EFORT open reviews

EFORT Open Reviews (2024) **9** 625–631
https://doi.org/10.1530/EOR-23-0211

HAND & WRIST

Bias in published randomized trials that compare collagenase injection with percutaneous needle fasciotomy in the treatment of Dupuytren disease: a systematic review

David Eckerdal[1,2,*], Hendrik Pakosta[1,*], Muhanned Ali[1,2] and Isam Atroshi[1,2]

[1]Department of Orthopedics, Hässleholm-Kristianstad Hospitals, Hässleholm, Sweden
[2]Department of Clinical Sciences - Orthopedics, Lund University, Lund, Sweden

Correspondence should be addressed to D Eckerdal Email david.eckerdal@med.lu.se

*(D Eckerdal and H Pakosta contributed equally to the study and are joint first authors)

- *Purpose:* Controversy exists regarding the comparative efficacy of collagenase injection and percutaneous needle fasciotomy in the treatment of Dupuytren contracture. The randomized controlled trials (RCTs) that have compared the two treatment methods have reported results mostly implying similar treatment efficacy, durability, and complications. We aimed to review these RCTs regarding methodical quality and risk of bias.
- *Methods*: We searched PubMed and Cochrane Library databases up to May 2023. All RCTs comparing collagenase injection with needle fasciotomy were included. Eligible articles were reviewed by two researchers, of whom one was blinded to each article's title, authors, year of publication, journal, and source of the studies. To assess methodical quality, we used the modified Jadad scale yielding a score of 0 (lowest quality) to 5 (highest quality). We assessed risk of bias with the Cochrane risk-of-bias tool (RoB 2).
- *Results*: Five studies were eligible, comprising 204 patients treated with collagenase injection and 209 patients treated with needle fasciotomy. The modified Jadad score ranged from 1 to 2 points in the five studies, and the overall risk of bias was high in all studies. Pretrial protocols could be retrieved for only two studies, revealing important discrepancies with the published articles.
- *Conclusion*: The published RCTs that have compared collagenase injection with needle fasciotomy in the treatment of Dupuytren contracture demonstrate a high risk of bias.

Keywords: Dupuytren disease; risk of bias; collagenase; percutaneous needle fasciotomy

Background

Treatment of Dupuytren's disease (DD) aims to reduce finger joint contractures through removal or disruption of the Dupuytren cords, with surgical fasciectomy having been the mainstay of treatment (1). Due to the postoperative morbidity associated with fasciectomy, less invasive techniques such as collagenase injection and percutaneous needle fasciotomy (PNF) have been increasingly used for treating DD (1, 2). Both these methods have been shown to be safe with good short-term efficacy (3, 4, 5, 6). Collagenase injection is a pharmacological treatment in which a mixture of two strands of collagenase is used to enzymatically divide

Published by Bioscientifica Ltd.
www.efortopenreviews.org

EFORT Open Reviews (2024) **9** 625–631
https://doi.org/10.1530/EOR-23-0211

type 1 and type 3 collagen in the Dupuytren cord. The finger is then manipulated into extension, disrupting the cord (3, 7). In PNF, a needle is used to divide the Dupuytren cord at one or more locations in the palm, allowing for finger extension (6). Because they differ substantially in initial treatment costs, a comparison of their efficacy has acquired importance. Randomized controlled trials (RCTs) are the gold standard for assessing treatment efficacy, providing a high level of evidence (8). They can, however, be influenced by various sources of bias. The validity of the reported results of an RCT is directly dependent on the design and conduct of the trial. The RCTs comparing collagenase injection with PNF have reported results implying similar treatment efficacy, durability, and complications (2, 9, 10, 11, 12).

We aimed to review published RCTs that have compared collagenase injection with PNF with regard to methodical quality and risk of bias.

Materials and methods

We conducted a structured literature search following the guidelines described in the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement (13). The search was performed, with the help of a librarian, in PubMed (MEDLINE) and Cochrane Central Register of Controlled Trials databases using the search terms 'Dupuytren', 'Collagenase', and 'Needle', and the search was limited to RCTs. The primary search was performed in September 2021, and an updated search was performed in May 2023. All studies published before May 2023 in English were screened. We performed manual searches for references of prior relevant systematic reviews for additional relevant studies and subjected them to a similar selection process.

Screening

Abstract screenings were performed by two reviewers, and full-text screenings were performed by the same two reviewers. All prospective randomized clinical trials in which one arm was PNF and the other was collagenase injection were included. Articles were excluded if they were follow-up studies to previously published articles utilizing the same patient population.

Quality and risk-of-bias assessments

All articles were independently reviewed by two reviewers, of whom one was blinded to each article's title, authors, year of publication, journal, and other information referring to the source of the research. This was done by masking these details in each manuscript. In the presence of disagreements between the researchers, a consensus was achieved after reassessment and discussion, and a third reviewer was consulted in case of continuous disagreement. To assess the quality of reporting, we used the Jadad scale as modified by Gummesson *et al.* (14, 15), and to assess the risk of bias, we used version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2) (16).

The modified Jadad scale assesses the randomization method, blinding, and dropouts/withdrawals, yielding a score from 0 (lowest quality) to 5 (highest quality). The RoB 2 is structured into 22 items in five domains (randomization, blinding, availability of data, outcome analysis, and adherence to a pre-specified protocol) focusing on different aspects of trial design, conduct, and reporting relevant to the risk of bias. An algorithm is used for judgment of risk of bias for each domain, and the results are expressed as 'Low', 'Some Concerns', or 'High' risk of bias. An overall judgment about the study using the same scoring and a separate algorithm was given based on the results from the individual domains.

To examine possible discrepancies between the published articles and the original study protocols that may affect the validity of the results, we attempted to retrieve the pre-trial study protocols that were submitted to the Ethics Review Boards. In case the Ethics Review Board did not provide the protocol, we then sent an e-mail to the article's authors and asked them to provide the protocol. We also sought to determine whether the study protocol was registered in an RCT registry and the time of registration in relation to the start date of the trial.

Analyses

For each article, two assessors extracted data about the number of patients that were screened, the number that were included, and the number that completed end-point analysis in each cohort. We also extracted data about mean age, number of patients in each cohort, the gender distribution in the cohorts, the joints that were treated, and the main result that was reported. We then calculated the Jadad score for each domain as well as the final score. Similarly, the different domains were graded for RoB, and these together with the overall RoB grade are presented in a standard diagram. One of the authors compared the pre-trial protocols and any RCT registry protocols with the published studies for possible discrepancies. We also examined the reported baseline characteristics of the patients randomized to the two treatment methods and analyzed potential imbalances that may favor one of the methods (17).

Results

The initial search for RCTs in MEDLINE and Cochrane Central Register provided 11 studies after exclusion of 94 studies that were not RCTs (Fig. 1). After screening,

EFORT Open Reviews (2024) **9** 625–631
https://doi.org/10.1530/EOR-23-0211

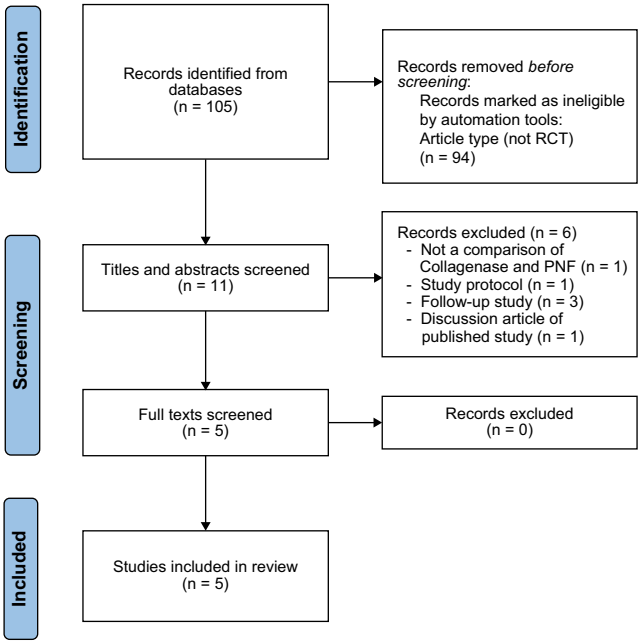

Figure 1

Flow diagram of the literature search.

one article was excluded because it was not an RCT comparing collagenase injection with PNF, and another article was excluded because it was a study protocol. Of the remaining nine published studies, three were excluded as they involved follow-up of previously published studies and one was excluded as it was a discussion article of a previously published RCT. After a full-text review, the remaining five studies were found eligible for inclusion.

Characteristics of the studies

The five eligible studies, hereafter referred to as study I (2), study II (9), study III (11), study IV (10), and study V (12), originated from Sweden (two studies), Denmark (two studies), and Japan (one study). The studies included 204 patients treated with collagenase injection and 209 patients treated with PNF (Table 1).

Modified Jadad scale

The modified Jadad score ranged from 1 to 2 points. All articles were described as randomized. In study I no description of the randomization method is reported. In study II the method of randomization was judged to be inappropriate because randomization was reportedly done 'in groups of 10 patients treated in 1 cycle with 5 patients randomized to PNF and collagenase injection each', which would potentially enable identification of the group to which the next patient will be assigned. Study V does not provide information regarding how the randomization sequence was created but also utilized block randomization 'allocating blocks of 15 patients equally to both groups'. With regard to blinding, study II was the only study described as blinded and the blinding method was deemed appropriate. Study V is described as blinded, but the blinding method is not described and the examiner at the early follow-up (30 days) was not blinded. Withdrawals/dropouts are described in study I, but the study provides no data about the number of patients screened and reasons for any exclusions. Studies II and III state that 716 and 772 screened patients, respectively, were excluded without providing the reasons for the exclusions. Study IV reported that 18 screened patients were excluded but without description. Study V states that 828 patients were excluded after screening but does not provide the reasons for exclusion. We therefore considered these unexplained pre-randomization exclusions as non-described withdrawals in the Jadad score (Table 2).

Risk of bias

All five studies were judged to have an overall high risk of bias (Fig. 2). Study I received high risk in one domain, some concerns in two domains, and low risk in two domains. Study II received high risk in two domains, some concern in one domain and low risk in two domains. Study III received high risk in one domain, some concern in three domains, and low risk in one domain. Study IV received high risk in one domain, some concern in two domains, and low risk in two domains. Study V received high risk in one domain, some concern in two domains, and low risk in two domains. Thus, the combined overall risk of bias for the five studies was high (Fig. 3).

Discrepancies with pretrial study protocols

Pretrial study protocols for study I and study II were retrieved from the Swedish Ethical Review Authority. For the remaining 3 studies, the protocols could not be retrieved from the respective Ethics Review Boards, and the corresponding authors did not respond to our e-mail request. In both studies for which the pretrial protocols could be reviewed, discrepancies were found with the published articles. In study I, the pretrial protocol states that patients with a palpable cord causing contracture in metacarpophalangeal (MCP) or proximal interphalangeal (PIP) joints were eligible for inclusion if the contracture was 'large enough'. This was later changed in the published article to DD 'primarily affecting the MCP joint'. In addition, the published article states that the inclusion criteria were total extension deficit of 30–135° with PIP contracture less than 60°, but no such specification was stated in the pretrial protocol, stating only that if the contracture was 'too small' the patient was to be excluded. In study II, the pretrial protocol states that contractures in '1 or more fingers' are eligible for inclusion, but in the published article this has been changed to a single finger with strict exclusion if more than 1 finger was affected. Furthermore, it is

EFORT Open Reviews (2024) **9** 625–631
https://doi.org/10.1530/EOR-23-0211

Table 1 Characteristics of the five studies.

	Study				
Characteristics	I (2)	II (9)	III (11)	IV (10)	V (12)
First author	Scherman	Strömberg	Skov	Abe	Jørgensen
Publication year	2016	2016	2017	2019	2022
Country of origin	Sweden	Sweden	Denmark	Japan	Denmark
Study period	December 2012–November 2013	October 2012–May 2014	March 2012–October 2013	October 2014–May 2016	2013–2015
Number of patients					
Screened	Unknown	856	772	97	905
Randomized					
Collagenase:PNF	38:45[†]	69:71	29:21	36:36	37:40
End-point analyzed					
Collagenase:PNF	37:41	67:71	23:19	36:34	32:36
Sex, men *n* (%)					
Collagenase	36 (95)[†]	56 (81)	21 (72)	?[‖,§]	24 (75)
PNF	36 (80)[†]	63 (89)	18 (85)	?[‖,§]	26 (72)
Age* (years)					
Collagenase	67[†,↑]	66 (42–80)	62 (58–66)	70[†,‖]	70 (50–90)
PNF	67[†,↑]	69 (29–86)	67 (64–70)	67[†,‖]	65 (48–91)
Follow-up time (years)	1	1	2	3	3
Treated joint	MCP	MCP	PIP	MCP and/or PIP	MCP
Main result reported	Similar reduction of contracture	No significant difference	Collagenase not superior in clinical improvement and complications	No significant difference	Less recurrence and disease progression after collagenase

[†]No standard deviation or other distribution measure reported; [↑]Data from the 3-month follow-up; [‖]Data from the 3-year follow-up; [§]Conflicting data in the published article, stating that the collagenase group included '36 patients' comprising '36 men and 3 women', and the PNF group included '34 patients' comprising '31 men and 2 women'; *data is either mean or median (range).
MCP, metacarpophalangeal joint; PIP, proximal interphalangeal joint; PNF, percutaneous needle fasciotomy.

stated in the pretrial protocol that contractures in both MCP and PIP joints are eligible for inclusion, which has later been changed in the published article that only patients with isolated MCP contractures were included unless the patient 'accepted that any PIP contracture would be left untreated'.

Trial registration

Trial registration was found for study III, registered in https://clinicaltrials.gov/ before patient inclusion commenced according to the published paper. The information provided in the trial registration did not differ from that later published in the article. A trial registration for Study II was found in a local database, but the information provided is brief and does not clearly specify any inclusion or exclusion criteria other than patients affected by DD in a single finger are eligible for inclusion. As stated above, this differs from the pretrial study protocol. The registration was created about 4 years after patient enrollment had started and 5 months after the manuscript was first submitted to the journal in which it was published. No trial registration could be found for study IV and study V.

Imbalance in baseline characteristics

In study III, there was an unexplained imbalance in the number of patients included in the collagenase and PNF groups (29 vs 21 patients, respectively). Also, the number of patients treated for contracture in the small finger PIP joint was in the collagenase group 28 of 29 (97%) and in the PNF group 15 of 21 (71%), a statistically significant difference (Fisher's exact test $P = 0.033$).

Discussion

Treatment of DD and recommendations regarding preferred treatment methods have been frequently discussed and debated after the introduction of collagenase injection, more than a decade ago. A Cochrane review of surgical treatments, including needle fasciotomy, found that the available evidence was insufficient to show the relative superiority of different surgical procedures, but collagenase treatment was not included (18).

In the present study, five peer-reviewed published studies comparing collagenase injection with PNF

EFORT Open Reviews (2024) **9** 625–631
https://doi.org/10.1530/EOR-23-0211

Table 2 Modified Jadad scale.

	Study				
Scale parameters	I (2)	II (9)	III (11)	IV (10)	V (12)
Randomization					
Study described as randomized	1	1	1	1	1
Method described and appropriate	0	0	1	1	0
Method described but inappropriate	0	−1	0	0	−1
Method not described	−1	0	0	0	0
Blinding					
Study described as double or single blind	0	1	0	0	1
Method described and appropriate	0	1	0	0	0
Method described but inappropriate	0	0	0	0	0
Method not described	0	0	0	0	0
Study not described as blind	0	0	0	0	0
Withdrawals and dropouts					
Described	1	0	0	0	0
Not described	0	0	0	0	0
Total score	1	2	2	2	1

were identified through literature search. All studies except study V showed similar outcomes for PNF and collagenase. Study III showed a slightly higher recurrence rate after collagenase compared to PNF as well as a higher number of minor complications in the collagenase group. However, study III had a statistically significant imbalance of baseline characteristics, where 97% of patients in the collagenase group received treatment for small finger PIP joint contracture (17). Furthermore, since PIP joint contractures of the small finger are more difficult to treat and more prone to recur (5, 19, 20) this imbalance favors PNF. Study V comparing collagenase with PNF in isolated MCP joint contracture showed that, at 3 years, contracture recurrence or progression leading to further treatment occurred in 17 of 36 patients (47%) in the PNF group compared to 6 of 32 patients (19%) in the collagenase group ($P = 0.007$) (12).

A previous systematic review of collagenase injection and PNF included three RCTs (also included in our review) and two retrospective cohort studies but with different assessment results (21). Judging the risk of bias is a complex procedure and requires meticulous reasoning and adequate knowledge of the subject of the study. For example, it is important that the evaluators have knowledge of the fact that it is easier to treat MCP joint contractures than PIP joint contractures and that the outcomes are generally better. Similarly, it is well known that small finger PIP joint contractures are more difficult to treat than other joints, and the outcomes are generally worse (5, 19, 20). The changes made during the conduct of the trial in relation to the pretrial protocol seem to suggest that the researchers aimed to avoid including patients with more severe PIP joint contractures that are specifically not suitable for PNF (either technically difficult or poor expected outcome) whereas collagenase can be used to treat severe PIP joint contractures. Studies I and II were publicized as having compared PNF and collagenase in the treatment of DD in general, despite that the results can only apply to the treatment of MCP joint contractures. In study III that involved PIP joint treatment, the authors did not respond to our request for the pretrial protocol, but the detected imbalance in the number of small fingers treated in each group favored PNF. Besides, there was an unexplained imbalance in the number of patients included in the collagenase and PNF groups (29 vs 21 patients, respectively).

All included studies scored low on the modified Jadad scale indicating low quality. All five studies were described as randomized, yet study I only stated 'sealed envelopes' without specification of how the sequence of randomization was generated. Thus, since it is impossible to know whether the method of randomization was concealed in study I and since study II had an inappropriate method of randomization, these studies cannot be considered as truly randomized. The

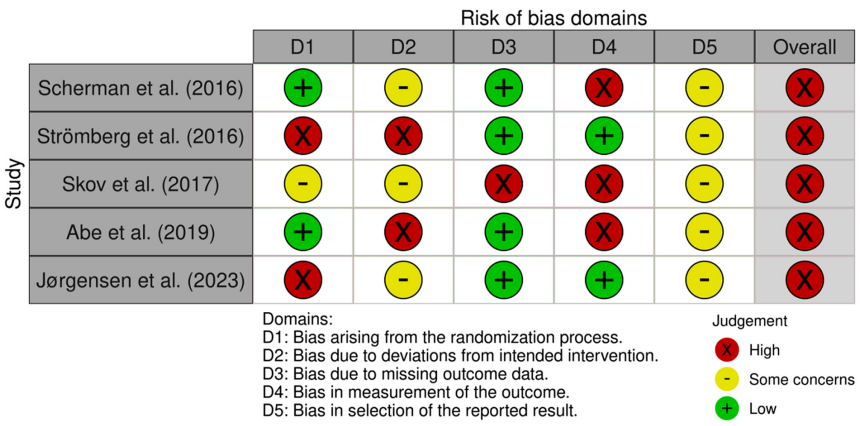

Figure 2

Risk of bias of the included studies according to the domains (2, 9, 10, 11, 12).

EFORT Open Reviews (2024) **9** 625–631
https://doi.org/10.1530/EOR-23-0211

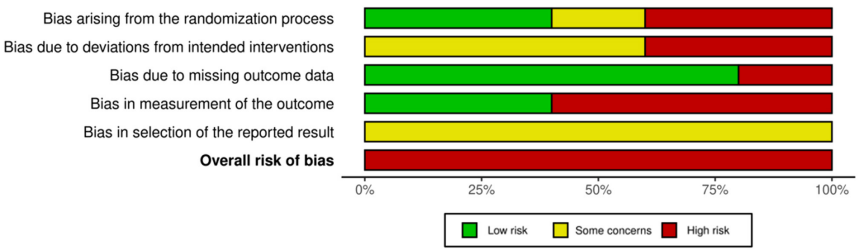

Figure 3

Risk-of-bias summary plot for the included studies.

modified Jadad scale also assesses blinding of studies, which is generally difficult in surgical trials but accepts blinding of outcome assessors (22). Despite this, only study II and study V were described as blinded and received points accordingly. However, study V was not blinded at the early follow-up (30 days), and they do not describe the blinding method. More surprisingly, none of the studies described the reasons for exclusions which is standard reporting according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines (8). Study I reported the number of patients included but not the number of patients screened. Studies II and III reported that more than 700 patients were screened, and the majority were excluded without providing the reasons for exclusions. Considering the few exclusion criteria stated in these studies, it would seem implausible that such a large number of patients with DD were ineligible for inclusion. Hypothetically, considering the nature of the treatments compared, the surgeon could exclude patients that are eligible but expected to have a poor outcome with one of the treatments. This would be a major source of bias that is not captured by post-randomization dropouts and becomes even more apparent since inconsistencies were found between pretrial protocols and published methodologies for study I and study II. As both these trial designs had been altered from initially stating in the protocols that contractures of both MCP and PIP joints were eligible for inclusion (primarily MCP joints but also PIP joints with a contracture of <60° in study I and only MCP joints in study II). It seems likely that a substantial number of patients with PIP joint contractures were excluded before randomization. It has previously been established that PIP joints have less favorable results than MCP joints after PNF, which would indicate that these exclusions constitute a major source of bias (5).

Another aspect that could be relevant is the treatment preference at the study center where the trial was conducted. Studies I, II, and III appear to have been conducted in centers that had used PNF routinely as the preferred method of treatment before collagenase was available. Allegiance bias has been recognized as another type of bias in randomized trials (23). Thus, the researchers' treatment preferences may have influenced the conduct of these studies. A problem with these trials is that, in order to be included, the patient had to be suitable for both collagenase and PNF, and it is unknown whether, for example, patients were excluded by the examining surgeon because their cords were too simple to justify the cost of collagenase or were too thick that PNF was not believed to be effective.

The high risk of bias found in the included studies highlights the need for quality assessment of current and future RCTs to ensure correct interpretation of results. It also highlights the need for correct reporting of RCTs in accordance with the CONSORT statement (8).

Previous reviews have approached the matter (21, 24), but to our knowledge, this is the first study that primarily investigates the methodological quality of RCTs comparing collagenase injection with PFN in the treatment of DD. Our results regarding the quality of the published studies would be helpful when proposing future practice guidelines, particularly since the results of these published RCTs may apply to the treatment of isolated MCP joint contractures but cannot be generalized to more severe DD with PIP involvement.

The limitations of this study include possible interobserver variability with regard to the Cochrane risk-of-bias tool, which may explain why our results differ from previous studies. Furthermore, the literature search was restricted to two databases, and no additional manual searches were conducted. However, the other published systematic reviews did not identify other potentially eligible studies. Another possible limitation is that the published follow-up articles of study I and study II were not included in the analysis. However, follow-up articles usually focus on results and do not add information to the initially reported methodology.

In conclusion, this study has revealed important limitations in the methodological quality and high risk of bias in published RCTs comparing collagenase injection with PNF in the treatment of DD. It is possible that the results of these published trials should be interpreted in light of these limitations when applied to clinical practice.

ICMJE Conflict of Interest Statement
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the study reported.

Funding Statement
This study did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

EFORT Open Reviews (2024) **9** 625–631
https://doi.org/10.1530/EOR-23-0211

Author contribution statement

IA designed the study. IA and DE performed the systematic search and screened for inclusion. HP and DE extracted the data. HP, DE, and IA analyzed all data. HP and DE wrote the manuscript with support from IA and MA. All authors reviewed the manuscript for important intellectual content and approved the final version of the manuscript.

Acknowledgements

The authors wish to thank Ylva Sundin, librarian at Kristianstad University, for her help with the literature search, and Jesper Nordenskjöld, MD, PhD, for his comments on the manuscript.

References

1 Soreide E, Murad MH, Denbeigh JM, Lewallen EA, Dudakovic A, Nordsletten L, van Wijnen AJ & Kakar S. Treatment of Dupuytren's contracture: a systematic review. *Bone and Joint Journal* 2018 **100–B** 1138–1145. (https://doi.org/10.1302/0301-620X.100B9.BJJ-2017-1194.R2)

2 Scherman P, Jenmalm P & Dahlin LB. One-year results of needle fasciotomy and collagenase injection in treatment of Dupuytren's contracture: a two-centre prospective randomized clinical trial. *Journal of Hand Surgery* 2016 **41** 577–582. (https://doi.org/10.1177/1753193415617385)

3 Hurst LC, Badalamente MA, Hentz VR, Hotchkiss RN, Kaplan FTD, Meals RA, Smith TM, Rodzvilla J & CORD I Study Group. Injectable collagenase Clostridium histolyticum for Dupuytren's contracture. *New England Journal of Medicine* 2009 **361** 968–979. (https://doi.org/10.1056/NEJMoa0810866)

4 Krefter C, Marks M, Hensler S, Herren DB & Calcagni M. Complications after treating Dupuytren's disease. A systematic literature review. *Hand Surgery and Rehabilitation* 2017 **36** 322–329. (https://doi.org/10.1016/j.hansur.2017.07.002)

5 van Rijssen AL, Ter Linden H & Werker PMN. Five-year results of a randomized clinical trial on treatment in Dupuytren's disease: percutaneous needle fasciotomy versus limited fasciectomy. *Plastic and Reconstructive Surgery* 2012 **129** 469–477. (https://doi.org/10.1097/PRS.0b013e31823aea95)

6 van Rijssen AL & Werker PM. Percutaneous needle fasciotomy in Dupuytren's disease. *Journal of Hand Surgery* 2006 **31** 498–501. (https://doi.org/10.1016/j.jhsb.2006.03.174)

7 Denkler KA, Park KM & Alser O. Treatment options for Dupuytren's disease: tips and tricks. *Plastic and Reconstructive Surgery* 2022 **10** e4046. (https://doi.org/10.1097/GOX.0000000000004046)

8 Schulz KF, Altman DG & Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *Journal of Pharmacology and Pharmacotherapeutics* 2010 **1** 100–107. (https://doi.org/10.4103/0976-500X.72352)

9 Strömberg J, Ibsen-Sörensen A & Fridén J. Comparison of treatment outcome after collagenase and needle fasciotomy for Dupuytren contracture: a randomized, single-blinded, clinical trial with a 1-year follow-up. *Journal of Hand Surgery* 2016 **41** 873–880. (https://doi.org/10.1016/j.jhsa.2016.06.014)

10 Abe Y. Comparison of treatment outcomes after collagenase injection and percutaneous needle fasciotomy for Dupuytren's contracture: objective and subjective comparisons with a 3-year follow-up. *Plastic and Reconstructive Surgery* 2020 **145** 1464–1474. (https://doi.org/10.1097/PRS.0000000000006828)

11 Skov ST, Bisgaard T, Søndergaard P & Lange J. Injectable collagenase versus percutaneous needle fasciotomy for Dupuytren contracture in proximal interphalangeal joints: a randomized controlled trial. *Journal of Hand Surgery* 2017 **42** 321–328.e3. (https://doi.org/10.1016/j.jhsa.2017.03.003)

12 Jørgensen RW, Jensen CH & Jørring S. Three-year recurrence of Dupuytren contracture after needle fasciotomy or collagenase injection: a randomized controlled trial. *Plastic and Reconstructive Surgery* 2023 **151** 365–371. (https://doi.org/10.1097/PRS.0000000000009847)

13 Moher D, Liberati A, Tetzlaff J, Altman DG & PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Medicine* 2009 **6** e1000097. (https://doi.org/10.1371/journal.pmed.1000097)

14 Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ & McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Controlled Clinical Trials* 1996 **17** 1–12. (https://doi.org/10.1016/0197-2456(95)00134-4)

15 Gummesson C, Atroshi I & Ekdahl C. The quality of reporting and outcome measures in randomized clinical trials related to upper-extremity disorders. *Journal of Hand Surgery* 2004 **29** 727–734. (https://doi.org/10.1016/j.jhsa.2004.04.003)

16 Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Elridge SM, *et al.* RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019 **366** l4898. (https://doi.org/10.1136/bmj.l4898)

17 Stang A & Baethge C. Imbalance *p* values for baseline covariates in randomized controlled trials: a last resort for the use of *p* values? A pro and contra debate. *Clinical Epidemiology* 2018 **10** 531–535. (https://doi.org/10.2147/CLEP.S161508)

18 Rodrigues JN, Becker GW, Ball C, Zhang W, Giele H, Hobby J, Pratt AL & Davis T. Surgery for Dupuytren's contracture of the fingers. *Cochrane Database of Systematic Reviews* 2015 **2015** CD010143. (https://doi.org/10.1002/14651858.CD010143.pub2)

19 Nordenskjold J, Lauritzson A, Akesson A & Atroshi I. Collagenase injections for Dupuytren disease: 3-year treatment outcomes and predictors of recurrence in 89 hands. *Acta Orthopaedica* 2019 **90** 517–522. (https://doi.org/10.1080/17453674.2019.1663472)

20 Peimer CA, Blazar P, Coleman S, Kaplan FTD, Smith T & Lindau T. Dupuytren contracture recurrence following treatment with collagenase Clostridium histolyticum (CORDLESS [Collagenase Option for Reduction of Dupuytren Long-Term Evaluation of Safety Study]): 5-year data. *Journal of Hand Surgery* 2015 **40** 1597–1605. (https://doi.org/10.1016/j.jhsa.2015.04.036)

21 Hirase T, Suresh R, Cotton MO, Han A, Burn MB, Harris JD & Liberman SR. Percutaneous needle fasciotomy versus collagenase injection for Dupuytren's contracture: a systematic review of comparative studies. *Journal of Hand and Microsurgery* 2021 **13** 150–156. (https://doi.org/10.1055/s-0040-1721876)

22 Tadjerbashi K, Rosales RS & Atroshi I. Intervention randomized controlled trials involving wrist and shoulder arthroscopy: a systematic review. *BMC Musculoskeletal Disorders* 2014 **15** 252. (https://doi.org/10.1186/1471-2474-15-252)

23 Dragioti E, Dimoliatis I, Fountoulakis KN & Evangelou E. A systematic appraisal of allegiance effect in randomized controlled trials of psychotherapy. *Annals of General Psychiatry* 2015 **14** 25. (https://doi.org/10.1186/s12991-015-0063-1)

24 Obed D, Salim M, Schlottmann F, Bingoel AS, Panayi AC, Dastagir K, Vogt PM & Koenneker S. Short-term efficacy and adverse effects of collagenase Clostridium histolyticum injections, percutaneous needle fasciotomy and limited fasciectomy in the treatment of Dupuytren's contracture: a network meta-analysis of randomized controlled trials. *BMC Musculoskeletal Disorders* 2022 **23** 939. (https://doi.org/10.1186/s12891-022-05894-6)