jiménez et al (31).

Most studies presented baseline pain scores, often on a 0-10 Numeric Rating Scale (NRS). Average baseline pain scores varied from 7.5 to 8.7 on NRS. Giesen et al (26). split the baseline scores into pain at rest, light activity and demanding activity. They reported median pain scores of 5, 7.5 and 10, respectively. Madsen et al. (30) used a five-point scale, reporting a median of 5/5. (table 4)

Of note, the study by Servasier et al. (29) included arthropathies of various types: degenerative (43 joints) and inflammatory (11 joints). Inflammatory was further divided into rheumatoid arthritis (7 joints), ankylosing spondylarthritis (1 joint), psoriatic arthritis (2 joints) and undetermined inflammatory rheumatism (1 joint).

Follow-up

Fifteen out of seventeen studies reported the follow-up duration, which ranged from four to 152 months. In most studies a physical follow-up was used, with the exception of the study by Ehrl et al. (22), in which 23 of the 60 patients only had a follow-up over the telephone, and Giesen et al. (26), where the final follow-up consisted of a questionnaire only, with a physical follow-up halfway through the follow-up period.

Outcomes

Fifteen of the seventeen groups reported post-operative pain outcomes, using a visual analogue scale (VAS) or NRS, or using their own scales or descriptions. Almost all studies reported good results, with 56-92% patients experiencing some measure of pain relief (19, 20, 24, 25, 34, 35). The mean change in NRS score ranged from 3 to 8.1 on a 10-point scale (21, 22, 24, 26, 27, 29-32). Salibi et al. (23) reported no differences in pain when comparing denervation to trapeziectomy from baseline to months 6, 12 and 60.

Fifteen out of seventeen studies reported other outcome measures. Six reported on patient satisfaction, which ranged from 70 to 92% (24, 28, 32-35). Three studies reported on range of motion of the joint after surgery; mean increase ranged from 3.5 to 27 degrees (29, 31, 32). Three other studies reported on grip strength, with average increase around 3.9 kg (20, 26) or 12 foot/lb (24) for grip strength and 2.1 kg for pinch grip strength (20, 26). Finally, various questionnaires and other physical examinations were reported; most showing beneficial results (19, 21, 22, 26, 30, 31). For details, see table 4.

Adverse events

Rates of adverse events varied between 0-75% (table 4) (20-22, 24-34). Most studies (n=9) reported rates of 20% or lower. The most frequently occurring complications were (temporary) sensory disturbances, such as pain, paresthesia or numbness (20-22, 24-26, 28-34). Other reported complications included wound infection, skin necrosis and complex regional pain syndrome type I. (21, 22, 24, 29, 34). Three studies (by Salibi et al., Suresh et al. and by Servasier et al. (19, 23, 29)) reported numbers of patients undergoing an additional type of surgery due to dissatisfaction. In the study by Salibi et al. 9 out of 35 (26%) underwent a trapeziectomy, Servasier et al. reported 7 out of 54 (13%) joints underwent either arthrodesis (n=2) of arthroplasty (n=5), Suresh et al. reported 3 out of 9, which underwent arthroplasty.

Table 1. Study characteristics

1st Author, publication year (ref)	Number of patients; joints	OA Diagnosis criteria	Additional intervention	Relevant inclusion and exclusion criteria	LoE
Case series					
CMCJ-I					
Arenas-Prat 2012 (34)	16;18	N/A	None	N/A	IV
Arenas-Prat 2022 (28)	17;17	N/A	None	N/A	IV
Dellon 2017 (27)	3;3	Radiological	None	Inclusion: Volar osteophyte on Radiograph, positive grind test, no response to conservative treatment	IV
Donato 2019 (24)	8;11	Clinical	None	Inclusion: ≥6 months follow-up, good response to bipuvacaine block. Exclusion: Incomplete preoperative testing or follow-up	IV
Ehrl 2016 (21)	42;42	Radiological (Eaton-Littler)	Lavage and imbrication	Inclusion: No sustained benefits from conservative treatment, including ≥1 steroid injection. Exclusion: Prior surgery, Eaton-Littler stages I or IV	IV
Ehrl 2016 (22)	60;60	Radiological (Eaton-Littler)	Lavage and imbrication	Inclusion: No sustained benefits from conservative treatment, including ≥1 steroid injection. Exclusion: Prior surgery, Eaton-Littler stages I or IV	IV
Giesen 2017 (26)	30;31	Radiological (Dell)	None	Inclusion: No Z-deformity, primary CMCJ-I OA.	IV
Lorea 2003 (25)	14;14	Clinical	None	Inclusion: OA	IV
Suresh 2022 (19)	12 (3 lost to follow-up);12	Clinical and radiological (Eaton)	None	Inclusion: Symptomatic OA	IV
Tuffaha 2019 (20)	12;12	Clinical	None	Inclusion: Good response to block at median nerve in mid-forearm or around joint capsule.	IV

Table 1. Study characteristics (continued)

1st Author, publication year (ref)	Number of patients; joints	OA Diagnosis criteria	Additional intervention	Relevant inclusion and exclusion criteria	LoE
PIPJ					
Braga-Silva 2001 (32)	21;24	Clinical	None	N/A	IV
Jiménez 2020 (31)	11;11	Clinical and radiological	None	Inclusion: Painful, disabling OA, resistant to conservative treatment, RoM >30 degrees, good lateral joint stability.	IV
Servasier 2021 (29)	42;54*	Clinical	None	Inclusion: pain with functional RoM (60° passive).	IV
DIPJ					
Arenas-Prat 2012 (33)	10; 10	N/A	None	N/A	IV
MCPJ					
Arenas-Prat 2014 (35)	9;9	N/A	None	N/A	IV
MCPJ/DIPJ/PIPJ					
Madsen 2018 (30)	11;23	Clinical	None	Inclusion: Painful OA with preserved motion, inadequately controlled with NSAIDs.	IV
Non- randomized Clinical Trial					
CMCJ-1					
Salibi 2019 (23)	45;45	Clinical	None	Inclusion: OA requiring surgery. Exclusion: Previous surgery.	II

LoE: Level of Evidence.

Table 2. Risk of bias assessment

Joint	Study	Clear inclusion criteria?[1]	Standard measurement of condition?[2]	Valid identification methods for condition?[3]	Consecutive inclusion of patients?[4]	Complete inclusion of participants?[5]	Clear reporting of patient demographics?[6]	Clear reporting of clinical information of patients?[7]	Outcomes or follow-up clearly reported?[8]	Clear reporting of demographics of clinic?[9]	Statistical analysis appropriate?[10]
CMCJ-I	Arenas-Prat 2012 (34)	N	U	U	U	U	N	N	N	N	N
	Arenas-Prat 2022 (28)	N	U	U	Y	Y	N	N	N	N	N
	Dellon 2017 (27)	Y	N	N	U	N	Y	Y	Y	N	N
	Donato 2019 (24)	Y	U	U	Y	Y	Y	Y	Y	N	Y
	Ehrl 2016 (21)	Y	Y	Y	U	N	Y	Y	Y	N	N
	Ehrl 2016 (22)	Y	Y	Y	U	N	Y	Y	Y	N	N
	Giesen 2017 (26)	Y	Y	Y	U	Y	Y	Y	Y	N	N
	Lorea (25)	Y	U	U	Y	Y	N	N	Y	N	N
	Suresh 2022 (19)	Y	Y	Y	Y	Y	Y	N	N	N	Y
	Tuffaha 2019 (20)	Y	Y	Y	N	N	Y	Y	Y	N	N
PIPJ	Braga-Silva 2001 (32)	N	N	U	U	Y	Y	Y	Y	N	N
	Jiménez 2020 (31)	Y	N	N	U	U	Y	Y	Y	N	Y
	Servasier 2021 (29)	Y	N	N	U	U	Y	Y	Y	N	Y
DIPJ	Arenas-Prat 2012 (33)	N	U	U	U	U	N	N	N	N	N
MCPJ	Arenas-Prat 2014 (35)	N	U	U	U	U	N	N	N	N	N
mixed	Madsen 2018 (30)	Y	N	N	Y	Y	Y	Y	Y	N	Y

Risk of bias assessment according to the Joanne Briggs Institute checklist for case series. 1. Were there clear criteria for inclusion in the case series? 2. Was the condition measured in a standard, reliable way for all participants included in the case series? 3. Were valid methods used for identification of the condition for all participants included in the case series? 4. Did the case series have consecutive inclusion of participants? 5. Did the case series have complete inclusion of participants? 6. Was there clear reporting of the demographics of the participants in the study? 7. Was there clear reporting of clinical information of the participants? 8. Were the outcomes or follow-up results of cases clearly reported? 9. Was there clear reporting of the presenting site(s)/clinic(s) demographic information? 10. Was statistical analysis appropriate? Y= Yes. N = No. U = Unclear. NA = Not applicable.

Table 3. Details surgical interventions

Author, publication year (ref)	Incision; figure	Nerves dissected	Additional intervention	Postoperative care
Case series				
CMCJ-I				
Arenas-Prat 2012 (34)	Wagner; A1	Articular branches of SBRN, PBMN, TBMN, CBLACN	None	Mobilization as pain allows after two weeks.
Arenas-Prat 2022 (28)	Wagner; A1	SBRN, PBMN, TBMN and CBLACN	Periosteal resection of first metacarpal	Sutures and soft bandage with splint for two weeks. Gradual mobilization after two wks.
Dellon 2017 (27)	Transverse at base of first metacarpal; A2	Unclear	Nerve injected with 1% lidocaine. Volar osteophyte removed.	Return to activities over two weeks after one week
Donato 2019 (24)	Palmar transverse; A4 1st interosseous space; A5	Articular branches of radial nerve, SBRN, PCBMN, TBMN, CBLACN. Dorsal articular nerve of the 1st interosseous space.	None	No activity restrictions.
Ehrl et al. 2016 (21)	Radial S shaped incision; A3	Dorso-radial and dorso-ulnar sensory branches from radial nerve to thumb, CBLACN, branches of PCBMN.	Synovectomy and excision of osteophytes, joint irrigated normal saline.	Plaster cast for two weeks, then splint for two weeks.
Ehrl et al. 2016 (22)	Radial S shaped incision; A3	Dorso-radial and dorso-ulnar sensory branches from radial nerve to thumb, CBLACN, branches of PCBMN.	Synovectomy and excision of osteophytes, joint irrigated normal saline.	Plaster cast for two weeks, then splint for two weeks.
Giesen et al. 2017 (26)	Transverse palmar; A4 1st interosseous space; A5 Fourth extensor compartment; A6	Articular branches of SBRN, PBMN, TBMN, CBLACN, PIN.	None	N/A
Lorea 2003 (25)	Transverse palmar; A4 Dorsal in 1st interosseous space; A5	Articular branches of the SBRN, PBMN, TBMN, CBLACN, nerve of the first interosseous space	None	Bulky, moist dressing. Rest for three weeks. Gradual resuming of normal activities after that.
Suresh et al. 2022 (19)	Wagner; A1	Branches from LABCN, SBRN, PCBMN.	Intraepineural 1% lidocaine of nerves.	Dressing for three days. Hand therapy and increasing activity over five to twelve days.
Tuffaha et al. 2019 (20)	Wagner; A1	Articular branches from RSN, LABCN, PCBMN.	None	N/A

Table 3. Details surgical interventions (continued)

Author, publication year (ref)	Incision; figure	Nerves dissected	Additional intervention	Postoperative care
PIPJ				
Braga-Silva 2001 (32)	Volar Brunner; A7	Articular branches of palmar digital nerves.	None	Early active mobilization of digits.
Jiménez et al. 2020 (31)	Brunner; A7	Articular branches of common digital nerve, dorsal digital nerves.	None	Active mobilization after five days
Servasier et al. 2021 (29)	4 as Foucher; A7 12 as Lorea; A8 38 with single dorsal on PIPJ; A9	All joint afferents.	None	N/A
DIPJ				
Arenas-Prat 2012 (33)	From eponichium to joint; A10	Articular branches of volar and dorsal digital nerves.	None	Mobilization as pain allows after two weeks.
MCPJ				
Arenas-Prat 2014 (35)	Volar Brunner; A11 Dorsal straight; A13	Articular branches of dorsal digital nerve, volar digital nerves, DBUN	None	Mobilization as pain allows after two weeks.
MCPJ/DIPJ/PIPJ				
Madsen et al. 2018 (30)	MCPJ: Volar Chevron; A12. Dorsal linear; A13 PIPJ: Brunner; A7. DIPJ: U shaped flap to eponychium; A10	MCPJ: Branches from radial and ulnar digital nerves. Articular branches of RSN or DSBUN. PIPJ: Radial, ulnar and dorsal digital nerve branches. DIPJ: Branches from digital nerves.	None	Movement and use of hand as possible encouraged. Return to activity as tolerated.
Non-randomized clinical trial				
CMCJ-I				
Salibi et al. 2019 (23)	Dorsoradial; A3	All branches leading to joint capsule.	None	N/A

Incisions: Wagner incision = slightly curved incision across the thenar eminence, towards the palmar aspect. (figure A1) Brunner incision = Zigzag incision across the palmar side of the finger. (figure A10)
Nerves: SBRN = Superficial branch of radial nerve. PBMN = Palmar branch of median nerve. TBMN = Thenar branch of median nerve. CBLACN = Cruveilhier branch from lateral antebrachial cutaneous nerve. DBUN = Deep branch of ulnar nerve. PCBMN = Palmar cutaneous branch of median nerve. DANFIS = Dorsal articular nerve of the first interosseous space. PIN = Posterior interosseous nerve. LABCN =: Lateral antebrachial cutaneous nerve. MRMN = median recurrent motor nerve. RSN = Radial sensory nerve. UMN = Ulnar motor nerve. DSBUN = dorsal sensory branch of ulnar nerve.
Other: N/A = Not available

Table 4. Patient characteristics and outcomes

1st Author, publication year (ref)	Patient age years (range); Female sex %	Baseline Pain	Follow-up (mths)	Outcomes at follow-up		Adverse events (number of joints)
				Pain	Other	
Case series						
CMCJ-I						
Arenas-Prat 2012 (34)	N/A; N/A	N/A	N/A	N/A	14/16 patients, 16/18 joints, very satisfied.	Hypertrophic scar (2). Hypoesthesia (1).
Arenas-Prat 2022 (28)	N/A; *N/A*	N/A	4-6[1]	N/A	15/17 satisfied/very satisfied	Mild paraesthaesia (4)
Dellon 2017 (27)	64.3 (54-83)[2]; *N/A*	8.7[3]	125.6 (48-152)[2]	0.67[3]; average ↓8.1 on NRS	N/A	None
Donato 2019 (24)	63.4 (55-77)[2]; *62.5*	7.9 (2.3)[4]	18.5 (7-30)[2]	1.9 (1.9)[4]; average ↓6 on NRS 7/8 patients reported improvement	Grip strength: 50.2 (10-99)[2]; average ↑11.8 87.5% patient satisfaction	Wound infection (1) Persistent focal pain (1)
Ehrl 2016 (21)	62.7 (47-81)[2]; 81	7.5 (1.6)[4]	46.5 (6-82)[2]	1.1 (1.1)[4]; average ↓6.4 NRS	DASH 18.1 (1.3)[4]; average ↓28.7 Cooney 73.7 (16.0)[4]; average ↑38.3 Krimmer 80.0 (14.1)[4]; average ↑41.7	Postoperative wound infection (1) Complex regional pain syndrome (1)
Ehrl 2016 (22)	Physical: 63 (10)[4]; 78 Phone: 61 (11)[4]; 70	7.5 (1.6)[4]	Physical: 46 (12-81)[2] Phone: 52 (14-93)[2]	Telephone FU: 87% improved complaints, 45% no complaints. Physical FU: 1.1 (1.4)[4]; Average ↓6.4	DASH 18.4 (14.9)[4] Cooney71.6 (15.7)[4] Krimmer 79.1 (13.7)[4] Subjective weakness/stiffness ↓	Postoperative wound infection (1) Complex regional pain syndrome (1)
Giesen 2017 (26)	62 (39-86)[2]; 73	At rest: 5 (5).[5] Gentle activity: 7.5 (1.5)[5] Heavy activity: 10 (2.5)[5]	12	*6 months*: Improved *12 months:* At rest: 2 (3)[5] Gentle activity: 5.0 (3.8)[5] Demanding activity: 6.0 (4.0)[5]	*6 months:* Key-pinch ↑2.5 (2.1)[4] kg. Grip strength ↑ 3.6 (6.0)[4] Kapandji score 9.3 (0.6); average ↑0.8 *12 months:* Kapandji score improved 1-2 points in 50% of cases.	Paresthesia of SBRN (3) Mild neuropathic pain>2 years (1) Mild synovitis, resolved with 1 month of splinting (1)
Lorea 2003 (25)	60 (30-77)[2]; N/A	N/A	8 (12)[8]	12/14 >80% ↓ pain. 1/14 70% ↓, 1/14 60% ↓.	Off work period 7 (4-10)[2] weeks.	Temporary paresthesias in most cases.
Suresh 2022 (19)	59 (46-74)[2]; 75	N/A	60.7 (20.9-77.8)[2]	Complete pain resolution in 4/12, partial in 1/12	Of 3/12 with in person follow-up, 3 scores 10/10 on Kapandji.	Three conversions to arthroplasty.

Table 4. Patient characteristics and outcomes (continued)

1st Author, publication year (ref)	Patient age years (range); Female sex %	Baseline Pain	Follow-up (mths)	Outcomes at follow-up		Adverse events (number of joints)
				Pain	Other	
Tuffaha 2019 (20)	59 (46-74)[2]; 75	N/A	Mean 15 (3-28)[2]	Pain resolution complete in 8/12, near complete in 3/12, none in 1/12.	Of 8/12 with strength measurements: Grip strength mean ↑4.1 (3.0)[4] lateral pinch strength ↑1.7 (0.5)[4]	Patchy numbness (8). Pin-point pain (1)
PIPJ						
Braga-Silver 2001 (32)	63 (50-75)[2]; *86*	8[3]	77 (64-90)[2]	2[3]; average ↓ 6	22/24 joints good improvement. RoM 67° (55-80)[2]; average ↑10°	Paraesthesia (5), resolved <30 days (3). Deformity increased in 3/11 deformed joints.
Jiménez 2020 (31)	52 (30-69)[2]; 36	7.8 (5-10)	24 (12-120)[6]	1.4 (0-3); average ↓6.4	DASH 8.7 (2.3-20.5); average ↓34.9 RoM mean 79°; average ↑27°	Transient digital paraesthesia (2)
Servasier 2021 (29)	66.5 (44-78)[2]; 98	7.5 (5-10)[2]	Mean 51 (4-168)[2]	In 47/54 unrevised joints: Average 1.1 (0-8)[2]; average ↓6.4	In 16/54 improved joints: Mean RoM ↑13.9°[3] in flexion, ↑3.5°[3] extension.	Transient skin sensitization (1) Complex regional pain syndrome (7) Failures (7)
DIPJ						
Arenas-Prat 2012 (33)	N/A; N/A	N/A	4-16[1]	7/10 good pain relief	7/10 pleased. 1/10 unchanged. 2/10 not satisfied	Necrosis of surgical area (1), hypersensitive scar (1)
MCPJ						
Arenas-Prat 2014 (35)	N/A; N/A	N/A	N/A	3/9 complete pain relief, 5/9 significant improvement, 1/9 minimal.	3/9 very satisfied, 5/9 satisfied.	N/A

Table 4. Patient characteristics and outcomes (continued)

1st Author, publication year (ref)	Patient age years (range); Female sex %	Baseline Pain	Follow-up (mths)	Outcomes at follow-up		Adverse events (number of joints)
				Pain	Other	
MCPJ/DIPJ/PIPJ						
Madsen 2018 (30)	57.8 (39-66)[2]; 55	5/5 (2-5)[6]	26.5 (9-46)[2]	0/5 (0-5)[6]; average ↓5	Function 2/5 (0-5) to 5/5 (1-5)[6]; average ↑3 Recovery time 96 (2-210)[2] days	Persistent numbness in overlying skin (5). Persistent fingertip numbness (1) No improvement in joint pain (1) Recurrence of pain (2)
Non-randomized clinical trial						
CMCJ-I						
Salibi 2019 (23)	Arm 1: 61 (55-72)[2]; 50 Arm 2: 58 (41-72)[3]; 83	N/A; N/A	60	Arm 1: ΔVAS pain at 6 months (0.19)[3], 12 months (0.21)[3], 60 months (0.15)[3]. Arm 2: ΔVAS pain at 6 months (0.09)[3], 12 months (0.13)[3], 60 months (0.10)[3].	No significant differences between groups.	denervations converted to trapeziectomy (9)

Pain reported on a 10-point NRS scale, unless specified otherwise. No. = Number. N/A = Not available. RoM = Range of motion. DASH = Disability of the arm, shoulder and hand. SD = Standard deviation. FU = Follow-up. VAS = Visual analog scale. Arm 1 = Trapeziectomy. Arm 2 = Denervation. Ext. = extension Kg = Kilograms. Wks = Weeks. Mths = Months.
[1] = Range. [2] = Mean (range). [3] = Mean. [4] = Mean (SD). [5] = Median (SD). [6] = Median (range). [7]Mean (max).

DISCUSSION

Pain in hand OA remains difficult to treat, and new therapies are required. Surgical denervation has been proposed as an option. In this review we gave an overview of the available literature describing the efficacy and safety of surgical denervation for OA in the PIPJ, DIPJ, MCPJ and CMCJ-I. No meta-analysis was performed due to the heterogeneity of the surgical techniques and the reported outcome measures.

The overall quality of the evidence was low. Most studies were case series (with the inherent shortcoming that there was no blinding or randomization) and all studies had methodological shortcomings. Most common were lack of clarity regarding the inclusion of patients (consecutive or not, stringency of diagnosis, use of diagnostic criteria) and statistical analysis of the results. Despite the fact that most included studies were case series, these shortcomings still stand out and therefore the results of these studies may be biased. The varying use of diagnostic criteria hampers generalizability. Furthermore, properly performed randomized clinical trials were unavailable, precluding adequate comparison to other (non)pharmacological treatments or surgical methods, as well as comparison to usual care or sham. In particular, it would be valuable to have trials comparing surgical denervation to other interventions targeting nerves, such as e.g. radiofrequency ablation. Ablation (using radiofrequency or cryoneurolysis) is conditionally recommended by the ACR guidelines for knee OA (3), based on two randomized clinical trials (RCTs) comparing it to sham (36, 37) and two RCTs comparing it to intra-articular injection with corticosteroids (38) or platelet rich plasma and hyaluronic acid (39), as well as one comparing it to oral analgesics (40).

The trial by Salibi et al. (23) started out as randomized, but diverted from this design due to slow inclusion, which arose from a strong patient preference for denervation. As such, their results are likely to be biased due to amongst others regression to the mean and placebo effects, as well as publication bias favoring positive outcomes. In total, the current state of the literature does not allow for definitive conclusions. However, the reported results of this intervention are generally positive. Most studies showed pain reduction, high patient satisfaction and retained or improved function. The pain reduction after denervation exceeded the minimal clinical important difference for NRS pain in most studies (41). This legitimizes further evaluation in randomized clinical trials.

Conversely, adverse events were frequent, with only one study reporting no adverse events (27). Sensory abnormalities frequently occurred, as well as postoperative infections and the need for other surgical interventions. However, the frequency and severity of adverse events after surgical denervation can currently not be assessed with certainty, as the described studies lack sufficient quality. Nine cases from the studies developed complex regional pain syndrome. This severe adverse event may be worse than hand OA, and as such should be taken seriously. Of these patients with complex regional pain syndrome, two were described to be settled with hand therapy and analgesics (by the same authors, which may describe the same patient in two papers) (21, 22). Of the remaining seven, three diagnoses were doubtful and showed swift regression of symptoms, one resolved within 6 months and 3 resolved withing 12 months (29). Another potential adverse event of denervation could be negative effects on the joint structure, given the concerns raised previously that removal of or interfering with pain signaling in the joint may exacerbate cartilage damage, both in clinical and basic science. (42, 43) Development of Charcot joint has also been described as a potential adverse outcome of surgical denervation, but was not seen in the studies covered in this review. (9, 10) The knowledge gap concerning adverse events needs be to be addressed before denervation surgery can be recommended as a standard part of treatment for hand OA, as no sufficient risk-benefit analysis can be done without adequate information on adverse events. Specifically, comparisons of the adverse events after surgical denervation compared to other surgical interventions and other therapies targeting nerves are needed.

Another aspect of surgical denervation to consider is the possibility of a second surgery should the denervation fail, previously described as a strong potential benefit (9, 10, 44, 45). Although it may technically be possible, it is unclear whether the outcomes of such an intervention are comparable to the outcomes of the same intervention without a preceding denervation. The reviewed studies offered insufficient evidence to answer this question.

Finally, techniques employed for denervation still vary greatly between surgeons. The studies included here differed in the incisions used, in the nerves targeted for denervation and in additional interventions performed. This makes direct comparison of the results difficult, and a consensus on at least the nerves to dissect and potential additional interventions to perform should be reached. For example, Giesen et al. (26) decided to make an extra incision to dissect the posterior interosseous nerve in addition to the nerves innervating the CMCJ-I. More uniformity in the surgical techniques may aid interpretation and evaluation of the effects of surgical denervation. The selection of the surgical techniques should be based on the innervation of the joint, and as such this innervation needs to be known.

There is an increasing understanding of the complexity of hand OA pain, which is thought to be nociceptive, but also nociplastic or neuropathic in nature, with central and peripheral sensitization influencing it (46). Studies in this review did not assess the type of hand pain. So, it is currently unknown for which type of hand pain surgical denervation might be beneficial. This lack of results stratified by pain phenotype needs to be addressed in future studies.

In conclusion, we currently cannot be sure the benefits of surgical denervation outweigh the harms to treat patients with hand OA, given the small number of cases and overall low quality of the evidence. Thus, we do not recommend denervation surgery for pain relief in hand OA. However, the available results indicate the outcomes may be favorable, although a considerable number of complications were reported. To further evaluate the use of surgical denervation in hand OA, we propose future studies should investigate 1) the innervation of the joints, 2) the best surgical technique to dissect all relevant nerves, 3) perform high-quality randomized clinical trials to investigate the efficacy of surgical denervation in comparison to sham in different patient groups, 4) to investigate other (non-surgical) therapies targeting the nerves, and finally 5) the safety of surgical denervation.

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Author contributions
MK, AC, MJPFR and AJHV designed the study. CvdM, AC, SEST and MK collected the data. CM, LAvdS, and MK analysed the data. CvdM, LAvdS, AC, FPBK, MJPFR, FRR, SEST, AJHV, and MK interpreted the data and wrote the report. All authors approved the final version of the manuscript.

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Data sharing statement
All data relevant to the study are included in the article or uploaded as supplementary information. The used search strategies are shown in the supplementary file and can be used to reproduce the search.

Competing interest statement
MK reports the following, all outside the current study: Grants from IMI-APPROACH and the Dutch Arthritis Society, paid to the institution. Royalties or licences from Wolters Kluwer and Springer Verlag, paid to the institution. Fees for consulting/advisory boards by Abbvie, Kiniksa, Galapagos, CHDR, Novartis, UCB, all paid to the institution. Payment or

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APPENDIX 1

Table A1. Nerves innervating the joints of the hand

Joint	Nerve	Branches
CMCJ-I	Radial	Superficial branch Sensory branch
	Median nerve	Thenar branch Palmar cutaneous branch
	Lateral antebrachial cutaneous nerve	Cruveilhier branch
PIPJ	Radial and median nerves	Dorsal and palmar digital nerves
DIPJ	Radial and median nerves	Dorsal and palmar digital nerves
MCPJ	Radial and median nerves	Dorsal and palmar digital nerves
	Radial nerve	Superficial branch
	Ulnary nerve	Motor branch Dorsal branch Deep branch

Anatomical description of innervation of the hand joints

CMCJ-I

The CMCJ-I is often described as the trapeziometacarpal joint in anatomical literature. The nerves supplying the CMCJ-I are branches of the radial nerve (specifically the superficial and sensory branch), branches of the median nerve (specifically the palmar cutaneous en thenar branches) and a branch of the lateral antebrachial cutaneous nerve (named the Cruveilhier branch). The last of these originates from the musculocutaneous nerve and runs along the radial side of the forearm down towards the hand. (11)

PIPJ

Innervation of the PIPJ is supplied by branches of the digital nerves. Up to four digital nerves can be present (two dorsal and two palmar, further divided into ulnar and radial based on their position relative to the phalanx), which run parallel to the phalanxes in the digits after originating from joining branches of the radial and median nerves. (15) All of these nerves have been described to give off branchlets innervating the PIPJ, although reports on the dorsal nerves vary. (11, 12, 14)

DIPJ

Nerves innervating this joint originate from the digital nerves. Studies agree that branches from the palmar digital nerve innervate the DIPJ. Reporting on the innervation by branches from the dorsal digital nerves varies, but this has also been described. (11-13)

MCPJ

The MCPJ-I has been described as being innervated by branchlets of the palmar digital nerves. The other four MCPJs additionally receive branches from the dorsal digital nerves, as well as the motor branch, dorsal branch and deep branch of the ulnary. The superficial branch of the radial nerve has also been described to innervate MCPJs. (11-14)

APPENDIX 2

Search strategy Pubmed

(“Hand”[Mesh] OR “Hand Joints”[Mesh] OR “Finger Joint”[Mesh] OR “Carpal Joints”[Mesh] OR “hand”[tiab] OR “hands”[tiab] OR “intermetacarp*”[tiab] OR “finger*”[tiab] OR “carpal”[tiab] OR “intercarp*”[tiab] OR “carpometacarp*”[tiab] OR “metacarpophalang*”[tiab] OR “thumb”[tiab] OR “thumbs”[tiab] OR “metacarp*”[tiab] OR “trapeziometacarp*”[tiab] OR “first metacarpal-carp*”[tiab] OR “carpometacarp*”[tiab] OR “interphalang*”[tiab] OR “scaphotrapeziotrapezoid*”[tiab]) AND (“Osteoarthritis”[Mesh] OR “osteoarthr*”[tiab] OR “osteo-arthr*”[tiab] OR “degenerative arthrit*”[tiab] OR “rhizarthros*”[tiab] OR “arthros*”[tiab] OR “Heberden”[tiab] OR “Bouchard”[tiab]) AND (“Denervation”[Mesh] OR “denervat*”[tiab] OR “nerve excision*”[tiab] OR “nerve ablation*”[tiab]OR “nerve exeresis”[tiab] OR “neurectom*”[tiab] OR “neuronectom*”[tiab] OR “radiculectom*”[tiab])

Search strategy Ovid

((exp hand/ or (hand or hands or intermetacarp* or finger* or carpal or intercarp* or carpometacarpal or thumb or thumbs or metacarp* or trapeziometacarp* or first metacarpal carp* or carpometacarp* or interphalang* or scaphotrapeziotrapezoid*).ti,ab,kw.) and (osteoarthritis/ or (osteoarthr* or osteo arthr* or degenerative arthrit* or rhizarthros* or arthros* or Heberden or bouchard).ti,ab,kw.) or (exp hand osteoarthritis/ or hand osteoarthr*.ti,ab,kw.)) and (exp denervation/ or exp neurectomy/ or (denervat* or nerve excision* or nerve ablation* or nerve exeresis or neurectom* or neuronectom* or radiculectom*).ti,ab,kw.)

Search strategy Cochrane

(hand or hands or intermetacarpal or finger* or carpal joint* or carpometacarapal or metacarpophalangeal or thumb or metacarpus or trapeziometacarpal or interphalangeal or scaphotrapeziotrapezoid*) AND (osteoarthr* or degenerative arthritis or rhizarthros* or arthros* or heberden or bouchard) AND (denervat* or neurectom*)

APPENDIX 3

Table A2. Risk of bias assessment of non-randomized clinical trial

Item	Salibi et al. (23) Risk
Bias due to confounding	Serious
Bias in selection of participants into the study	Low
Bas in classification of interventions	Low
Bias due to deviations from intended interventions	Serious
Bias due to missing data	Serious
Bias in measurement of outcomes	Serious
Bias in selection of reported results	Low
Overall risk of bias	Serious

APPENDIX 4

	A1. Wagner incision	**A2. Transverse incision**	**A3. Radial incision**	**A4. Palmar transverse incision**
CMCJ-I				
	A5. Dorsal transverse incision of first interosseous space	**A6. Dorsal straight incision of fourth extensor compartment**		
CMCJ-I				
	A7. Brunner Incision	**A8.1 Double lateral incision**	**A8.2 Double lateral incision**	**A9. Dorsal incision for PIPJ denervation**
PIPJ				
	A10. Skin flap			
DIPJ				
	A11. Brunner incision	**A12. Chevron incision**	**A13. Dorsal straight incision**	
MCPJ