Medicine®

Effectiveness and safety of moxibustion for De Quervain disease
A protocol for systematic review and meta-analysis

Min Liu, PhD, Meinian Liu, MM, Wenlong Yang, MM, Ou Mei, PhD, Hanting Xia, PhD, Hong Tu, MM, Li Wang, PhD, Xuyong Deng, PhD, Fengyun Yang, MM*

Abstract

Background: De Quervain disease (DQD) is a common clinical disease. As a strainingdisease, DQD is more common in women who frequently engage in manual operations. The main clinical symptoms are local pain and dysfunction. Many clinical studies have reported that moxibustion has a good effect on the treatment of DQD, but there is no relevant systematic review. So the purpose of this study is to evaluate the effectiveness and safety of moxibustion in treating DQD.

Methods: The following 8 electronic databases will be searched, including PubMed, Embase, the Cochrane Library, China National Knowledge Infrastructure (CNKI), Web of Science, Chinese Scientific Journal Database (VIP), Wanfang Database, and Chinese Biomedical Literatures Database (CBM) from their inception to 1 October 2020 without any restrictions. Researchers retrieve the literature and extracted the data, evaluation of research methods, quality of literature. The outcomes will include a visual analogue scale, Finkelsteins, resisted thumb extension, total effective rate, incidence of any adverse events. We use the Cochrane Risk of a bias assessment tool to evaluate methodological qualities. Data synthesis will be completed by RevMan 5.3.0.

Results: We will show the results of this study in a peer-reviewed journal.

Conclusions: This meta-analysis will provide reliable evidence for moxibustion treatment of DQD.

INPLASY registration number: INPLASY2020100111.

Abbreviations: CI = confidence interval, DQD = de Quervain disease, RCT = randomized controlled trials, RR = risk ratios, WMD = weight mean differences.

Keywords: de quervain disease, moxibustion, protocol, randomized controlled trial, systematic review and meta-analysis

1. Introduction

De Quervain diseas (DQD) is a clinical symptom caused by frequent movement of the thumb or wrist, local exudation,

oedema, and fibrosis of the tendon and tendon sheath, resulting in obstruction of the sliding of the tendon in the tendon sheath.[1] The disease mostly occurs in people between 30 and 50 years old.[2] The incidence rate of men is 0.05%, and the incidence rate of women is 1.3%.[3] The clinical manifestations are finger-snapping with obvious pain, in severe cases, the affected finger flexes and dare not move. Pain is often on the palm side of the metacarpophalangeal joints. Painful nodules can be palpated at the distal palmar transverse lines during physical examination. It moves up and down with the flexor tendons during a physical examination and can cause bounce. Each fingers incidence frequency was the most in the middle and ring fingers, followed by the thumb and the little finger the least. DQD is manifested in pain at the radius styloid process, local tenderness, and sometimes painful nodules.[4] The diagnosis is mainly pain, tenderness, and localized swelling at the carpal radius stem. Pain worsens when the thumb and wrist joints move, and Finkelstein's positive.[5]

The current main treatments include corticosteroid injections,[6,7,8] NSAIDs, stretching, and strengthening,[9,10] a high success rate has been shown in the treatment of DQD with corticosteroid injection,[11] However, the injection may be complicated by local depigmentation, postinjection flare, atrophy of subcutaneous fat, infection, and tendon rupture.[2] Moxibustion, as a complementary and alternative therapy, has been developed in China for thousands of years. Moxibustion has a relatively good effect in the treatment of DQD.[12] A large

number of clinical studies on the treatment of DQD with moxibustion have been reported, but there is no relevant systematic review. So this research aims to systematically and comprehensively evaluate the safety and efficacy of moxibustion in the treatment of DQD.

2. Methods

2.1. Study registration

This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on October 28, 2020 (registration number INPLASY2020100111). It could be obtained from https://inplasy.com/inplasy-2020–10-0111. This report will be conducted based on the preferred reporting items for systematic reviews and meta-analyses protocols (PRISMA) statement guidelines.[13]

2.2. Inclusion criteria

2.2.1. Study type. All randomized controlled trials (RCT) and quasi-RCTs study on moxibustion in the treatment of DQD will be included.

2.2.2. Participants. All patients included in the study were diagnosed with DQD, regardless of age, gender, race.

2.2.3. Type of intervention. The trail group uses moxibustion or combination therapy with other treatments. The acupuncture method, acupoint selection, and needles are not limited; the control group uses the corticosteroid injection, and other adjuvant treatments can be appropriately added. The trail group and the control group are not limited in terms of medication, dosage, and treatment course.

2.2.4. Type of outcome measures

2.2.4.1. Primary outcomes. Primary outcome measures will include:

1. The effective rate.
2. Visual analogue scale.

2.2.4.2. Secondary outcomes. Secondary outcome measures will include:

1. Finkelstein's
2. Resisted thumb extension.
3. Incidence of any adverse events.

2.3. Exclusion criteria

The following exclusion criteria are presented:

1. The same study or duplicated publications.
2. Case report.
3. Theoretical or basic research.
4. Unable to get available data through various means.

2.4. Search strategy

The following 8 electronic databases will be searched, including PubMed, Embase, the Cochrane Library, China National Knowledge Infrastructure (CNKI), Web of Science, Chinese Scientific Journal Database (VIP), Wanfang Database, and Chinese Biomedical Literatures Database (CBM) from their inception to October 2020 without any restrictions. We strictly follow the PRISMA[14] statement, The research only includes human subjects, The main search terms: "moxibustion," "de Quervain disease," and "randomized controlled trial." will be included. We use similar search strategies for all electronic databases. We will also search for eligible trial, which is unpublished or ongoing. The search strategy for PubMed is shown in Table 1.

2.5. Study selection

All literature retrieved from electronic databases will be imported into NoteExpress 3.2.0 software for category management, excluding double-checked and published literature. All researchers will discuss and define the selection criteria before selecting the literature. Two reviewers will independently assess the retrieved studies against the inclusion criteria. In the initial selection of studies, only titles and abstracts will be reviewed to exclude inappropriate publications. Studies that do not match will be removed to the trash folder in the software. Reasons for exclusion will be recorded as an Excel dataset. The next step will be to further evaluate the included studies by reading the full text. Two reviewers will check the reference list to identify trials that may have been missed. Two reviewers will cross-check the screening results. The reviewers, if they disagree, will resolve their disagreement by consensus. Any disagreement will be resolved by discussion between the 2 authors and the third author, arbitration, if necessary. The above process will be presented in the form of a PRISMA flowchart. (Fig. 1)

2.6. Data extraction and management

Data will be extracted independently from a pre-established data extraction table. The following basic information will be

Table 1

The search strategy used in the PubMed database.

| Search	Query
#1	"De Quervain Disease"[Mesh]
#2	((De Quervain Stenosing Tenosynovitis [Title/Abstract]) OR (Stenosing Tenosynovitis, De Quervain [Title/Abstract])) OR (De Quervain's Disease [Title/Abstract])
#3	#1 or #2
#4	"Moxibustion"[Mesh]
#5	(Moxabustion [Title/Abstract]) OR (Acupuncture [Title/Abstract])
#6	#4 or #5
#7	randomized controlled trial [Publication Type] OR randomized [Title/Abstract] OR placebo [Title/Abstract]
#8	#3 and #6 and #7
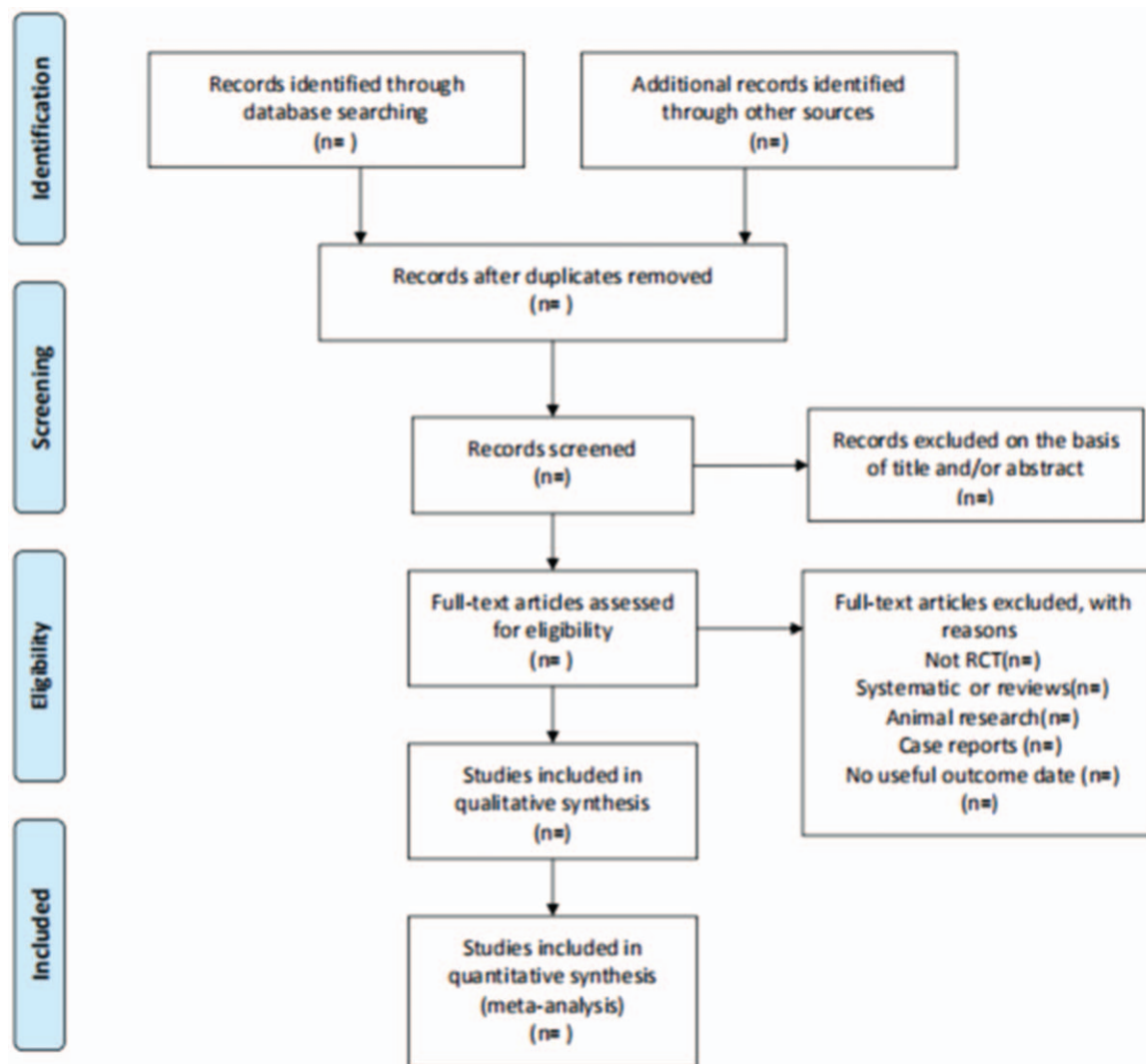
Figure 1. Flowchart of literature selection.

extracted: author, year, country, sample size, mean age, randomized method, intervention, control measures, follow-up time, outcome measures, and adverse effects. Three reviewers will cross-check the results. They are (Min Liu, Meinian Liu, and Wenlong Yang). If there is any disagreement, it will be negotiated or arbitrated by the fourth investigator (Fengyun Yang). Besides, the intention-to-treat analysis of this study will be used to address missing data. Data NoteExpress 3.2.0 and Excel 2007 software will be applied. To extract the eligible data. When vital data in the study are incomplete or missing, we will have the option to contact the first author or the corresponding author to obtain the data by phone or email.

2.7. Assessment of risk of bias in included studies

The risk of bias in the included studies will be assessed by 2 independent reviewers (Min Liu and Meinian Liu) using the assessment tool of Cochrane Reviewer's Handbook 5.0.24.[15] We will assess the risk of bias in the following areas: allocation sequence generation, allocation sequence concealment, blinding of personnel and outcome assessors, incomplete information.

Outcome data, selective reporting of outcomes, and other sources of data bias. The assessment will be divided into 3 levels: low risk, high risk, and Unclear Risk. Ambiguous items in the study will be queried by Contact the appropriate author for details. Any disagreement will be resolved through discussion with the third reviewer (Fengyun Yang).

2.8. Data synthesis
2.8.1. Measures of treatment effect. We will use RevManV.5.3.0 software for data analysis and quantitative data synthesis. Dichotomous data will be analyzed using risk ratios with 95% confidence intervals (95% CI). For continuous outcomes, we will analyze using the mean difference or standardized mean difference with 95% CI,[16] when fewer than 2 studies are included for each outcome measure, only descriptive analyses will be performed to summarize the results.

2.8.2. Heterogeneity analysis. Statistical heterogeneity between included studies will be assessed strictly according to the criteria ($P > .1$ and $I^2 < 50\%$) and displayed as a forest plot. When $P > .1$ and $I^2 < 50\%$, lower heterogeneity was analyzed

using a fixed-effects model; when $P < .1$ and $I^2 > 50\%$, higher heterogeneity was analyzed using a random-effects model. When the included studies' heterogeneity is significant, we will choose subgroup analysis or sensitivity analysis to search for possible sources clinically and methodologically.

2.8.3. Subgroup analysis. If sufficient data are available, we will conduct subgroup analyses based on the following themes: age, duration of treatment, study quality, type of intervention in the control or study group, and so on.

2.8.4. Sensitivity analysis. Sensitivity analysis will be used to validate the robustness of the review findings. We will consider several decision points in the systematic review process to implement the sensitivity review, such as sample size, missing data results, and methodological quality. Besides, the analysis will be repeated after excluding studies with low methodological quality.

2.8.5. Publication bias. When the number of eligible RCTs is $\geq$ 10,[17] publication bias will be detected using a funnel plot developed by Egger test.

2.8.6. Grading the quality of evidence. A summary table of findings will be generated and included in the final report. Three investigators will assess the quality of each selected study through a tiered proposal assessment, development, and evaluation methodology. The following areas will be assessed: risk of bias, consistency, directness, precision, publication bias, and additional scores. There will be 4 levels of assessment: high, medium, low, and very low quality.[18]

2.8.7. Ethics and dissemination. Ethical approval is not required as data from individual patients are not included, and there are no privacy implications. We will disseminate the results of this systematic review by publishing the manuscript in a peer-reviewed journal or presenting the relevant conference findings.

3. Discussion

DQD is a widespread clinical condition, and with the proliferation of cell phones and computers, more and more people are suffering from it. The main symptom is pain in the wrist joint and low mobility, which affects peoples learning and life. Currently, the primary conservative treatment including corticosteroid injections, tui na, massage, and so on, when conventional therapy does not work, surgery can also be used, but people are often reluctant to accept surgical treatment, and there is a specific recurrence rate. Moxibustion has been developed in China for thousands of years as a traditional healing method. The main effect is to invigorate blood circulation and eliminate stasis, warming the meridians. There are many clinical reports of using moxibustion to treat DQD, and it has the characteristics of sound effect, low cost, short course, low recurrence rate, and few side effects. However, there is a lack of systematic reviews and meta-analyses of moxibustion treatment for DQD. Therefore, we intend to demonstrate the efficacy and safety of moxibustion for DQD through this systematic review and meta-analysis. Finally, we hope that the results of this review will provide clinicians with more reliable, evidence-based evidence for the treatment of DQD.

Author contributions

Conceptualization: Min Liu, Fengyun Yang.
Data curation: Min Liu, Meinian Liu, Wenlong Yang.
Formal analysis: Min Liu, Meinian Liu, Wenlong Yang.
Investigation: Min Liu, Fengyun Yang.
Methodology: Ou Mei, Hanting Xia, Hong Tu.
Software: Meinian Liu, Xuyong Deng.
Supervision: Li Wang, Fengyun Yang.
Writing – original draft: Min Liu, Meinian Liu, Wenlong Yang, Ou Mei.
Writing – review & editing: Hanting Xia, Hong Tu, Li Wang, Xuyong Deng, Fengyun Yang.

References

[1] Awan WA, Babur MN, Masood T. Effectiveness of therapeutic ultrasound with or without thumb spica splint in the management of De Quervain's disease. J Back Musculoskelet Rehabil 2017;30:691–7.

[2] Mardani-Kivi M, Karimi Mobarakeh M, Bahrami F, et al. Corticosteroid injection with or without Thumb Spica Cast for de Quervain Tenosynovitis. J Hand Surg Am 2014;39:37–41.

[3] Abi-Rafeh J, Kazan R, Safran T, et al. Conservative management of de Quervain stenosing tenosynovitis: review and presentation of the treatment algorithm. Plast Reconstr Surg 2020;146:105–26.

[4] Bernstein DT, Gonzalez MA, Hendrick RG, et al. Impact of septated first dorsal compartments on symptomatic de Quervain Disease. Plast Reconstr Surg 2019;144:389–94.

[5] Mcdermott JD, Ilyas AM, Nazarian LN, et al. Ultrasound-guided injections for de Quervain's Tenosynovitis. Clin Orthop Relat Res 2012;470:1925–31.

[6] Jeyapalan K, Choudhary S. Ultrasound-guided injection of triamcinolone and bupivacaine in the management of de Quervain's disease. Skeletal Radiol 2009;38:1099–103.

[7] Di Sante L, Martino M, Manganiello I, et al. Santilli V.Ultrasound-guided corticosteroid injection for the treatment of de Quervain's tenosynovitis. Am J Phys Med Rehabil 2014;93:278.

[8] McKenzie JM. Conservative treatment of de Quervain's disease. Br Med J 1972;4:659–60.

[9] Roh YH, Hong SW, Gong HS, et al. RETRACTED: Ultrasound-guided versus blind corticosteroid injections for De Quervain tendinopathy: a prospective randomized trial. J Hand Surg Eur Vol 2018;43:820–4.

[10] Ilyas AM. Nonsurgical Treatment for de Quervain's Tenosynovitis. J Hand Surg Am 2009;34:928–9.

[11] Shin YH, Choi SW, Kim JK. Prospective randomized comparison of ultrasonography-guided and blind corticosteroid injection for de Quervain's disease. Orthop Traumatol Surg Res 2020;106:301–6.

[12] Oh JK, Messing S, Hyrien O, et al. Effectiveness of corticosteroid injections for Treatment of de Quervain's Tenosynovitis. HAND 2016;12:357–61.

[13] Stewart LA, Clarke M, Rovers M, et al. Preferred reporting items for systematic review and meta-analyses of individual participant data: the PRISMA-IPD statement. JAMA 2015;313:1657–65.

[14] Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: Elaboration and explanation. BMJ 2015;349:7647–17647.

[15] Higgins Julian P, Altman A, Sterne J, et al. Assessing risk of bias in included studies. Cochrane Handbook for Systematic Reviews of Interventions: Cochrane Book Series. New York: John Wiley & Sons, Ltd; 2011.

[16] Akl EA, Johnston BC, Alonso-Coello FP, et al. Addressing dichotomous data for participants excluded from trial analysis: a guide for systematic reviewers. PLoS One 2013;8:e57132.

[17] Vandenbroucke JP. Bias in meta-analysis detected by a simple, graphical test. Experts' views are still needed. BMJ 1997;316:469–71.

[18] Deng T, Wang Y, Huang D, et al. Methods for formulating clinical practice guidelines: GRADE method theory. Chin J Evid Based Cardiovasc Med 2018;10:1441–5.