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Efficacy of treatments and pain management for trapeziometacarpal (thumb base) osteoarthritis: protocol for a systematic review

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ABSTRACT

Introduction: The thumb is essential for daily activities. Unfortunately, this digit is commonly affected by trapeziometacarpal osteoarthritis (TMO), handicapping a large number of individuals. TMO constitutes an increasing human and economic burden for our society whose population is ageing. Limited access to adequate treatment is among the most important obstacles to optimal TMO management. Poor understanding of TMO characteristics, lack of knowledge about evidence-based treatments, simplistic pain management plans based solely on the patient's physical condition, absence of interprofessional communication and lack of multidisciplinary treatment guidelines contribute to inadequate TMO management. On the long term, our research project aims at improving the quality of care and services offered to patients with TMO by developing a patient-centred, evidence-based multidisciplinary management clinical pathway coordinated across the healthcare system. This proposed systematic review is a prerequisite to ensuring evidence-based practices and aims to document the efficacy of all the existing modalities for TMO management.

Methods and analysis: The protocol of the systematic review is registered with PROSPERO and will be conducted using the guidelines *Cochrane Handbook for Systematic Reviews of Interventions*. We will identify studies in English and French concerning TMO treatments through searches in Cochrane Central, EMBASE, MEDLINE, PsychINFO, CINHAL, PubMed, OT Seekers, PEDRO and the grey literature. 2 reviewers will independently screen study eligibility, extract data and appraise studies using published assessment tools. Meta-analyses will be undertaken where feasible; otherwise, narrative syntheses will be carried out. The robustness of evidence will be assessed using the GRADE system.

Ethics and dissemination: Ethics approval is not required for this study. A comprehensive knowledge exchange and transfer plan incorporating effective strategies will be used to disseminate the findings of this review and utilise them to optimise TMO management.

Trial registration number: PROSPERO CRD42015015623.

Strengths and limitations of this study

- This review is the first to carry out an extensive and comprehensive systematic review of all the existing treatments specific to trapeziometacarpal osteoarthritis (TMO) including pharmacological, non-pharmacological and surgical ones, not limited to any one discipline. Subsequently, the findings will allow us to develop and design an evidence-based multidisciplinary TMO management pathway usable for clinicians of various disciplines across the healthcare continuum.
- An extensive knowledge exchange and transfer plan incorporating effective strategies to disseminate and share the results with end-users is proposed. The findings will be used in a future study aimed at developing an active collaborative partnership between researchers and end-users to optimise care for patients with TMO.
- Language restriction to English and French for the literature search is a limitation of the proposed protocol such that language bias is possible.

INTRODUCTION

Trapeziometacarpal osteoarthritis: an understudied but important health problem

The most prevalent cause of chronic pain in the world is osteoarthritis (OA).[1 2] Its prevalence is increasing in an alarming manner with the ageing of the population, and it is estimated it will double before the year 2020.[3] This anticipated increase is somewhat frightening considering that OA is associated with numerous adverse consequences for affected individuals as well as increasing economic costs for our society.[3–6] Based on the meta-analysis of Pereira *et al*[7] on OA prevalence, hand OA is more prevalent than knee/hip OA, yet hand OA has been much less studied. Despite the fact that the thumb accounts for approximately 50% of overall hand function and is essential in our daily

activities,[8] relatively few studies have documented the prevalence of trapeziometacarpal osteoarthritis (TMO). Most of our knowledge comes from American and European studies which are based solely on radiographic findings: the prevalence rates of TMO ≥ grade 2 (on 4-point or 5-point severity scale) are highly variable ranging from 11.5% to 50.5%.[9–13] TMO was found to be more prevalent in women than men, but the prevalence steadily increases with age in both genders. The prevalence of symptomatic TMO (as defined by the presence of clinical symptoms with or without radiographic findings) and the rates vary between 1.0% and 15.9%.[14–21] Some studies have revealed that only a weak to modest association between TMO radiographic findings and clinical symptoms (pain and/or functional disability) exists[10 15]—that is, patients may exhibit important structural changes, yet report little or no pain; or patients may experience severe pain with little radiological evidence of TMO. Botha-Scheepers *et al*[22] followed a group of patients with hand OA over a 2-year period and found that the progression of pain intensity and physical functioning was unrelated to X-ray findings.[22] Based on the extensive clinical experience of three of the co-authors (PH, NB, TH) of this article, the above rates of symptomatic TMO are most likely to be underestimated because healthcare professionals commonly have insufficient knowledge of TMO characteristics and misdiagnose the origin of the pain (eg, tendinopathy vs TMO). As a result, these patients are referred to a hand specialist long after TMO first appears.

The patients with TMO reported persistent pain at the thumb base[23–25] which limits their hand functions,[25–27] reducing both thumb mobility[28] and hand strength,[29–31] thereby affecting their daily activities (eg, holding objects, preparing meals, writing).[26 29 32] However, only a few studies have either quantified the severity of TMO pain and/or its impact on various aspects of daily living other than physical functioning.[22 32]

Management of TMO and pain-related symptoms

Despite decades of research on pain assessment and management, it is well documented that chronic pain disorders of various origins continue to be commonly undertreated, mistreated or untreated, with a large number of patients going from one doctor to another seeking pain relief.[33] One of the major barriers to optimal management of persistent pain disorders including OA is the limited access to adequate healthcare services. Patients commonly have difficulty gaining *timely* access to *appropriate* pain care[34–36] leading to a premature or an increased deterioration of their physical functioning, psychological well-being and health-related quality of life while waiting for treatment. Management of TMO and pain-related symptoms can be provided by different healthcare professionals including primary care physicians, rheumatologists, physiatrists, orthopaedic surgeons, plastic surgeons, radiologists, pharmacists, physical therapists and/or occupational therapists. However, these clinicians (including hand specialists) often work in silos and manage patients with TMO based on their own clinical experience rather than on well-documented scientific evidence. Other obstacles to adequate TMO management include (1) poor awareness and understanding of the characteristics of TMO (and especially in the primary sector of care), (2) lack of knowledge about evidence-based effective treatments and (3) simplistic pain management plans based solely on patients' physical condition which do not necessarily meet all their needs. Finally, the fact that healthcare professionals commonly have insufficient knowledge and training for managing chronic pain disorders should not be neglected.[37 38]

Management of TMO involves various modalities including pharmacological therapy,[23 39 40] corticosteroid/hyaluronic acid injections,[23 25 40] hand exercises,[40–42] orthoses,[25 39 40 42 43] joint protection education,[39] assistive devices,[39 42] physical agent modality[39 40 43] and surgery.[40 42 44] However, the relative efficacy of these modalities remains poorly documented, some of them recommended for the treatment of hand OA in general while others are specifically for TMO. Furthermore, earlier systematic reviews examining the efficacy of TMO treatment have focused solely on one type of modality (eg, surgery, orthoses).[45 46] Chronic pain disorders commonly have significant adverse consequences in various domains of a patient's life,[26 39] and it is widely acknowledged that a multidisciplinary approach which takes into account the biopsychosocial components of the pain experience constitutes the 'gold standard' for managing this type of disorder.[47 48] Therefore, there is a need to conduct a systematic review from a multidisciplinary perspective which integrates all the existing therapeutic modalities for TMO in order to (1) document their relative efficacy, and (2) examine the modalities whose efficacy for TMO is supported by scientific evidence and those which are not, without creating confusion between effective modalities with absence of documented evidence and ineffective modalities supported by evidence.

Objectives

Our ultimate aim is to improve the quality of care and delivery of services for patients with TMO by developing a patient-centred, evidence-based TMO management clinical pathway[49] coupled to most optimal treatments which are evidence-based. As a prerequisite, a systematic review of the literature is needed to document the efficacy of the existing pharmacological, non-pharmacological and surgical modalities to relieve pain and improve function in patients with TMO. This paper aims at presenting the protocol for this systematic review of the literature.

METHODS AND ANALYSIS

The guidelines for systematic review of the literature *Cochrane Handbook for Systematic Reviews of Interventions*[50]

were referred to to prepare this protocol. The review will involve five steps (see figure 1).

Research team

The team combines relevant and complementary disciplines with members in pain psychology and pharmacology (MC), epidemiology and biostatistics (LL), plastic surgery (PH), radiology (NB), physiotherapy (NG), occupational therapy (TH) and library information science (DZ). The research expertise of MC is in the field of pain assessment/management and knowledge translation. The second author's research expertise (LL) focuses on knowledge transfer on primary care clinical practices in the cardiovascular and pain fields. The third author (PH) runs the largest hand clinic in the province of Quebec (Canada) and follows about 50 patients with TMO yearly. The fourth author (NB), a radiologist and a researcher, routinely performs image-guided steroid injections. The fifth author (NG) has research expertise in systematic reviews of the literature, lower limb OA and technology assessment. The sixth author (DZ) has collaborated on a series of systematic reviews. Finally, TH, a PhD student and occupational therapist, has treated patients with TMO for over 13 years.

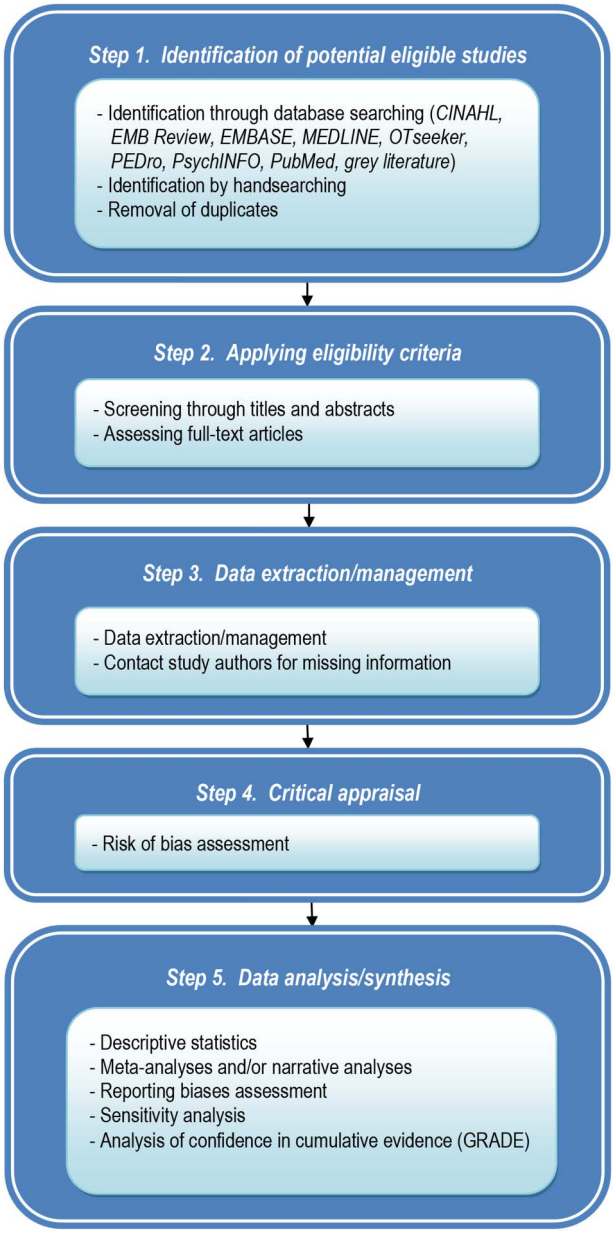

Figure 1 Process of the systematic review.

Step 1: Identification of potential eligible studies

Our academic librarian informationist (DZ) will search through bibliographic electronic databases CINAHL (from 1937 onwards), EMB Review (from 1991 onwards), EMBASE (from 1974 onwards), MEDLINE (from 1946 onwards), OTseeker, PEDro, PsychINFO (from 1806 onwards), PubMed and the grey literature (CADTH, Clinical Trials, National Guideline Clearing House, National Institute for Health and Care Excellence (NICE), MedNar, Google Scholar, OAIster and Open Grey). The first search will combine words and expressions for three conceptual groups: trapeziometacarpal joint, OA and treatment. To ensure that psychotherapeutic modalities for TMO will be picked up, the following keywords will be added: *cognitive therapy, cognitive behavior therapy, relaxation, biofeedback, supportive psychotherapy, group therapy* and *counseling*. For the second search, the first two conceptual groups will be the same while the third group will focus on 'pain' (see online supplementary annex 1 for details on the search strategy for MEDLINE). For each database, we will use words and expressions from controlled vocabulary (MeSH, EMTREE and others) and free-text searching. The searches will be restricted to articles published in English and French. Handsearching will also be used to identify other references (TH and MC). A pilot search through the CINAHL, EMB Review, EMBASE, MEDLINE, OTseeker, PEDro, PsychINFO and PubMed have identified approximately 2000 references, demonstrating the study's feasibility.

Step 2: Applying eligibility criteria

Once the results from multiple searches will be merged by the librarian (DZ) using the reference management software EndNote, duplicate records will be removed (DZ and TH). Titles and abstracts of studies will be screened independently by two reviewers for eligibility (MC and TH). Agreement between the two reviewers will be established using κ statistic.[50] Full-text copies of potentially relevant reports will be retrieved (TH). They will be analysed against eligibility criteria and the results will be recorded in part 1 (General Information) and part 2 (Eligibility) of the *Cochrane Effective Practice and Organisation of Care Group (EPOC) Data Abstraction Form*[50] by the two screeners. In the cases where no consensus is reached by the two reviewers, a third reviewer (PH) will determine the eligibility of the study. Part 1 of the EPOC form includes study identification (surname of first author and year of first full report of study), date form

completed, name of person extracting data, report title, publication type, study funding source and possible conflicts of interest. Part 2 consists of study characteristics (type of study, participants, types of intervention/outcome measure).

Criteria for considering studies for this review

Types of studies

Meta-analyses, systematic reviews of the literature, randomised controlled trials (RCT) will be included. If there are no RCT, non-RCTs, controlled before-after studies, interrupted time series (ITS) and repeated measures studies will be considered as well as observational studies (cohort, case–control).[40 39] Case series, review articles, editorials and commentaries will be excluded. The studies with higher evidence will be prioritised to determine the efficacy of therapeutic modalities. Results of most recent systematic reviews and those of reviews including more studies will be prioritised if there is more than one systematic review on a given intervention.

Types of participants

Studies conducted among TMO adults who had received treatment to decrease pain and/or improve function will be included. Studies on diseases other than primary TMO (eg, traumatic OA, rheumatoid arthritis), on OA other than the trapeziometacarpal joint or on animals will be excluded. Studies including OA of different joints will be included if the data of TMO are separately presented.

Types of interventions

All the existing therapeutic modalities for TMO treatments (eg, pharmacological, non-pharmacological, surgical) to reduce pain and improve function will be included. The possible interventions are 'drug therapy', 'surgery', 'manual therapy', 'psychotherapy', 'orthoses', 'acupuncture', 'hand exercises', 'assistive devices', 'education', 'joint injections', 'joint protection', 'laser therapy' and 'thermotherapy'. The comparators are another intervention or a non-exposed control group.

Type of outcomes

Primary outcomes are pain and function, considered core outcomes for OA clinical trials according to the international consensus group Outcome Measures in Rheumatology (OMERACT).[51 52] Secondary outcomes are patients' psychological well-being, health-related quality of life and treatment satisfaction.

Step 3: Data extraction/management

Data will be independently extracted by two persons (MC and TH) using part 3 of the EPOC data abstract form[50] (Population and Setting) which explores population description, setting, inclusion criteria, exclusion criteria and methods of recruitment. Part 4 (Methods) looks at aims of study, design, unit of allocation, start date, end date and duration of participation. Part 5 (Risk of bias) will be used at step 4. Part 6 (Participants) considers total number of participants, withdrawals and exclusion, severity of illness, comorbidities, other treatment, relevant sociodemographics, and subgroups. Part 7 (Intervention group) takes into account description of intervention, duration of treatment period and others. Part 8 (Outcomes) records outcome name, time points measured/reported, outcome definition, person measuring/reporting, unit of measurement, scales and others. Part 9 (Results) varies according to study design and nature of outcome (dichotomous/continuous). It mainly concerns comparison, outcome, subgroup, results, baseline data, number of missing participants, statistical methods and appropriateness of these methods, and others. Part 10 (Applicability) questions if important populations have been excluded from the study, if the intervention is likely to be aimed at disadvantaged groups and if the study directly addresses the review question. Part 11 (Other information) includes key conclusions, references to other relevant studies, correspondence required for further study information and others. In cases where data are missing, study authors will be contacted.

Step 4: Critical appraisal

Risk of bias in individual studies will be separately assessed by two reviewers (MC and TH). In the cases of disagreement, discussion will take place to achieve consensus. If necessary, the third one (PH) will appraise the study. Different assessment tools will be used depending on study design: *Assessment of Multiple Systematic Reviews* (AMSTAR) for systematic reviews of the literature,[53] EPOC *Risk of Bias Tool* for controlled studies and for ITS studies,[54] *Effective Public Health Practice Project* (EPHPP) *Quality Assessment Tool for Quantitative Studies* for cohort studies or case–control study.[55]

Assessment of Multiple Systematic Reviews

The questionnaire is composed of 11 items.[53] It examines the methodological quality of a systematic review including double review, exhaustive research strategy, heterogenic analysis and publication bias. It scores each criterion on four scales 'yes', 'no', 'can't answer' and 'not applicable', and total score on seven scales. Its inter-rater reliability for each item is moderate to perfect ($0.51<\kappa<1.00$) and excellent for the global score ($\kappa=0.84$, 95% CI 0.67 to 1.00). Its construct validity (Pearson coefficient) is 0.72 (95% CI 0.53 to 0.84). The minimal detectable difference is 0.64.[56]

EPOC Risk of Bias Tool for studies with a separate control group

This tool includes the five domains of bias determined by the *Cochrane Risk of Bias Tool*[55 57]—selection (random sequence generation and allocation concealment), performance, attrition (method addressing incomplete outcome), detection and reporting (selective outcome reporting)—and two other criteria regarding 'similarity

of baseline outcome measurements between experimental and control groups' and 'similarity of baseline characteristics between experimental and control groups'. Each item is scored 'yes' for high risk, 'no' for low risk and 'unclear' if not specified in the paper.

EPOC Risk of Bias Tool for ITS studies

This tool examines four domains of risks of bias determined by the *Cochrane Risk of Bias Tool*[54 57] (performance, attrition, detection and reporting bias) and three risks of bias associated with the ITS study design; 'was the intervention independent of other changes?', 'was the shape of the intervention effect prespecified?' and 'was the intervention unlikely to affect data collection?'

EPHPP Quality Assessment Tool for Quantitative Studies

This tool will be used to assess cohort and case–control studies.[55] It includes the items defined by the *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE) *Statement*.[58] It includes 21 items from eight categories (selection, study design, confounders, blinding, data collection methods, withdrawals and drop-outs, intervention integrity and analyses). This tool is considered one of the best tools for systematic review.[59] Content validity and construct validity, and inter-rater and intra-rater reliability have been demonstrated (κ=0.74, intraclass correlation coefficient=0.77).[55 60] Administration time is 10–15 min, and its ease of use has been reported.[55 59]

Step 5: Data analysis/synthesis

Characteristics of included studies

Descriptive statistics will present features of included studies in terms of study design, clinical and sociodemographic characteristics of participants, studied TMO treatments and their results.

Efficacy analysis of each therapeutic modality

Meta-analyses will be undertaken using the Cochrane Group's Review Manager software (RevMan V.5.1)[61] unless heterogeneity among studies is demonstrated by the I^2 statistic, that is, $I^2 \geq 50\%$.[62] For continuous outcomes, mean differences and standardised mean differences will be used for meta-analysis. For dichotomous outcomes, ORs, risk ratios, absolute risk reduction and number needed to treat will be computed. For longitudinal studies, risk ratios or HRs will be calculated; for case–control studies, ORs will be computed. In the presence of substantial variation among studies, narrative syntheses will be favoured and studies will be classified in logical categories.[63] In cases where data are missing, study authors will be contacted; otherwise, participant attrition will be treated by intention-to-treat analysis.[50] Missing statistics (eg, SD) will be calculated from available data (eg, SE will be reported from p values or 95% CIs).[50]

Reporting biases assessment and sensitivity analyses

Reporting biases across studies will be analysed by funnel plots when feasible—that is, at least 10 studies are included in the meta-analysis to ensure the power of the tests.[50] Sensitivity analyses will be undertaken in case the eligibility of some studies in the meta-analysis is doubtful (eg, low-quality studies).[50]

Confidence in cumulative evidence

The robustness of evidence will be assessed by using the GRADE classification[64–77] and its software GRADEpro.[78] Two tables will be dressed for each therapeutic modality. 'Clinical Evidence Profile' tables present quality of evidence for each outcome, while 'Clinical Evidence Summary of Findings' tables will provide end-users (administrators, healthcare professionals, patients) with key information helping them with decision-making in choosing the right treatments.[64]

ETHICS AND DISSEMINATION

Ethics approval is not required for this study. Once completed, the systematic review findings will be presented to a group of stakeholders during a 1-day workshop where researchers, clinicians from various disciplines, managers/decision-makers and patients will work together to elaborate a TMO management clinical pathway. This partnership between researchers and end-users will contribute to effective knowledge exchange and transfer.[79] With regard to our end-of-project knowledge transfer plan, we will draw on three key principles: (1) developing communication vehicles adapted to the target audience; (2) presenting concise messages; and (3) creating settings for exchange and discussion.[80] We consider the target audiences to be the: (1) scientific community, (2) healthcare professionals, (3) general public including patients with TMO or those afflicted with other types of OA or chronic pain disorders, and (4) administrators. In addition to traditional vehicles (eg, scientific meetings, publications), we will also create a module tab on the website of the Quebec Pain Research Network and on the *Centre hospitalier de l'Université de Montréal* (CHUM) website where the results of the project will be made accessible to the different targeted audiences. The final product (TMO management clinical pathway) will be made available in the form of a twofold pamphlet, one will be specifically for healthcare professionals, while the other for patients with TMO (ie, patient decision aids), elaborated by following the recommendations of the *International Patient Decision Aids Standards Collaboration*.[81 82] They will be duly delivered and subsequently presented to different institutions from the primary to tertiary sectors of care.

DISCUSSION

TMO is a chronic and degenerative disease which can seriously handicap patients, hence affecting their quality

of life. However, TMO management is far from optimal due to several obstacles including limited access to adequate healthcare services. Developing a patient-centred, evidence-based multidisciplinary treatment algorithm for TMO is paramount to improving the quality of care to this patient clientele. It will help guide the decision-making process of clinicians and patients with TMO in choosing the most suitable therapeutic modalities. To do so, a systematic review is a prerequisite, and to our knowledge, we are the first to propose the conduct of an extensive and comprehensive literature review of all the existing treatments for TMO including pharmacological, non-pharmacological and surgical modalities, not limited to any one discipline. Language restriction to English and French for the literature search is a limitation of the proposed protocol such that language bias is possible. However, the obtained findings will be crucial in developing a TMO treatment algorithm useful to all stakeholders across the healthcare continuum.

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