No Rules of Thumb:

Outcome Measurement and Treatment for Thumb Base Osteoarthritis

Robbert Wouters

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CONTENT

CHAPTER 1

GENERAL INTRODUCTION AND THESIS OUTLINE

INTRODUCTION TO THUMB BASE OSTEOARTHRITIS

The thumb base joint (CMC-1) is a saddle joint, connecting the trapezium and first metacarpal bone into a highly mobile joint. Located at the base of the thumb, the CMC-1 allows positioning the thumb relative to the fingers, enabling functional grasps and dexterity.

While allowing a large Range Of Motion (ROM), the CMC-1 is relatively unstable by nature due to limited ligamentary support and the CMC-1 suffers from high joint loading.[1-6]

Osteoarthritis (OA) of the CMC-1 arises due to multiple factors, such as biological factors, genetic associations and several factors related to characteristics of the joint, such as CMC-1 instability.[1-3,7-11] CMC-1 OA can be classified by the Eaton classification, which runs from stage I (no degeneration) to IV (extensive degeneration of both the CMC-1 and scaphotrapeziotrapezoid joint (STT))[11], but radiographically-diagnosed CMC-1 OA is only modestly associated with clinical symptoms.[12,13]

WHAT IS THE IMPACT ON PATIENTS AND SOCIETY?

CMC-1 OA is a common condition in the elderly, with a symptomatic prevalence of 7% and 2% amongst females and males aged ≥50 years; the radiographic prevalence is even higher.[7,12,14] These prevalence numbers are likely to increase due to the aging population[15,16] and the associated direct treatment costs and societal costs are substantial.[17]

Patients with CMC-1 OA often experience thumb pain and limitations in hand function and activities of daily life (ADL).[12,13] Furthermore, as ligamentous laxity increases, dorsoradial subluxation may occur in the CMC-1 joint, followed by metacarpophalangeal (MCP-1) hyperextension, interphalangeal (IP-1) hyperflexion, and limited first web space: a typical z-deformity.[1-3,6] Additionally, patients with CMC-OA often present clinical features such as thenar muscle wasting, nodes and joint synovitis.[3,6,7,12,13]

HOW TO TREAT PATIENTS WITH CMC-1 INSTABILITY OR OA?

Present treatment for CMC-1 instability or subsequent OA aims to reduce pain intensity and improve hand function and ADL. Current guidelines and systematic reviews advise starting with non-surgical treatment, which may include analgesics, intra-articular injections, orthotics and exercise programs.[18-20] While these interventions are used widely, evidence supporting these non-surgical treatments, especially exercise programs, is limited.[6,18-25] Nonetheless, while analgesics, intra-articular injections, and orthotics provide short-term results[18-21,23], exercise programs aim to provide a long-term solution by improving lifestyle, joint mechanics and function.[6,22,24,25] Theoretically, improving joint mechanics might be very beneficial, both for patients with CMC-1 instability as patients with CMC-1 OA, since improving joint mechanics might reduce subluxation and synovitis, thereby preventing further joint degeneration in later life.[1-3,9-11]Most exercise programs aim to improve active stability and positioning of the CMC-1 into a more stable position of extension/abduction, since the CMC-1 becomes unstable during flexion and adduction.[1-3,9,22,24,25] Additionally, exercises focus on maintaining the first web space and pinch strength.[3,6,23-25] Usually, this includes coordination and strengthening exercises of the intrinsic thenar muscles (except the adductor pollicis), extensor pollicis brevis and the first dorsal interosseous.[3,6,24] Exercises are often complemented by orthotics, to reduce subluxation and inflammation, but orthotics are also prescribed as a stand-alone treatment.[3,23] Despite this clear treatment rationale, the effectiveness of non-surgical treatment, or exercises in particular, remains unclear since non-surgical treatment is only studied to a limited extent.

When non-surgical treatment fails to alleviate symptoms, conversion to surgery may be considered. In the past years, a variety of surgical techniques are described, which may include a trapeziectomy, with or without Ligament Reconstruction and/or Tendon Interposition (LRTI).[19,26,27] CMC-1 arthrodeses and implants are also used, but these techniques are associated with a higher risk of complications (e.g., non-union or dislocation).[19,26,27] Surgical treatment comes with prolonged recovery, discomfort, and limitations for the patient and high costs for society.[19,28,29] Furthermore, it has been reported that for a trapeziectomy both with or without LRTI, 11-33% of the patients would not consider the same treatment again under the same circumstances.[28,30-33] Some studies emphasize the importance of postoperative rehabilitation for patients who underwent CMC-1 arthroplasty to reduce pain and improve hand function and ADL.[19,26] However, the

lack of consensus on the content of postoperative rehabilitation for patients who underwent CMC-1 arthroplasty is acknowledged as well and optimal immobilization period and time points for the initiation of ROM or strengthening exercises are unclear.[19,26] It is, for example, unclear if concepts such as early active rehabilitation are equally safe and effective in CMC-1 resection arthroplasty as in other surgical treatments, such as hip replacement[34], tendon repair in the hand[35,36] or open reduction and internal fixation for distal radius fracture.[37]

WHAT FACTORS PREDICT OUTCOMES AND TREATMENT CHOICES?

It is unclear which factors predict outcomes of treatment for CMC-1 OA, such as conversion to surgical treatment following non-surgical treatment or acute postoperative pain following surgical treatment. Over the last decade, multiple studies demonstrated that psychological characteristics, such as depression, anxiety, negative illness perception and pain catastrophizing are highly prevalent in patients with several types of OA.[38-47] However, little is known about (differences in) psychological characteristics and treatment expectations in patients with CMC-1 OA scheduled for non-surgical or surgical treatment. Furthermore, previous studies indicate that pain catastrophizing[48-53], female sex[48,49,51], preoperative pain[48-50,52,53], expected pain[53], higher age[48-50,52,53], previous chronic pain[48,50], higher anxiety[48-50,52,53], surgical fear[53], and less optimism[48,49] results in higher acute postoperative pain after hip, knee or other elective surgery. However, it is unknown if these factors also predict acute postoperative pain in patients surgically treated for CMC-1 OA.

HOW TO MEASURE OUTCOMES PATIENTS WITH HAND AND WRIST CONDITIONS?

In the past years, the value-based healthcare (VBHC) framework by Porter and Teisberg[54,55] has been recognized as a model to improve the quality of healthcare against affordable costs. Within this framework, value is defined as the outcomes achieved divided by the costs.[54,55] Measuring outcome is therefore a key aspect of VBHC, preferably by using a condition-based standard set of outcome tools at predetermined time points independent of treatment type or healthcare profession.[54,55] To implement VBHC, government organizations endorse the standard sets developed by the International Consortium for Health Outcome Measurement (ICHOM).[56,57] Although some efforts on standardizing outcome

measurement exist in hand and wrist care[58,59], such an internationally adopted standard set for measuring outcomes of hand and wrist care is currently unavailable. The lack of such a standard set makes it very difficult to make valid comparisons, both in daily clinical practice and research, e.g., following different treatments for patients with CMC-1 OA. Furthermore, the creation of a standard set will allow benchmarking and comparing different treatment centers, facilitate shared decision making and improve quality of healthcare.[54,55] Therefore, an international, minimum standard set of outcome measures that matter most to patients with hand and wrist conditions is needed. In addition, innovative approaches for measuring outcome in routine daily hand and wrist care are needed.

GENERAL AIMS AND OUTLINE

The outcomes of non-operative and postoperative treatment, predictors for treatment choices and predictors for treatment outcome are insufficiently studied in patients with CMC-1 OA. Further, standardization of and innovative approaches for outcome measurement in hand and wrist conditions are needed. Simple *rules of thumb* are not sufficient or applicable for treating patients with CMC-1 OA, but in contrast, evidence-based, patient-, and treatment-specific guidelines are needed.

Therefore, in **Part 1** of this thesis, the outcomes following non-surgical treatment for CMC-1 OA and CMC-1 instability are presented in **Chapter 2 and 4,** respectively. Additionally, Part 1 investigates the added value of exercise therapy in addition to an orthosis in patients with CMC-1 OA in **Chapter 3**, and Part 1 investigates predictors for the outcomes of non-surgical treatment in **Chapter 5**. Subsequently, in **Chapter 6,** patients scheduled for CMC-1 resection arthroplasty are compared with their non-surgical counterparts in terms of sociodemographics, clinical, and psychological factors.

In **Part 2** of this thesis, a systematic review on the postoperative rehabilitation following CMC-1 resection arthroplasty is performed in **Chapter 7** and the outcomes following shorter and longer immobilization after CMC-1 resection arthroplasty are compared in **Chapter 8**. Additionally, Part 2 investigates predictors for acute postoperative pain following CMC-1 resection arthroplasty in **Chapter 9**.

Part 3 presents the development, design, and implementation of the hand and wrist study cohort in **Chapter 10**. Moreover, Part 3 describes the process of international standardization of outcome measurement in hand and wrist care by developing the ICHOM standard set for hand and wrist conditions in **Chapter 11**.

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PART 1

NON-OPERATIVE TREATMENT AND CONVERSION TO SURGERY

CHAPTER 2

OUTCOME OF A HAND ORTHOSIS AND HAND THERAPY FOR CARPOMETACARPAL OSTEOARTHRITIS IN DAILY PRACTICE: A PROSPECTIVE COHORT STUDY

Jonathan Tsehaie
Kim R. Spekreijse
Robbert M. Wouters
Harm P. Slijper
Reinier Feitz
Steven E.R. Hovius
Ruud W. Selles

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ABSTRACT

Introduction: Initial treatment for symptomatic carpometacarpal (CMC) osteoarthritis (OA) of the thumb is usually non-surgical. However, evidence on the effect of a hand orthosis and hand therapy for mid and long-term results is limited, and it is unknown how many patients undergo additional surgical treatment. Therefore, the aim of this study is to describe the outcome of a hand orthosis and hand therapy for CMC OA in a large cohort study, and to evaluate the conversion rate to surgical treatment.

Methods: In this multicenter, prospective cohort study, patients treated with a hand orthosis and hand therapy for primary CMC OA between 2011 and 2014 were included. Pain (visual analog scale) and function (Michigan Hand Questionnaire) were measured at baseline, 6 weeks, 3 months, and at 12 months after the start of treatment. All patients converted to surgery were recorded between 2012 and 2016. Outcome was compared with baseline, and post hoc comparisons were made between patients who were not converted to surgery and patients who were converted to surgery after initially receiving a hand orthosis and hand therapy. Lastly, subgroup analysis was performed based on baseline pain levels.

Results: After a mean follow-up of 2.2 ± 0.9 years, 15% of all patients were surgically treated. In the group that was not converted to surgery, pain (visual analog scale) significantly improved from 49 ± 20 at baseline to 36 ± 24 at 12 months. The Michigan Hand Questionnaire score was essentially unchanged from 65 ± 15 at baseline to 69 ± 10 at 12 months. Post hoc testing showed that improvement in pain was only significant between baseline and 6weeks, and thereafter stabilized until 1 year after the start of treatment. The group that eventually converted to surgery did not show any improvement in pain and function during conservative treatment.

Conclusions: In this cohort of patients with thumb CMC OA who underwent hand therapy including an orthosis, 15% of the patients underwent additional surgical treatment. The patients (85%) who did not undergo surgery improved in pain and function, although only improvements in pain were significant and clinically relevant. Most improvement was seen in the first 6 weeks and stabilized till 1 year after the start of treatment.

INTRODUCTION

Treatment guidelines for carpometacarpal (CMC) osteoarthritis (OA) of the thumb usually advise a period of non-surgical treatment before considering surgical treatment for all patients with primary CMC OA.[1-4] Non-surgical treatment for CMC OA can consist of orthosis immobilization, intra-articular steroid injections, hand therapy, or a combination of modalities.[5-7] When non-surgical treatment fails to provide enough pain relief or functional improvement in daily life, a decision may be made to proceed to surgical treatment.

However, the existing evidence on the effectiveness of non-surgical treatment is of poor quality, primarily due to small sample sizes, non-generalizable study samples, or short follow-up time. In addition, most of these studies are limited to only comparing different types of orthoses and not the effect of combination therapy, that is, an orthosis with hand therapy.[8-10] For example, a systematic review by Egan and Brousseau[8] showed that hand orthoses may help to relieve pain, but sample sizes of the included studies were very small (N= 10-37) and follow-up times relatively short (1 wk to 6 mo). In addition, hand function was not measured. Another systematic review on comparative studies of hand orthoses or hand therapy of CMC OA[9] concluded that a hand orthosis or hand therapy may provide pain reduction, but all studies had a short follow-up time (2 wk to 3 mo) and study samples comprising only older individuals (70-90 y). In addition, none of the studies evaluated outcome after a combination of a hand orthosis and hand therapy.[1,2,4,11]

A recent meta-analysis of Aebischer et al.[10] based on studies on hand orthoses, hand therapy, and nonpharmaceutical treatment for CMC OA concluded that combination therapy is more effective for pain than single interventions. Because of the paucity of available evidence, it is unknown how many patients respond favorably, and how many patients who initially received a hand orthosis and hand therapy are eventually converted to surgical treatment. In addition, the timing of surgical intervention, in relation to receiving a hand orthosis and hand therapy (e.g., how long should surgery be delayed if patients do not respond to a hand orthosis and hand therapy), is unknown as well.

Therefore, the aim of this study was to describe the one-year outcome of providing a hand orthosis and hand therapy for thumb CMC OA, and to identify when and how many patients need additional surgical treatment.

METHODS

Study population

This study was conducted as an observational, prospective cohort study, performed in a private hand surgery clinic (Xpert Clinic, the Netherlands), consisting of 11 locations, with 13 European board-certified hand surgeons delivering care. Hand therapy was given by more than 50 hand therapists at specialized hand therapy clinics, located in or near an Xpert clinic (Handtherapie Nederland, the Netherlands).

All patients evaluated at the outpatient clinic between January 2011 and November 2014, clinically diagnosed with CMC OA and treated with a hand orthosis and hand therapy, were asked to participate in this study. All patients received an x-ray of their hand to confirm the clinical diagnosis and to grade the severity of CMC OA. However, because the grading of the osteoarthritis was done in a nonsystematic way, we did not further analyze the CMC OA severity based on the x-ray images. The study was approved by the local institutional review board, and all patients signed an informed consent. Exclusion criteria were previous CMC surgery, post-traumatic OA, isolated scaphotrapeziotrapezoid OA on the x-ray, or a history of prior intra-articular corticosteroid injections in the thumb CMC joint. Furthermore, patients with active trigger finger, carpal tunnel syndrome, OA of the interphalangeal joints, or de Quervain tendonitis were excluded when they received simultaneous treatment for these conditions at the start of treatment.

Intervention

Treatment was based on the Dutch treatment guideline.[1] In general, treatment consisted of prescribing a custom-made or prefabricated orthosis (based on the preference of the surgeon, hand therapists, and insurance of the patient) and 2 sessions of hand therapy per week of an average duration of 25 minutes per session. The hand therapists all received the same internal training on how to treat CMC OA with hand therapy. However, this was a pragmatic study in the sense that the hand therapy was not strictly protocolled and controlled, but evaluated, based on clinical practice. Therapy sessions were planned by judgment of the therapist and ability and availability of the patient. In some cases, patients received only a hand orthosis without further treatment, for example because of their insurance or schedules.

The treatment was divided into 2 phases: phase I (week 0-6) included instructions to wear the hand orthosis almost 24 hours per day and consisted of hand therapy for optimizing thumb position (training pinch and grasping movements without hyperextension in the metacarpophalangeal thumb joint and without CMC adduction) and using a full thumb range of motion (where the specific coordination of the intrinsic and extrinsic muscles of the thumb is trained); in phase II (week 7-12), the hand orthosis was slowly phased out: the patient was advised to use the hand orthosis only during heavy activities, depending on pain level and the patient's ability to perform activities with a stable thumb position. The hand therapy during this phase focused on maintaining the pain reduction, introducing the learned stability during daily activities and improving thenar muscle strength. In this phase, fewer hand therapy sessions were scheduled and patients performed more home exercises, up to 4-6 times a day. The number of prescribed home exercises ranged between 3 and 6 exercises per day, with 10-15 repetitions each, depending on the individual patient and the level of pain.

After this period of supervised therapy, patients were encouraged to keep doing the exercises, and patients were allowed to use the hand orthosis when necessary. No corticosteroid injections were given for their CMC OA during or after hand therapy, and no anti-inflammatory medication was prescribed by the surgeon.

Measures

Baseline demographics of all patients, including duration of complaints, comorbidity, and hand medical history, were collected before the start of treatment. Outcome measures were recorded before the start of the treatment, at 6 weeks, at 3 months, and at 12 months through our web-based outcome registration. All patients had a follow-up appointment with their hand surgeon after approximately 3 months, during which progress was evaluated.

Pain and function

Pain was measured with a visual analog scale (VAS) during 2 situations: pain during activities and pain experienced during the last week. To measure patient-rated hand function, the Michigan Hand Questionnaire was used (MHQ, Dutch Language Version; 0 = poorest function, 100 = ideal function).[12-14] The MHQ is a self-reported questionnaire with 6 domains and 37 items. The Minimal Clinically Important Difference ranges between 9 and 13 points for total MHQ and between 11 and 14 points for the subdomain pain, for nontraumatic hand conditions.[15]

Surgery

All patients had a follow-up appointment with their hand surgeon after approximately 3 months; further follow-up was only scheduled when indicated. Surgical intervention was discussed when patients did not respond well to the hand orthosis and hand therapy and had functional impairments and/or residual pain. Together with the surgeon, the decision to operate was made based on the symptoms of the patient. All surgeries performed between January 2012 and February 2016, together with time until surgery, were retrieved from the clinical records, independent of whether patients responded to the questionnaires. These results were separately analyzed and not combined with the results of the questionnaires, which made it possible to report conversion to surgery on all patients eligible for inclusion (Figure 1).

Statistical analysis

We performed a sample size calculation to determine the number of patients required to detect a conventional effect size of 0.15 for pain (VAS) after receiving a hand orthosis and hand therapy. The required sample was 90 participants.[16]

Baseline demographics were available in more than 98% of the patients. Because data were collected during daily clinical practice, we had a substantial proportion of nonresponse during follow-up (Figure 1). In addition, the data that were missing at 12 months consisted of both patients who did not fill in the questionnaires and patients who had already converted to surgery. Because of this, a thorough non-responder analysis on the whole group was performed using $\chi 2$ statistics or t-tests for all variables measured at baseline based on the response at 1 year. No significant differences were found at baseline between patients who filled in the questionnaires at follow-up and patients who did not fill the questionnaires at follow-up. In addition, Little's MCAR test[17] for all separate outcome variables showed that more than 95% of the outcome variables were missing at random. We therefore performed all main analysis with patients who responded at all follow-up measurements (complete case analysis). As a secondary analysis, we performed multiple imputations to compare the outcome for consistency with the complete case analysis. We performed multiple imputation by chained equations by fully conditional specification and used all patients. We imputed 10 times and compared the imputed data with the complete case data using t-tests (Appendix A). Here again, no significant differences were found between the imputed analysis and the complete case analysis.

Hereafter, analysis of variance tests with repeated measures were performed to compare baseline and follow-up measurements, combined with Tukey's post-hoc tests, to determine between which follow-up points the significant difference existed. In addition, we compared patients who eventually received surgery with patients who did not convert to surgery using independent samples t-tests. Because the decision to operate was made from 3 months onward, patients who eventually received surgery filled in the questionnaires only until 3 months. This allowed us to compare the group that was not operated with the group that converted to surgery up to 3 months without having to impute any data.

To study the influence of different baseline pain levels on outcome after treatment, we divided patients into 4 subgroups based on baseline pain level (VAS), correcting for regression to the mean, which can occur if a variable is extreme on its first measurement; in that case, it will tend to be closer to the average on its second measurement.[18] Corrections were made based on a test-retest reliability of 0.85 for VAS pain.[19] For all tests, we considered a P-value smaller than .05 as statistically significant.

Table 1. Baseline characteristics

Baseline Characteristics		**Total (n=122)**	
Variables		*N*	*% or mean ± SD*
Age (years)		126	60 ± 8
Duration symptoms (weeks)		126	40 ± 72
Sex	Female	91	72
Treated hand	Right	63	50
Workload	No work	67	53
	Light physical work	22	18
	Moderate physical work	30	24
	Heavy physical work	7	6
Dominance	Left	14	11
	Right	107	85
	Both	5	4

Abbreviations: SD = Standard deviation

RESULTS

Study population

Between January 2012 and November 2014, 1,033 patients with complaints of CMC OA visited Xpert Clinic, of whom 809 were eligible for inclusion. Of those patients eligible for inclusion, 122 completed all follow-up measurements without undergoing surgery and were used to analyze the primary outcomes: pain and function. In addition, 28 patients who underwent surgery completed all follow-up measurements until 3 months. Figure 1 shows the flowchart and Table 1 shows the baseline characteristics.

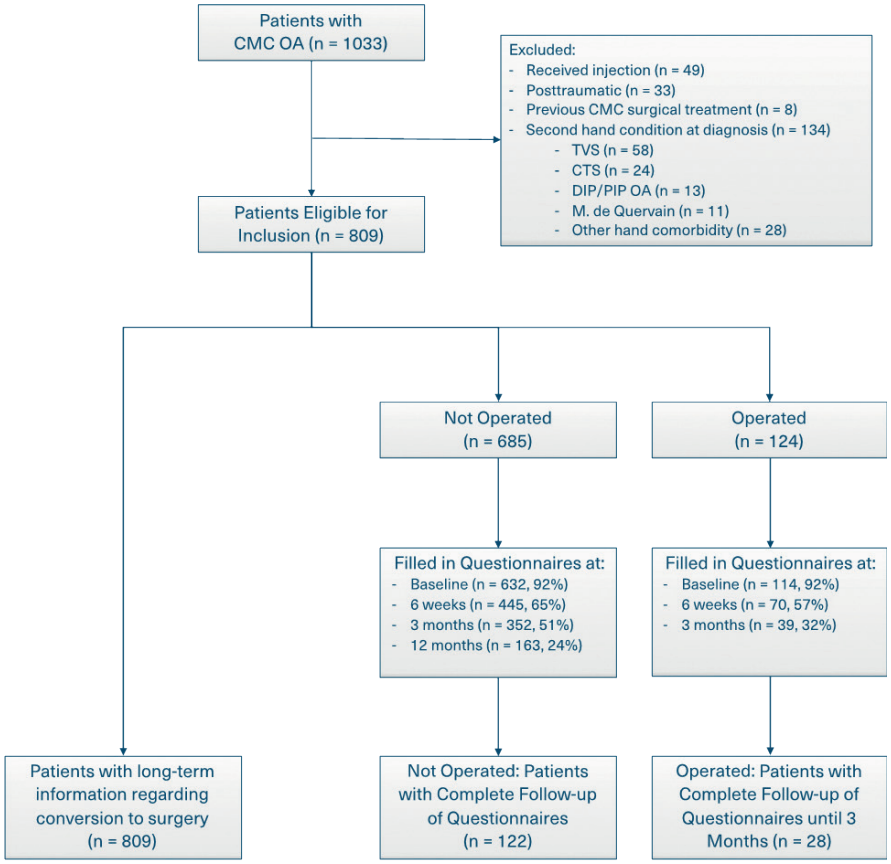

Figure 1. Flowchart of the study. CTS, carpal tunnel syndrome; DIP, distal interphalangeal joint; PIP, proximal interphalangeal joint.

To study conversion to surgery, we included all 809 patients, because the recording of conversion to surgery was independent of the response of the

patients to the questionnaires. Patients were followed for a minimum of 1.5 years to verify whether they had undergone surgical intervention. After a mean follow-up of 2.2 ± 0.9 (±standard deviation) years, 124 patients (15%) were surgically treated (Figure 2). The majority of the surgically treated patients (n = 93; 75%) were operated on within the first year after the start of hand therapy and the median number of days until surgery was 160 (interquartile range, 40-280) days.

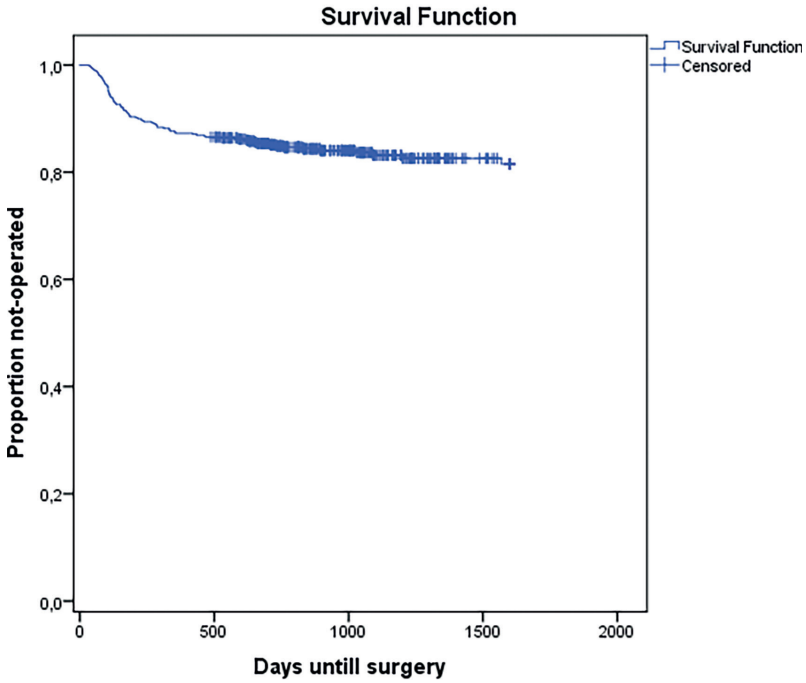

Figure 2. Survival analysis. Chart shows the duration of time until receiving surgery. On the y axis the proportion of patients not operated is shown, and on the x axis the number of days since the start of a hand orthosis and hand therapy. A total of 15.3% converted to surgery with a median number of days until surgery of 5 months.

Pain

The patients who did not convert to surgery showed a significant decrease in pain during the last week, VAS from 49 ± 20 (mean ± standard deviation) at baseline to 36 ± 24 at 12 months after the start of treatment ($P < .05$), and showed a significant decrease in pain during activities (VAS) from 60 ± 21 to 44 ± 27 after 12 months ($P < .05$) (Figure 3A).

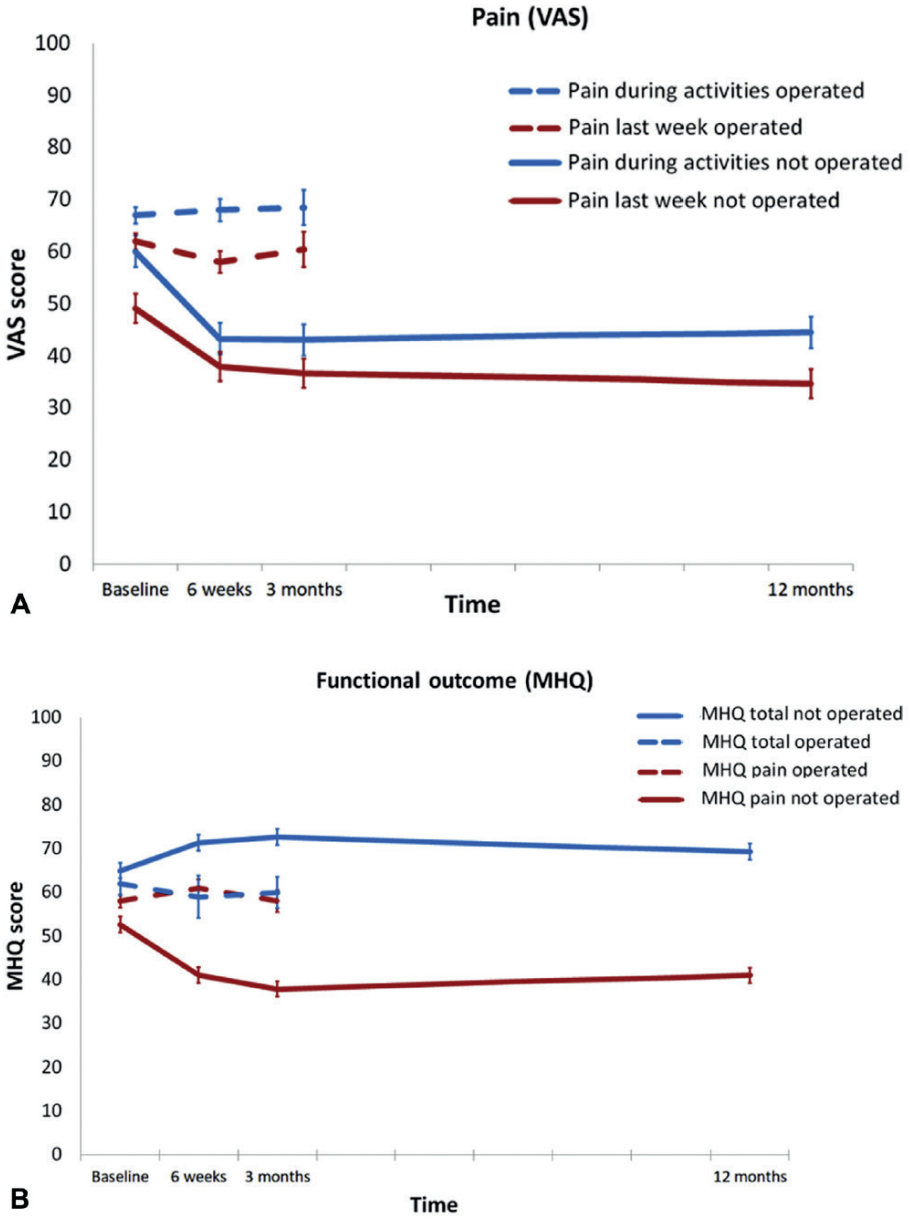

Figure 3. Outcome in pain (VAS) and function (MHQ). In the group that was not operated, there was a significant improvement in pain between baseline and 12 months. Furthermore, most improvement was seen in the first 6 week. In the group that was eventually operated, there was no significant improvement between baseline and 3 months after receiving a hand orthosis and hand therapy. Error bars indicate standard errors.

Post hoc tests showed that improvements were only significant between baseline and 6 weeks: 14.5 points improvement (95% confidence interval [CI], 7.2 - 21.8; P < .05) for pain during the last week and 17.6 points improvement (95% CI, 9.8-25.4; P < .05) for pain during activities. Between 6 weeks and 12 months, no significant change occurred: 1.8 points mean difference (95% CI, -9.1 to 5.5; P = .922) for pain during the last week and 1.7 points mean difference (95% CI, -9.5 to 6.1; P = .945) for pain during activities.

The patients who chose to convert to surgery after 3 months had at baseline (at the start of receiving a hand orthosis and hand therapy) a mean score of pain experienced during the last week of 62 ± 17, and a mean score of pain during activities of 67 ± 25. At follow-up, no significant change was seen between baseline and 3 months in pain experienced during the last week (1.6 points mean difference, 95% CI, -6.1 to 9.2; P = .677) or pain during activities (1.5 points mean difference, 95% CI, -11.0 to 8.0; P = .749).

When comparing patients who were converted to surgery with the patients who were not converted, we observed that the converted patients had at baseline 13.0 (95% CI, 5.0-21.0; P < .05) points higher pain experienced during the last week and 6.6 (95% CI, -2.3 to 15.5; P = .143) points higher pain during activities compared with the patients who were not converted. At 3 months the differences increased, with patients who were converted having 22.4 (95% CI, 12.9-32.0; P < .05) points higher pain experienced during the last week and 25.6 (95% CI, 15.9-35.4; P < .05) points higher pain during activities compared with the patients who were not converted.

Function

The patients who did not convert to surgery showed a significant change in function (total MHQ score) from 65 ± 15 at baseline to 69 ± 10 after 12 months (P < .05) (Figure 3B). Post hoc tests showed that for function, improvement was significant between baseline and 6 weeks: 6.2 (95% CI, 1.2-11.2; P < .05) points improvement, but the improvement in function was no longer significant at 1 year after the start of treatment (mean difference + 3.7 points; 95% CI, -0.95 to 11.2; P = .172) (Figure 3B).

The patients who chose to convert to surgery after 3 months had at baseline a mean function score of 58 ± 18. At follow-up, no significant improvement was

seen between baseline and 3 months in function (0.2 points mean difference; 95% CI, -4.4 to 4.1; P = .939).

When comparing patients who were converted with the patients who were not converted, we observed that the converted patients had at baseline 7.0 (95% CI, 0.2-13.7; P = .044) points less function compared with the patients who were not converted. At 3 months the differences increased, with patients who were converted having 15.0 (95% CI, 8.5-21.4; P < .05) points less function compared with the patients who were not converted.

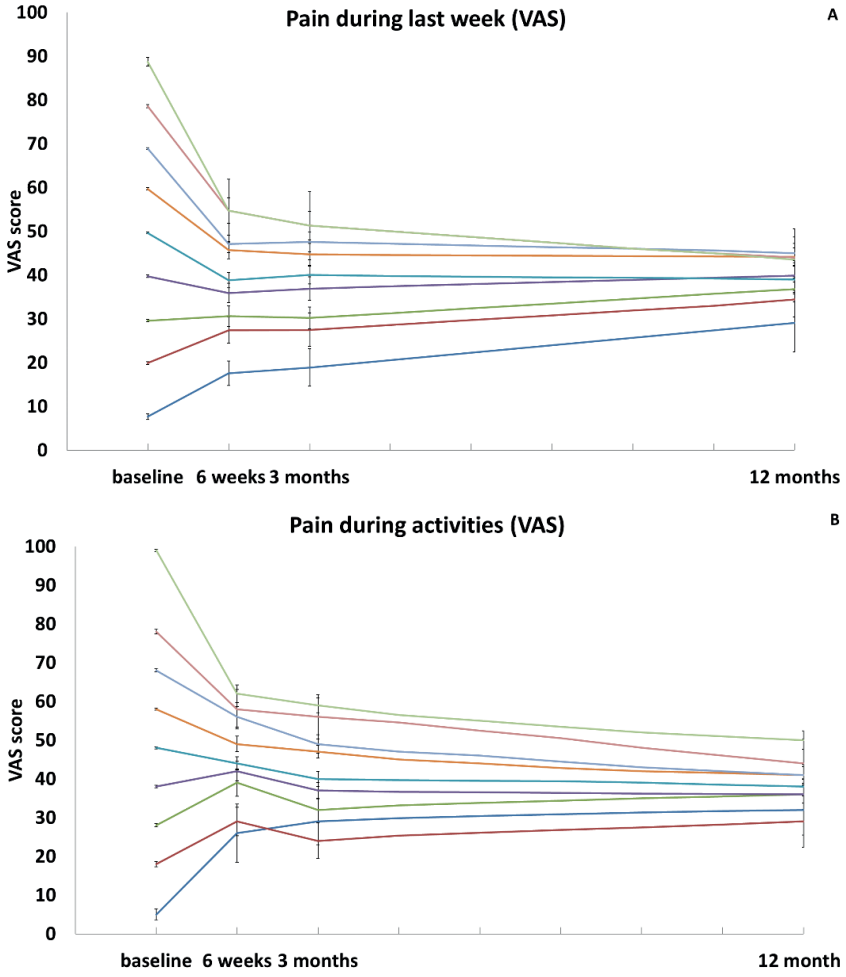

Figure 4. Subgroup analysis of Visual Analogue Scales (VAS) for pain during last week (A) and pain during activities (B) based on baseline pain levels. The figure shows the outcome of treatment on subgroups. Patients with high baseline pain improved in outcome, whereas patients with low baseline pain deteriorated in outcome. Error bars indicate standard errors.

Subgroup analysis

When grouping patients who were not converted to surgery based on the severity of baseline pain (Figure 4), pain only improved significantly in groups where pain at baseline was higher than 50 on average (VAS); the higher the average pain level at baseline, the higher the reduction in pain. In contrast, patients with a baseline level of 25 or lower (VAS) showed a significant increase in pain after a hand orthosis and hand therapy.

DISCUSSION

In this prospective cohort study using data collected as part of routine clinical care, we found that after a mean follow-up of 2.2 years, 15% of the patients treated with a hand orthosis and hand therapy underwent surgical treatment, after a median duration of 5 months from receiving a hand orthosis and hand therapy. When we divided patients who eventually did or did not convert to surgery, we found that the group that was not converted to surgery showed significant improvement in pain within 1 year after being treated with a hand orthosis and hand therapy for CMC OA. Most of this improvement was gained in the first 6 weeks of treatment, where after improvements were maintained. In addition, we saw that both pain and functional outcome were worse in the group that eventually received surgery, both at baseline and at the follow-up measurements. In the group that was converted to surgery, no improvement in pain and function was seen at follow-up measurements. Subgroup analysis, based on baseline pain levels, showed that patients with mean baseline pain levels of 50 or higher had a significant reduction in the amount of pain experienced, whereas patients with mean baseline pain levels of 25 or lower had a significant increase in pain.

The improvements on a group level in pain and function after a hand orthosis and hand therapy are in line with the limited available evidence. For example, Villafañe et al.[20] randomized 60 patients with CMC OA to manual therapy or a placebo intervention and found that the manual therapy group had a significant pain reduction after 1 month, whereas the placebo intervention did not reduce pain. Between 1 and 2 months after the start of manual therapy, pain did not change in this study, which is in line with our finding that pain reduced mostly within the first 6 weeks, although manual therapy in their study had a very different treatment protocol compared with our study, including passive nerve mobilization and joint mobilization. Similarly, the small retrospective study of

O'Brien and Giveans[21] described that, within 90 days, hand therapy significantly reduced pain from 3.3 to 2.7 on a 1-5 Likert scale.

It should be noted that not all significant improvements in this study were clinically relevant. In our study, we found a clinically relevant improvement of 12 on the MHQ subdomain pain.[15] However, the improvement on the total MHQ score of 4 points did not exceed the Minimal Clinically Important Difference of 9-13 points[15], indicating that the improvement in function may not be clinically relevant. Because Frouzakis et al.[22] found that pain reduction is the primary reason for patients to seek treatment, the clinically relevant pain reduction in this study supports the implementation of a hand orthosis and hand therapy in these patients.

Although we found that only approximately 15% of our patients received additional surgical treatment, we are not aware of any other studies reporting this outcome after a hand orthosis and hand therapy. Wajon et al.[23] concluded in a Cochrane review that they could not provide any information on the right time to convert to surgical treatment. Berggren et al.[24] reported that 23 of 33 patients (70%) waiting for operation could be treated successfully with hand therapy within 7 months before surgery, and within 7 years, only 2 more patients underwent additional surgical treatment. However, because patients in this study were already planned for surgery, we cannot compare this rate with our study.

This study has a number of specific strengths and limitations. An important strength of this study is the large sample size of 122 patients. Another strength is the pragmatic nature of this study, recording how hand therapy is performed in actual clinical practice, outside of the more controlled and potentially less natural setting of a randomized controlled trial. At the same time, the natural setting is also a limitation of the study because treatment was not completely standardized. Therapists adjusted treatment to the specific condition of the patient, severity of the complaints, time schedule, and type of insurance of the patient. Treatment in the form of purely an orthosis is very different compared with an orthosis and hand therapy. In addition, compliance with the treatment protocol by the participants was not recorded. The natural setting also resulted in the proportion of missing data, another limitation of our study. An important reason for missing data is that patients who had residual pain or functional complaints after being treated with hand therapy and an orthosis received surgical treatment and therefore were "missing" after 12 months. Another possible reason for our

missing data is that patients may have gone elsewhere to receive treatment. However, because these patients visited this center seeking treatment and, as a part of protocol, first received hand therapy and orthosis, our experience is that only a very small portion of patients elect to undergo surgery elsewhere when hand therapy leads to insufficient relief of symptoms.

Another limitation of this study is that it focuses only on the combination of an orthosis and hand therapy, but cannot conclude anything on the outcome of other treatment strategies, such as topical or oral anti-inflammatory medication or intra-articular corticosteroid injections. We did not perform radiological staging, because the Dutch guideline1 for the treatment of CMC OA indicates that x-rays can support the diagnosis of CMC OA but that radiological staging according to Eaton and Glickel does not have added value, due to only fair interobserver reliability and only fair correlation with symptoms. Inherent to the cohort nature of this study is that a control group is lacking. Therefore, this study does not provide information on what the relative effectiveness is compared with, for example, no treatment or direct surgical treatment. Finally, the relatively short follow-up is a limitation, because decisions regarding surgical treatment in patients with OA usually develop over years, and are influenced by various other factors.

Our results support clinical guidelines stating that treatment for CMC OA should first be non-surgical, because, at a group level, outcome significantly improved up to 1 year after treatment and the majority of patients did not undergo additional surgical treatment within the first 2 years. Subgroup analysis indicates that initial non-surgical treatment with an orthosis and hand therapy is also relevant, particularly for patients with higher baseline pain levels, because this subgroup showed the largest improvement in pain. The implication of our findings for patients with relatively low baseline pain levels is less clear. In this group, pain significantly increased at follow-up. However, they had a relatively low conversion to surgery rate. A possible explanation may be that these patients had only minor impairments before treatment, and became more aware of the pain in their thumb and the impairments in daily living during their treatment, which could contribute to the increased pain at 12 months after receiving an orthosis and hand therapy.

Although we found that the median duration to surgery was 5 months, this finding was subject to multiple local factors, and therefore, may be less generalizable. For example, as a rule, decision making on additional surgical treatment was scheduled at the outpatient clinic after 3 months, when treatment was

completed. In addition, factors such as waiting lists, personal factors, holidays, or financial reasons and insurance policies influenced the timing of surgery. To answer the question about the best timing to convert to surgery, a different study design would be preferred, using more frequent measurements.

For future research, it would be interesting to study the effect of patient adherence to therapy on treatment outcome. Future studies should also focus on identifying prognostic factors to predict which patients will have a good outcome after a hand orthosis and hand therapy and which can benefit more from early surgery. In addition, future research should focus on the optimal timing of this decision. Moreover, other possible predictors that can influence treatment outcome should be evaluated, such as coping mechanisms, catastrophizing, quality of life, emotional, and mental health.

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Supplementary Table 1. When applying Bonferroni correction to account for multiple testing, a P-value of <.003 was required to find a significant difference. No significant differences were found for all variables.

Variable	Mean complete cases ± SD	Mean imputed data ± SD	P-value
VAS Pain during activities baseline	57.4 ± 22	61.0 ± 22	0.154
VAS Pain during activities 6 weeks	45.3 ± 22	48.8 + 23	0.205
VAS Pain during activities 3 months	44.4 ± 23	47.2 ± 23	0.288
VAS Pain during activities 12 months	42.7 ± 26	45.7 ± 22	0.330
VAS Pain in the last week baseline	48.1 ± 19	49.6 ± 20	0.537
VAS Pain in the last week 6 weeks	35.2 ± 19	39.7 ± 21	0.060
VAS Pain in the last week 3 months	38.3 ± 22	40.4 ± 21	0.396
VAS Pain in the last week 12 months	35.1 ± 25	39.8 ± 19	0.099
MHQ Total baseline	64.3 ± 15	63.9 ± 14	0.820
MHQ Total 6 weeks	70.0 ± 9	68.7 ± 9	0.428
MHQ Total 3 months	70.8 ± 15	70.3 ± 11	0.791
MHQ Total 12 months	73.1 ± 15	71.9 ± 9.8	0.502
MHQ Pain baseline	57.7 ± 24	62.0 ± 26	0.151
MHQ Pain 6 weeks	43.8 ± 20	49.7 ± 20	0.011
MHQ Pain 3 months	41.2 ± 21	46.3 ± 21	0.040
MHQ Pain 12 months	39.1 ± 25	40.8 ± 20	0.557

Abbreviations: MHQ = Michigan Hand Questionnaire; SD =Standard Deviation; VAS = Visual Analog Scale

CHAPTER 3

EXERCISE THERAPY IN ADDITION TO AN ORTHOSIS REDUCES PAIN MORE THAN AN ORTHOSIS ALONE IN PATIENTS WITH THUMB BASE OSTEOARTHRITIS: A PROPENSITY SCORE MATCHING STUDY

Robbert M. Wouters
Jonathan Tsehaie
Harm P. Slijper
Steven E.R. Hovius
Reinier Feitz
The Hand-Wrist Study Group
Ruud W. Selles

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ABSTRACT

Objective: To compare the effect of exercises and orthotics with orthotics alone on pain and hand function in patients with thumb base (CMC-1) osteoarthritis (OA) and to predict outcomes on pain and hand function of exercises and orthotics.

Design: Prospective cohort study with propensity score matching

Setting: Data collection took place in thirteen outpatient clinics for hand surgery and hand therapy in the Netherlands.

Participants: A consecutive, population-based sample of 173 patients with CMC-1 OA was included in this study of which 84 were matched on baseline demographics and baseline primary outcomes.

Interventions: Exercises and orthotics versus orthotics alone.

Main Outcome Measure(s): Primary outcomes included pain and hand function at three months, measured using Visual Analogue Scales (0-100, VAS) and the Michigan Hand outcomes Questionnaire (0-100, MHQ).

Results: A larger decrease in VAS pain at rest (11.1 points difference, 95% Confidence interval(CI): 1.9, 20.3, p=0.002) and during physical load (22.7 points difference, 95% CI: 13.6, 31.0, p<0.001,) was found in the exercise + orthotic group compared to the orthotic group. Additionally, larger improvement was found for the MHQ subscales pain, work performance, aesthetics and satisfaction in the exercise + orthotic group. No differences were found on other outcomes. Baseline scores of metacarpophalangeal flexion, presence of scapho-trapezio-trapezoid OA, VAS pain at rest, heavy physical labor and MHQ total predicted primary outcomes for the total exercise + orthotic group (N=131).

Conclusions: Conservative treatment for patients with CMC-1 OA should include exercises, since there is a relatively large treatment effect compared to using an orthosis alone. Future research should study exercises and predictors in a more standardized setting to confirm this finding.

INTRODUCTION

Osteoarthritis (OA) of the thumb base joint (CMC-1) is a common disorder, with a radiologically diagnosed prevalence amongst females aged ≥50 years of 33-40%.[1-3] Patients with CMC-1 OA often experience thumb pain, limitations in activities of daily life (ADL) and present clinical features such as thenar muscle wasting or thumb deformity.[1,4]

Guidelines and reviews advise to start with non-surgical treatment, including analgesics, intra-articular injections, orthotics and exercise programs.[5-7] While these interventions are widely used, evidence that supports these non-surgical treatments, especially exercise programs, is limited.[5-13] Nonetheless, while analgesics, intra-articular injections or orthotics provide short-term results, exercise programs may provide a long-term solution by improving lifestyle, joint mechanics and function.[12]

Most exercise programs intend to improve active stability and positioning of the CMC-1 into a more stable position of extension/abduction, since the CMC-1 becomes less stable during flexion/adduction.[9,12-17] Additionally, exercises focus on maintaining the first web space and pinch strength.[10-14] Orthotics often complements exercises, to reduce subluxation and inflammation, but are also prescribed as a stand-alone treatment.[11,14]

If non-surgical treatment fails to alleviate symptoms, conversion to surgical treatment may be considered. However, disadvantages of surgical treatment are its long recovery, prolonged patient discomfort & limitations and high costs.[6,18,19] Furthermore, it has been reported that for a trapeziectomy with/without ligament reconstruction and tendon interposition, 11-33% of the patients would not consider the same treatment again under the same circumstances.[19-23] Hence, because of the potential advantages compared to surgical treatment, more research on the added value of exercises in addition to orthotics is needed, since few studies are conducted and those available are of low methodological quality.[5,7,8,11] Furthermore, it is unclear if there are predictors for outcome of exercises.[12] It is, for example, unclear if exercises are equally effective in patients with scapho-trapezio-trapezoid (STT) OA (Eaton stage >III[24]) compared to isolated CMC-1 OA (Eaton stages I-III).[12] This prospective cohort study compares the effect of a combination therapy consisting of range of motion, coordination and strengthening exercises and orthotics versus orthotics alone on pain and hand

function in patients with CMC-1 OA. Furthermore, predictors of outcome for the combination therapy are studied to optimize treatment selection for patients with CMC-1 OA.

METHODS

Study design

This is a prospective cohort study with propensity score matching (PSM) using a consecutive, population-based sample, reported following the STROBE statement.[25]

Setting

This study was performed at thirteen outpatient clinics for hand therapy and hand surgery in The Netherlands. Data collection took place between October 2015 and February 2017 and the local Medical Research Ethical Committee approved this study. Data collection was part of routine outcome measurement using GemsTracker electronic data capture tools.[26] GemsTracker (GEneric Medical Survey Tracker) is a secure web-based application for distribution of questionnaires and forms during clinical research and quality registrations.[27,28]

A certified hand surgeon diagnosed patients with CMC-1 OA by physical examination and radiographic evaluation to determine Eaton stage.[6,24] Subsequently, patients were referred for hand therapy and follow-up with the hand surgeon took place after three months to decide if further treatment was needed.

Participants

Participants were eligible for inclusion when they were adult and diagnosed with stage I-IV[24] CMC-1 OA. Exclusion criteria were: 1) secondary CMC-1 OA (i.e. due Bennett's fracture); 2) comorbidity interfering with treatment/outcome (i.e. Quervain's tenosynovitis); 3) patient history includes surgery interfering with treatment/outcome; or 4) steroid injection <6 weeks in hand/wrist.

Treatment

Due the observational design, treatment was not completely standardized as in randomized controlled trials. However, the hand therapists were trained to use and carry out treatment following a strict guideline.[29] The guideline prescribes the use of both orthotics and exercises. However, the exercises are not applied for every patient, depending on considerations made by the hand therapist and

patient (i.e. influenced by therapy costs/traveling distance). Therefore, the hand therapists completed surveys at baseline, six weeks and three months on the treatment content and potential deviations to ensure guideline usage.[29]

Participants with more than two hand therapy sessions were classified into the exercise + orthotic group, received exercises and a static orthosis to reduce synovitis and instability.[11,30] The orthosis was thermoplastic, custom-made and immobilized the CMC-1 in extension/abduction and the first metacarpophalangeal joint (MCP-1) in flexion. The exercise program included hand therapy sessions and exercises performed at home by the patient, aiming to improve active stability of the CMC-1 during pinch in extension/abduction as instability and degeneration occurs in flexion/adduction.[10,12,14-17] In the first treatment phase (week 0-6), coordination of the intrinsic thenar muscles (except the adductor pollicis), extensor pollicis brevis and the first dorsal interosseous was exercised.[10,12,14] Participants were instructed to use the orthosis 24h/day in this phase, except during exercises. In the second phase (week 6-3 months), orthosis usage was reduced, guided by the hand therapist and strengthening exercises for the thenar muscles (except adductor pollicis) were initiated (details in Appendix 1).[10,12] Participants in the orthotic group were provided with the same orthosis, usage instructions and wearing time, but only two or less hand therapy sessions were scheduled in which general advice and information on CMC-1 OA was provided and no structured exercises were performed.

Variables, data sources/measurement

Primary & secondary outcomes

Primary outcomes were pain and hand function. Pain at rest and during physical load (i.e. activities needing pinch force, such as opening a jar or turning a key) was measured at baseline, six weeks and three months using a Visual Analogue Scale (VAS, 0-100, higher scores indicate more pain). The VAS is a reliable and valid instrument to measure pain intensity in patients with rheumatic diseases and has a minimal clinical important difference (MCID) of eleven.[31] Hand function was measured at baseline and three months using the Michigan Hand Outcomes Questionnaire (MHQ).[32] The MHQ total score was used as primary outcome while the subscales were secondary outcomes (0-100, higher scores indicate better performance except for the subscale pain).[32] The MHQ has a high internal consistency, high internal validity, acceptable reliability and is particularly applicable for patients with hand OA.[32] The MCID for the MHQ is 8-13 (3-23

for the subscales).[33,34] Additionally, patient satisfaction was assessed at three months using a self-designed questionnaire on treatment effect and willingness to undergo treatment again. Conversion to surgery within 12 months was derived from patient charts.

Additional measurements

Stage of CMC-1 OA[6,24], age, gender, type of work, therapy frequency, symptom duration and dominant side treated was derived from patient charts and surveys completed by the hand therapists. The hand therapists performed and registered measurements using standardized forms and were trained to conduct standardized measurements.[35] Additional baseline characteristics included MCP-1 flexion/hyperextension and inter metacarpal distance (IMD). MCP-1 flexion/hyperextension was measured using the American Society of Hand Therapists recommendations.[35] Presence of hyperextension at MCP-1 was dichotomized while MCP-1 flexion was used as continuous variable. IMD was measured using a caliper, because its reliability is superior to goniometric measurements of abduction.[36,37] Measurements of IMD were dichotomized, where 3.3mm difference between the unaffected and affected side was defined as limited IMD, since 3.3mm is the smallest detectable difference for IMD.[37] In bilateral involvement, the hand with the worst baseline MHQ score was used.

Initially, our study protocol included pinch & grip strength measurements. However, due to substantial missing data we considered the available data as potentially biased, hence we chose not to include these measurements.

Study size

No recommendations on power analysis for PSM were found in literature. A study on Dupuytren's disease by Zhou et al.[28] used PSM, where 60% of the total sample was matched. Therefore, we estimated that at least 60% of the total sample would be matched, resulting in an estimated sample of 124 before PSM and 74 after PSM for a F-test, a conventional medium effect size of .15 (defined by Cohen[38]) and a power of 0.80. Since group ratio between the orthotic and exercise + orthotic group was unclear prior to analysis, we enlarged the sample to >200.

Statistical methods

At baseline, 91.7% of the demographic characteristics and primary outcomes were available. When data was missing, we checked whether it could be retrieved

from patient charts. Missing value analysis on demographics and outcomes at three months showed a non-significant Little's test (p=0.495 and p=0.341 respectively), which confirmed that missing values were missing completely at random (MCAR).[39-41] To further evaluate missing data at three months, significant testing was performed on demographic characteristics and baseline primary outcomes to compare participants with the presence of a primary outcome at three months with participants without the presence of a primary outcome at three months. No significant differences between were found (Appendix 2). Since data were MCAR and no differences were found between participants with and without the presence of a primary outcome at three months, multiple imputation was used to obtain missing data for continuous variables with <75% missing, resulting in excluding the patient satisfaction questionnaire from multiple imputation.[39,42,43]

Since comparing groups in observational studies is usually difficult due to differences between groups in covariates, we used PSM.[44] PSM involves a propensity score, which is the probability for an individual to be assigned to a particular treatment given observed covariates.[45,46] PSM allows comparing matched individuals, the only difference being whether they are treated with the intervention of interest or not.[45]

Propensity scores were estimated using logistic regression, where treatment status was regressed on baseline characteristics,[45-47] using: VAS pain at rest and during physical load, MHQ total score, MCP-1 hyperextension, MCP-1 flexion, limited IMD, presence of STT OA (Eaton >III[24]), age, gender, type of work, symptom duration and dominant side treated. The propensity scores were subsequently used to match participants on a one-to-one basis using a nearest-neighbor algorithm with a matching tolerance width of 0.2 SD of the logit of the propensity score.[45,47] Between-group differences in demographic characteristics were analyzed before and after matching using standardized mean differences.[47-49]

Continuous outcomes were analyzed using univariate linear mixed model analysis and paired sample t-tests. The threshold for significance is lowered to 0.0125 from a conventional 0.05 to correct for multiple testing. The patient satisfaction questionnaire was analyzed on item level using Wilcoxon signed rank and McNemar tests.

To predict primary outcomes at three months, multivariate backward regression analysis was used on the complete exercise + orthotic group (including

unmatched participants). The same characteristics as in PSM were used, with therapy frequency added. Data were checked for multicollinearity using correlation coefficients and variance inflation factor (VIF). A VIF >10 was considered an indication for multicollinearity.[50]

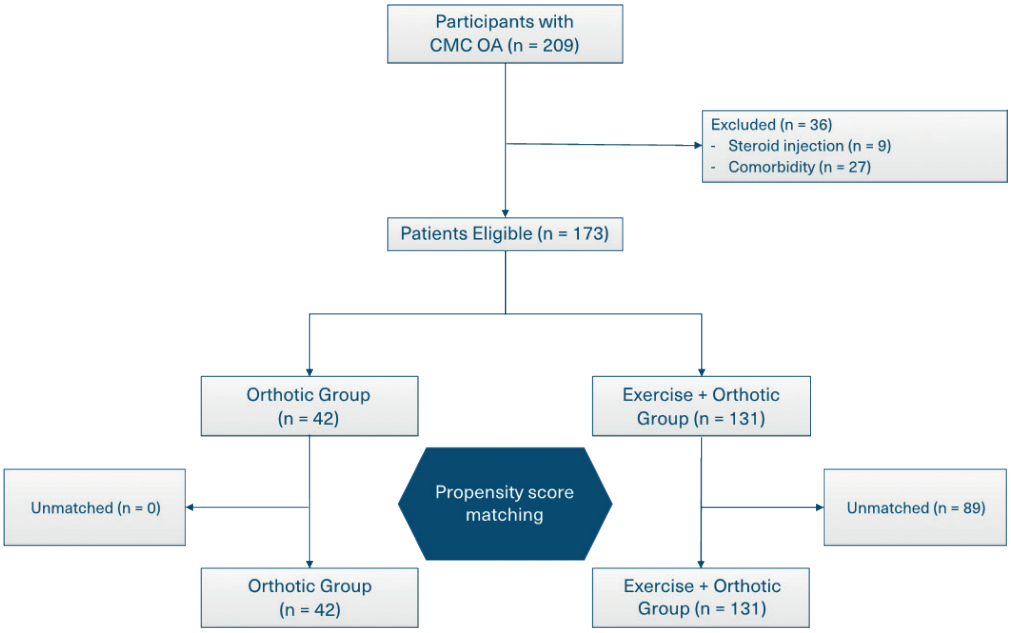

Figure 1. Flow chart of this study, demonstrating that 42 participants per group were matched using propensity score matching

RESULTS

Initially, 209 participants were included (Figure 1). Twenty-seven participants were excluded due to comorbidity and nine participants were excluded because of corticosteroid injection(s). Hence, 173 participants were finally included. The orthotic group contained 42 participants while the exercise + orthotic group contained 131 participants. After matching, both groups contained 42 participants. Small[38] between-group differences remained after matching (Table 1). The mean number of therapy sessions was 6.7 (SD=1.9) in the exercise + orthotic group.

Table 1. Demographic characteristics at baseline. The unmatched and matched participants are displayed. Characteristics between the groups were compared using standardized mean differences. SD = standard deviation, OA = Osteoarthritis, MCP-1 = first metacarpophalangeal joint, IMD = inter metacarpal distance. VAS = Visual Analogue Scale, MHQ = Michigan Hand outcomes Questionnaire

		All Participants			**Matched Participants**		
		Orthotic group	*Exercise + orthotic group*	*Standardized mean difference*	*Orthotic group*	*Exercise + orthotic group*	*Standardized mean difference*
Participants, N		42	131		42	42	
Age in years, mean (SD)		60.8 (9.1)	60.2 (8.4)	0.06	60.8 (9.1)	58.9 (7.6)	0.23
Females, N (%)		31 (73.8%)	99 (75.6%)	0.04	31 (73.8%)	32 (76.2%)	0.06
Dominant side treated, N (%)		20 (47.6%)	62 (47.3%)	0.01	20 (47.6%)	17 (40.5%)	0.14
VAS, 0-100 (SD)	*At rest*	34.5 (23.1)	26.1 (23.5)	0.36	34.5 (23.1)	29.7 (24.6)	0.20
	During physical load	70.9 (14.5)	66.8 (16.7)	0.26	70.9 (14.5)	70.9 (15.6)	0.00
MHQ total, 0-100 (SD)		54.1 (14.4)	56.3 (19.4)	0.12	54.1 (14.4)	54.6 (17.6)	0.03
Type of work, N (%)	*Unemployed*	21 (50%)	51 (38.9%)	0.22	21 (50%)	15 (35.7%)	0.29
	Light physical labor	8 (19%)	30 (22.9%)	0.10	8 (19%)	8 (19%)	0.00
	Moderate physical labor	9 (21.4%)	34 (26%)	0.11	9 (21.4%)	12 (28.6%)	0.17
	Heavy physical labor	4 (9.5%)	16 (12.2%)	0.09	4 (9.5%)	7 (16.7%)	0.21
Symptom Duration in months, mean (SD)		22.1 (17.2)	27.3 (35)	0.18	22.1 (17.2)	31.0 (33.1)	0.33
Eaton Stage OA, N (%)	*I-III*	37 (88.1%)	114 (87%)	0.03	37 (88.1%)	37 (88.1%)	0.00
	IV	5 (11.9%)	17 (13%)	0.03	5 (11.9%)	5 (11.9%)	0.00
MCP-1 Hyperextension, N (%)		30 (71.4%)	96 (73.3%)	0.04	30 (71.4%)	29 (69%)	0.05
MCP-1 flexion in degrees, mean (SD)		49.8 (11.6)	52 (12.5)	0.18	49.8 (11.6)	52.7 (13.7)	0.23
IMD limited, N (%)		12 (28.6%)	45 (34.4%)	0.13	12 (28.6%)	14 (33.3 %)	0.10

Primary & secondary outcomes

VAS pain at rest decreased 11.1 points more in the exercise + orthotic group compared to the orthotic group at three months (95% Confidence interval (CI): 1.9, 20.3, p=0.002, Figure 2). Furthermore, VAS pain during physical load decreased 22.7 points more in the exercise + orthotic group compared to the orthotic group (95% CI: 13.6, 31.0, p<0.001, Figure 3).

No significant between-group differences were found on the MHQ total score (Table 2, p=0.273), but the subscales pain, work performance, aesthetics and satisfaction improved more in the exercise + orthotic group compared to the orthotic group with 8, 10.1, 5 and 12.9 points difference respectively (Figures 4-5, Table 2, p<0.001-0.008). No significant differences were found on other MHQ subscales or the patient satisfaction questionnaire (Table 2). Conversion to surgery was 7% (N=3) in the exercise + orthotic group and 10% (N=4) for the orthotic group (p=0.693).

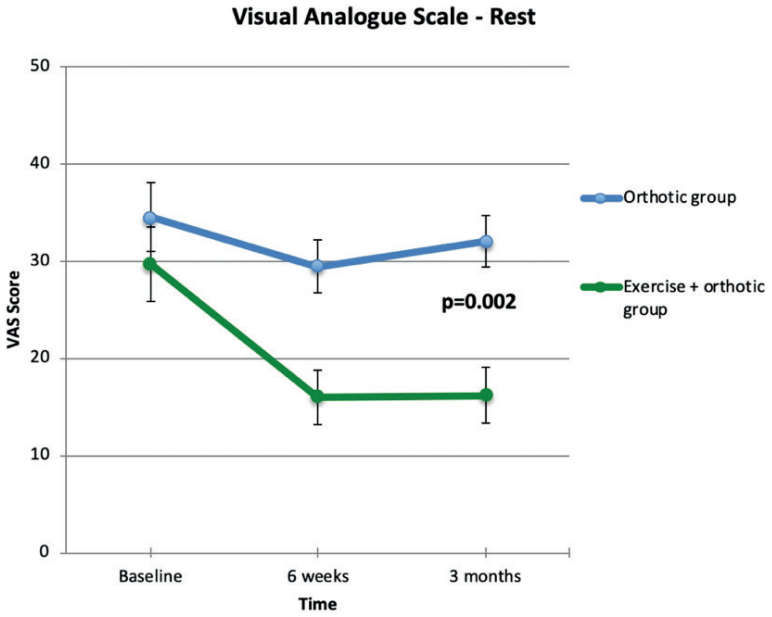

Figure 2. Pain at rest as measured with a Visual Analogue Scale (VAS) for the orthotic group (blue line) and the exercise + orthotic group (green line). Group means and standard errors are plotted. Linear mixed model analysis demonstrates a significant difference between the groups (p=0.002).

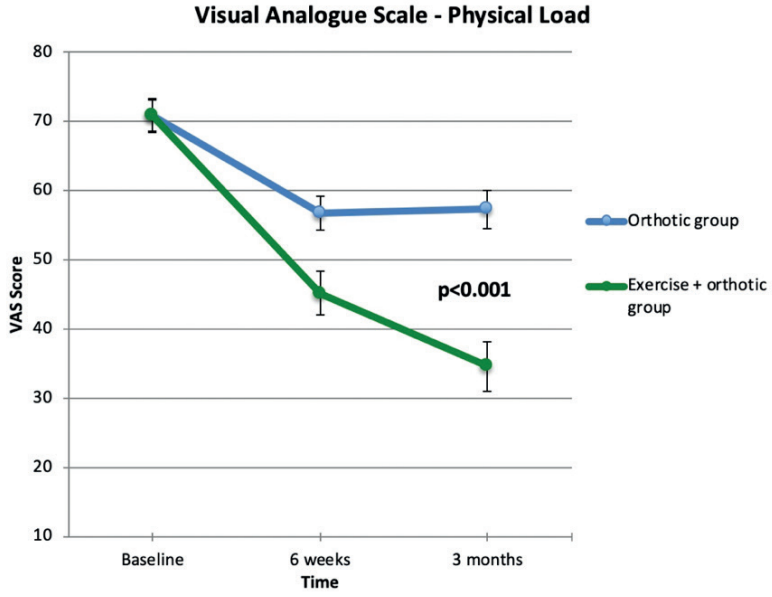

Figure 3. Pain during physical load as measured with a Visual Analogue Scale (VAS) for the orthotic group (blue line) and the exercise + orthotic group (green line). Group means and standard errors are plotted. Linear mixed model analysis demonstrates a significant difference between the groups (p<0.001).

Table 2. Outcomes of matched participants. The p-values displayed indicate significance of treatment effect in linear mixed model analysis, paired samples t-tests, Wilcoxon signed rank tests and McNemar tests. VAS = Visual Analogue Scale, SD = standard deviation, MHQ = Michigan Hand Outcomes Questionnaire – Dutch Version, ADL = activities in daily life.

	Splint group				**Exercise program group**					**p-value**
	Baseline	*6 weeks*	*3 months*	*Δ Within group*	*Baseline*	*6 weeks*	*3 months*	*Δ Within group*	*Δ Between groups*	
VAS pain rest, mean (SD)	34.5 (23.1)	29.4 (17.0)	32.0 (16.9)	-2.4	29.7 (24.6)	16.0 (18.4)	16.2 (18.7)	-13.5	-11.1	0.002
VAS pain physical load, mean (SD)	70.9 (14.5)	56.8 (14.4)	57.3 (17.2)	-13.6	70.9 (15.6)	45.2 (20.5)	34.6 (22.8)	-36.3	-22.7	<0.001
MHQ, mean (SD) Total	54.1 (14.4)	-	61.1 (10.0)	7	54.6 (17.6)	-	66.0 (13.4)	11.4	4.4	0.071
Subscales:										
- Overall hand function	51.5 (5.9)	-	56.6 (9.9)	5.1	54.2 (9.9)	-	59.8 (10.8)	5.6	0.5	0.258
- ADL	61.5 (8.9)	-	66.4 (13.8)	4.9	58.3 (17.2)	-	63.9 (16.5)	5.6	0.7	0.505
- Work performance	55.3 (15.6)	-	57.6 (17.1)	2.3	56.7 (18.7)	-	69.1 (15.8)	12.4	10.1	0.008
- Pain	66.8 (12.9)	-	55.6 (14.7)	-11.2	61.6 (19.0)	-	42.4 (17.7)	-19.2	-8.0	0.001
- Aesthetics	73.4 (8.2)	-	74.7 (14.5)	1.3	82.8 (14.6)	-	89.1 (10.4)	6.3	5.0	<0.001
- Satisfaction	44.0 (9.7)	-	50.6 (13.6)	6.6	46.9 (17.2)	-	66.4 (16.5)	19.5	12.9	<0.001
Experienced treatment result, %										0.317
- Excellent			0 %				6.3%			
- Good			40%				50%			
- Fair			10%				25%			
- Moderate			50%				12.5%			
- Poor		-	0%	-		-	6.3%	-		
Participants that would undergo treatment again, %		-	60 %	-		-	75%	-		1.000

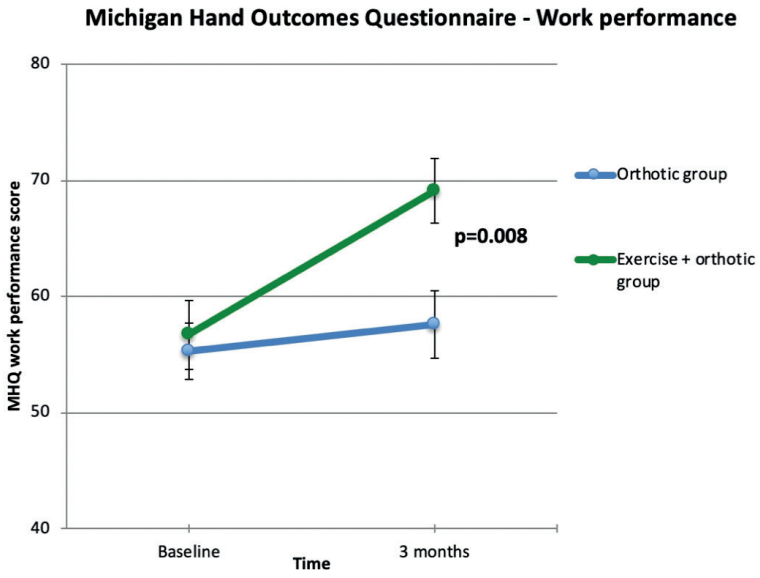

Figure 4. Work performance as measured with the Michigan Hand outcomes Questionnaire (MHQ) for the orthotic group (blue line) and the exercise + orthotic group (green line). Group means and standard errors are plotted. Paired samples T-tests demonstrate a significant difference between the groups (p=0.008).

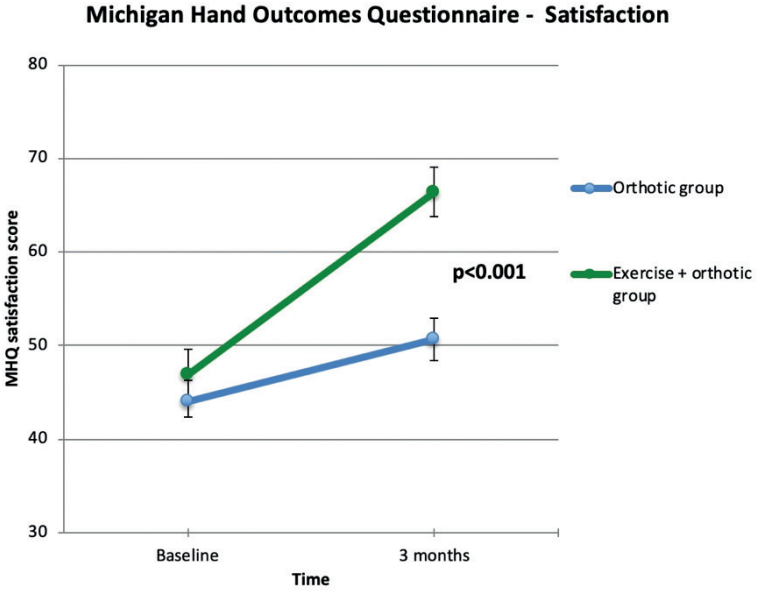

Figure 5. Satisfaction as measured with Michigan Hand outcomes Questionnaire (MHQ) for the orthotic group (blue line) and the exercise + orthotic group (green line). Group means and standard errors are plotted. Paired samples T-tests demonstrate a significant difference between the groups (p<0.001).

Prediction of outcome

Multiple regression identified several predictors in the total exercise + orthotic group (N=131), with a relatively small explained variance of 16% (VAS pain at rest), 19% (VAS pain during physical load) and 26% (MHQ total score, Table 3). Higher baseline score for VAS pain at rest predicted a higher score at three months. Furthermore, lower MCP-1 flexion, higher VAS pain at rest baseline score and presence of STT OA predicted a higher VAS pain score during physical load at three months. However, when comparing participants with (N=17) and without (N=114) STT OA within the total exercise + orthotic group, pain during physical load significantly decreased at three months in both subgroups, by 29.5 and 36.4 points respectively (p<0.001). Type of work with heavy physical labor (i.e. working in construction) predicted a lower MHQ total score at three months while a higher MHQ total baseline score predicted a higher score at three months.

Table 3. Predictors for outcomes in the total exercise + orthotic group (N=131) on Visual Analogue Scale (VAS) pain during physical load and at rest and the Michigan Hand outcomes Questionnaire (MHQ) total score. MCP-1 = first metacarpophalangeal joint, STT = scaphotrapeziotrapezoid joint, OA = osteoarthritis

Predictor	Beta coefficient	Adjusted R square	p-value
VAS pain rest at 3 months		0.161	
- VAS rest baseline score	0.286		<0.001
VAS pain physical load at 3 months		0.190	
- MCP-1 flexion	-0.424		0.011
- Presence of STT OA	11.976		0.063
- VAS rest baseline score	0.424		<0.001
MHQ total score at 3 months		0.255	
- Type of work: heavy physical labor	-13.782		0.034
- MHQ total baseline score	0.522		<0.001

DISCUSSION

This study found superior and clinically relevant results for the exercise + orthotic group compared to the orthotic group on VAS pain (at rest and during physical load) and the MHQ subscales pain, work performance, aesthetics and satisfaction. No significant differences were found on MHQ total score, its subscales and the patient satisfaction questionnaire. Furthermore, predictors for outcomes of a combination of exercises and orthotics were baseline MCP-1 flexion,

presence of STT OA, VAS pain at rest, type of work with a heavy physical labor and MHQ total.

Our findings on treatment effect are not completely in line with literature. Several studies [7,9,11,13] found positive outcomes on pain and hand function for exercises, while other studies[5,8] found insufficient or low evidence for the use of exercises. This contradiction may be related to the fact that systematic reviews reported that most studies on exercises for patients with CMC-1 OA are of low methodological quality.[5,7,8,11] Additionally, some studies[9,13] used similar exercises as in this study, while some studies included in the systematic reviews for example applied manual mobilizations to the CMC-1 or mainly applied exercises for general hand OA instead of CMC-1 OA specifically.[5,7,8] Hence, more high-quality studies on exercises for patients with CMC-1 OA are needed.

We found that within the exercise + orthotic group, baseline MCP-1 flexion, presence of STT OA, VAS pain at rest, type of work with a heavy physical labor and MHQ total were predictors of the primary outcomes at three months, although the explained variance was only 16-26%. STT OA was a predictor for worse outcomes on VAS pain during physical load, but despite this, pain during physical load significantly decreased on average still 29.5 points in the exercise + orthotic group. This suggests that exercises are also feasible and effective for patients with Eaton stage IV[24], but future research should investigate if exercises need to be adapted for patients with STT OA since the STT is presumably also influenced by wrist motion.[51]

The findings on MCP-1 flexion suggest that the exercises positively influenced biomechanics during pinch, since prevention of MCP-1 hyperextension and applying MCP-1 flexion might prevent further subluxation and degeneration of the CMC-1.[12,14-17] However, future studies should investigate the influence of MCP-1 flexion on the disease course of CMC-1 OA.

Additionally, heavy physical labor predicted a lower MHQ total score, possibly because it is more difficult for patients with heavy physical labor to adapt in ADL.

Study Limitations

The significant and clinically relevant benefits of exercises may be a result of improved thumb positioning and the strengthening exercises improving pinch strength. However, a limitation is that insufficient data was available to report

outcomes on strength. Additionally, the use of multiple imputation on other outcomes may have introduced bias, despite missing value analyses and the non-significant Little's test. Furthermore, substantial statistical power was lost in the variables where no multiple imputation was used. For example, outcomes on patient satisfaction demonstrated superior but non-significant results in the exercise + orthotic group. Hence, it is recommended that future research on this topic is employed with emphasis on prevention of missing data.

While a limitation of this study is its observational character, a strength is that the results are collected in daily practice and are therefore representative for actual daily care. However, despite that the hand therapists received training in guideline usage, complete standardization of treatment could not be ensured as in randomized controlled trials. Additionally, blinding was not possible in the present design and i.e. analgesics usage is not controlled. Furthermore, indication bias may have occurred in treatment allocation if unidentified covariates were present. Further exploration on (predictors for) outcomes of exercises is needed in a standardized, randomized controlled trial. However, the small differences[38] in baseline characteristics (with a highest SMD of 0.33), largely already present prior to PSM gives us confidence that the results of a randomized controlled trial would be similar.

Additionally, a limitation is that large variation on MCID's of the MHQ is reported in literature. Hence, the significant differences in MHQ subscales should be interpreted with caution.[33,34]

Another limitation is that contextual or placebo effects may be present, since the exercise + orthotic group received more attention from the hand therapists compared to the orthotic group. Hence, studies investigating contextual effects of exercises are needed.

Lastly, a limitation of the exercise program may be the costs compared to an orthosis only. Potential cost saving could be achieved if exercise programs reduce the conversion to surgery compared to no exercises. In the present study, conversion to surgery within 12 months was not significantly different between the exercise + orthotic group (7%) and the orthotic group (10%), but this may be due to the low number of events does not allowing to detect significant differences. Therefore, it is recommended that future studies investigate

the cost-effectiveness of exercise programs (including conversion to surgery) in addition to an orthosis in a larger, standardized randomized controlled trial.

CONCLUSIONS

In conclusion, positive effects of exercises were found on pain in patients with CMC-1 OA. Therefore, exercise programs are recommended in the treatment for patients with CMC-1 OA, particularly because of the relatively large treatment effects compared to an orthosis alone. Furthermore, baseline MCP-1 flexion, presence of STT OA, VAS pain at rest, type of work with a heavy physical labor and MHQ total predict outcomes for exercises combined with orthotics. Future research should study exercises in randomized controlled trials.

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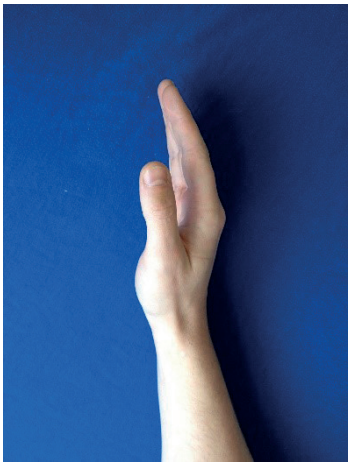
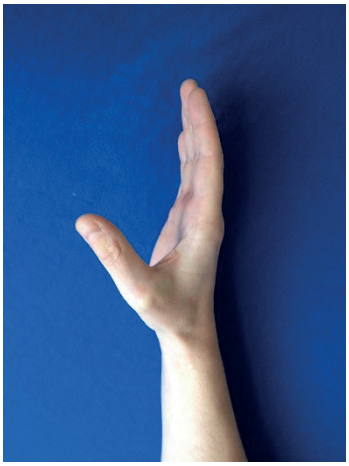
APPENDIX 1

First phase of treatment (week 0-6)

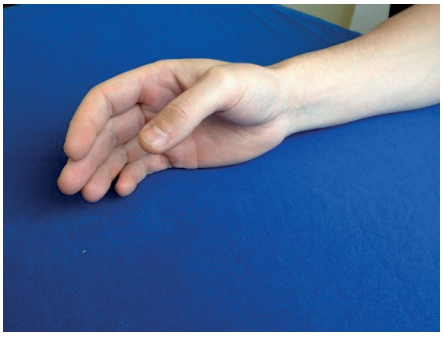
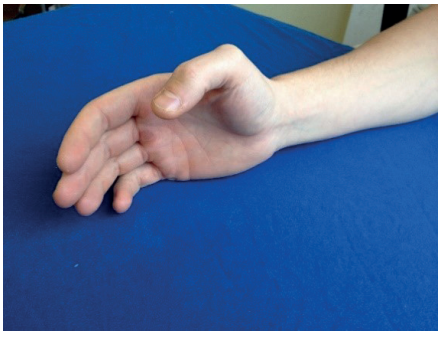
Examples of the exercises, performed 4-6 times a day, 10-15 repetitions.[12,23]

The exercises aim to improve the specific function of the intrinsic thenar muscles (except the adductor pollicis), the extensor pollicis brevis and the first dorsal interosseous.

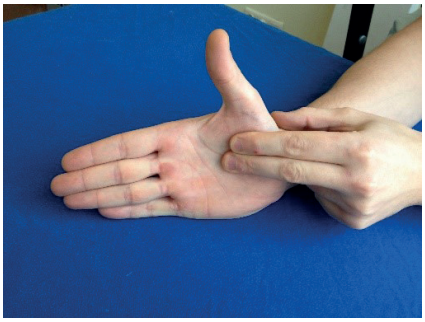
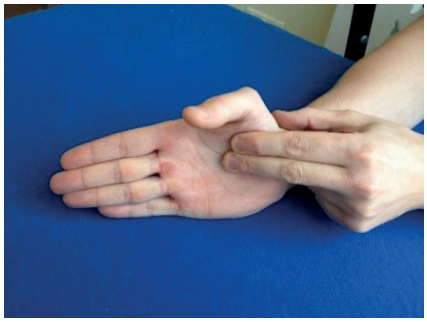
1 – Abductor pollicis brevis / longus coordination exercise

A.  B. 

2 – Extensor pollicis brevis coordination exercise

A.  B. 

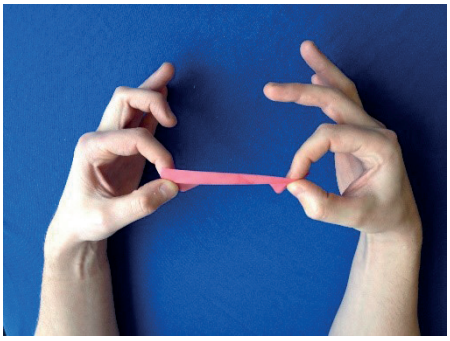
3 – Flexor pollicis brevis coordination exercise

A.  B. 

Second phase of treatment (week 6 – 3 months)

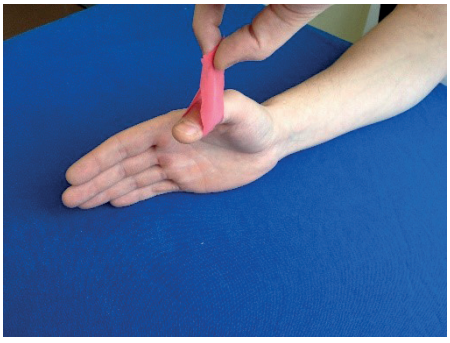
Examples of the exercises, performed 2-3 times a day. Force is applied for 2-3 seconds and build up until 50-100 repetitions. [12,23]

4 – Pulling a rubber band in closed and correct key pinch

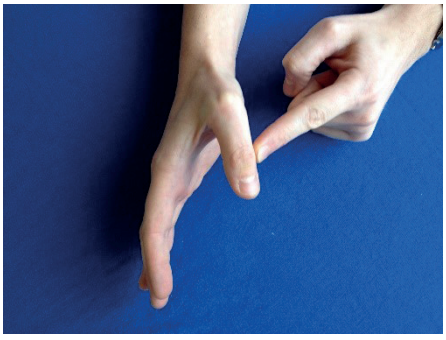


5 – Applying manual resistance at the radial, ulnar and dorsal aspect of the proximal phalanx in closed and correct key pinch

6 – Pulling a rubber band in open chain



7 – Applying manual resistance at the radial, ulnar and dorsal aspect of the proximal phalanx in open chain



APPENDIX 2

Supplementary Table 1. Non-responder analysis, where participants with the presence of a primary outcome at three months were compared with participants without a primary outcome at three months using independent samples t-tests, Chi square tests and Fisher's exact tests. SD = standard deviation, OA = Osteoarthritis, MCP-1 = first metacarpophalangeal joint, IMD = inter metacarpal distance. VAS = Visual Analogue Scale, MHQ = Michigan Hand outcomes Questionnaire

Non-responder analysis				
		Primary outcome at three months present	*Primary outcome at three months absent*	*p-value*
Participants, N		127 (73,4%)	46 (26,6%)	
Age in years, mean (SD)		60.2 (8.6)	60.9 (8.6)	0.662
Females, N (%)		96 (75.6%)	34 (73.9%)	0.844
Dominant side treated, N (%)		57 (44.9%)	15 (32.6%)	0.166
Type of work, N (%)	*Unemployed*	53 (41.7%)	19 (41.3%)	0.983
	Light physical labor	27 (21.3%)	11 (23.9%)	0.983
	Moderate physical labor	32 (25.2%)	11 (23.9%)	0.983
	Heavy physical labor	15 (11.8%)	5 (10.9%)	0.983
Duration of symptoms in months, mean (SD)		29.1 (28.7	24.9 (32.7)	0.443
Eaton Stage OA, N (%)	*I-III*	113 (89%)	38 (82.6%)	0.304
	IV	14 (11%)	8 (17.4%)	0.304
MCP-1 Hyperextension, N (%)		94 (80.3%)	32 (78%)	0.822
MCP-1 flexion in degrees, mean (SD)		51.0 (12.1)	52.9 (12.4)	0.394
IMD limited, N (%)		32 (32.3%)	12 (33.3%)	1.000
VAS, 0-100 (SD)	*At rest*	26.9 (24.4)	30.3 (21.2)	0.416
	During physical load	67.1 (16.4)	69.8(15.9)	0.353
MHQ total, 0-100 (SD)		57.8 (16.4)	57.1 (14.4)	0.916

CHAPTER 4

BENEFICIAL EFFECTS OF NON-SURGICAL TREATMENT FOR SYMPTOMATIC THUMB CARPOMETACARPAL INSTABILITY IN CLINICAL PRACTICE: A COHORT STUDY

Robbert M. Wouters
Harm P. Slijper
Lisa Esteban Lopez
Steven E.R. Hovius
Ruud W. Selles
for the Hand-Wrist Study Group

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ABSTRACT

Objective: To describe outcomes of non-surgical treatment for symptomatic thumb carpometacarpal (CMC-1) instability. Secondary, to evaluate the conversion rate to surgical treatment.

Design: Prospective cohort study

Setting: 20 outpatient clinics for hand surgery and hand therapy in the Netherlands.

Participants: A consecutive sample of 431 patients with symptomatic CMC-1 instability

Intervention: non-surgical treatment including exercise therapy and an orthosis

Main Outcome Measure(s): Pain (Visual Analog Scale, VAS, 0-100) and hand function (Michigan Hand Questionnaire, MHQ 0-100) at baseline, 6 weeks and 3 months. Conversion to surgery was recorded for all patients with a median follow-up of 2.8 years (range 0.8-6.7y).

Results: VAS scores for pain during the last week, at rest and during physical load improved with a mean difference at 3 months of 17 [97.5% Confidence interval: 9:25], 13 [9:18] and 19 [12:27] respectively ($p<0.001$). No difference was present at 3 months for MHQ total score, but the subscales ADL, work, pain and satisfaction improved by 7 [1:14], 10 [4:16], 5 [2:9] and 12 [2:22] points respectively ($p<0.001$-0.007). After median follow-up of 2.8y, only 59 (14%) participants were surgically treated. Both in the subgroups that did and did not convert to surgery, VAS pain scores decreased at 3 months compared to baseline ($p<0.001$-0.010), whereas MHQ total score did not improve in both subgroups. However, VAS and MHQ scores remained worse for patients that eventually converted to surgery ($p<0.001$).

Conclusions: In this large sample of patients with symptomatic CMC-1 instability, non-surgical treatment demonstrated clinically relevant improvements in pain and aspects of hand function. Furthermore, after 2.8 years, only 14% of all patients were surgically treated, indicating that non-surgical treatment is a successful treatment of choice.

INTRODUCTION

Symptomatic thumb carpometacarpal (CMC-1) instability can arise from multiple causes, such as generalized hypermobility, congenital disorders, or trauma and may cause pain and limitations in activities of daily living (ADL).[1-4] Furthermore, it has been suggested in literature that CMC-1 instability may predispose CMC-1 osteoarthritis (OA) later in life.[5-10]

Whereas multiple studies have investigated non-surgical treatment for CMC-1 OA[11-15], to our knowledge, there are no studies describing outcome of non-surgical treatment for symptomatic CMC-1 instability. Similar to patients with CMC-1 OA, orthotics and exercise programs may provide a long-term solution by improving lifestyle, joint mechanics and function, but evidence for their effectiveness in symptomatic CMC-1 instability is lacking.[11-15]

Exercise therapy for CMC-1 instability intends to improve active stability and positioning of the CMC-1 into a more stable position of extension/abduction, since the CMC-1 is less stable during flexion/adduction.[6,8-10,16-18] Additionally, exercise therapy aims to maintain the first web space and improve thumb pinch strength.[3,6,12,17,18] Furthermore, (temporary use of) orthotics often complement exercise therapy to reduce subluxation and inflammation.[6,12] Theoretically, improving joint mechanics in patients with CMC-1 instability might be very beneficial since CMC-1 instability may precede CMC-1 osteoarthritis (OA) later in life.[5-10]

In cases of symptomatic CMC-1 instability where insufficient improvement occurs following non-surgical treatment, surgical stabilization of the CMC-1 joint can be considered.[2,19,20] However, the outcome of these procedures are not very predictable and it has been reported that results of these surgical procedures are unsatisfactory in 12-55%[2,19]. In addition, surgical treatment comes with long recovery, prolonged patient discomfort & limitations and high costs.[21-23]. Hence, since non-surgical treatment potentially has many advantages compared to surgical treatment and since no studies are available on this topic, more research on non-surgical treatment for CMC-1 instability is needed. Therefore, the aim of this study is to describe the outcomes of non-surgical treatment, exercise therapy and an orthosis, for symptomatic CMC-1 instability. Secondary, the objective was to evaluate the conversion rate to surgical treatment.

METHODS

Study design

This is a prospective cohort study using a consecutive, population-based sample, reported following the STROBE statement.[24]

Setting

Data were collected at Xpert Clinic and Handtherapie Nederland, comprising 20 outpatient clinics for hand surgery and therapy in The Netherlands, and took place between January 2012 and September 2018 after approval by the local Medical Research Ethical Committee. Data collection was part of routine outcome measurement using GemsTracker electronic data capture tools.[25] GemsTracker (GEneric Medical Survey Tracker) is a secure web-based application for distribution of questionnaires and forms during clinical research and quality registrations, details have been published earlier.[11,15,26]

Participants

All patients were initially diagnosed with CMC-1 instability by one of the certified hand surgeons by physical examination. Radiographic evaluation of the CMC-1 joint was not systematically performed but radiographs were obtained if CMC-1 OA was suspected. Subsequently, patients were referred for hand therapy. Follow-up with the hand surgeon took place after three months to decide if additional treatment was needed. For this study, we excluded patients that: 1) were diagnosed with CMC-1 OA (including radiographic confirmation); 2) had comorbidity interfering with treatment/outcome (i.e. de Quervain's tenosynovitis); 3) had a patient history includes surgery interfering with treatment/outcome; or 4) received a steroid injection <6 weeks in hand or wrist.

Treatment

The treatment in this study was not completely standardized as in randomized controlled trials, since data collection was part of usual care. However, treatment by the hand therapists was carried out using a strict guideline,[27] which prescribes the use of both exercises and orthotics when needed. The exercises and orthotics were not applied in every patient, since the treatment was tailored to the patient's needs and based on a shared-decision making process (e.g., influenced by patient preferences, therapy costs and traveling distance).

If an orthosis was provided, this included a static orthosis to reduce synovitis and instability.[12,28] The orthosis was custom-made, thermoplastic and immobilized the CMC-1 in extension/abduction and the first metacarpophalangeal joint (MCP-1) in slight flexion. The exercise program included hand therapy sessions and exercises performed by the patient at home. These exercises aimed to improve the active stability of the thumb during pinch in extension/abduction, since flexion/adduction causes instability, and eventually degeneration.[3,6,8-10,18] In the first six weeks, the exercises aimed to improve coordination of the intrinsic thenar muscles (except the adductor pollicis), extensor pollicis brevis and the first dorsal interosseous.[3,6,11,18] Due to the observational design of this study, no strict prescriptions regarding orthotic usage were provided, but in general, if an orthosis was applied, participants were instructed to use it during heavy and provocative activities. Guided by the hand therapist, orthosis usage was reduced in the subsequent six weeks. Furthermore, strengthening exercises for the thenar muscles (except adductor pollicis) were initiated in this phase in addition to the coordination exercises.[3,6,11,18]

Variables, data sources/measurement

Primary & secondary outcomes

Primary outcomes in this study were pain and hand function at three months. Mean pain in the last week, pain at rest and pain during physical load were measured at baseline, six weeks and three months using a Visual Analogue Scale (VAS, 0-100, higher scores indicate more pain). The VAS is a widely used, reliable and valid tool for measuring pain intensity and has a minimal clinical important difference (MCID) of eleven points.[29] Hand function at baseline and three months was evaluated using the Michigan Hand outcomes Questionnaire (MHQ).[30] We used the MHQ total score as primary outcome while its six subscales were secondary outcomes (0-100, higher scores indicate better performance except for the subscale pain).[30] The MHQ is a widely used tool for measuring hand function and has a high internal consistency, high internal validity, acceptable reliability.[30] The MHQ has a MCID of 8-13 points (3-23 for the subscales).[31,32] Additional measurements included patient satisfaction at six weeks, three months and 12 months, assessed using a self-designed questionnaire on the perceived treatment effect and the patients' willingness to undergo the treatment again. Conversion to surgery within a median follow-up of 2.8 years (range 0.8 - 6.7 years) was derived from patient charts and additional questionnaires distributed one year after start of non-surgical treatment. If a patient converted to surgery,

we measured the time in months between the start of the non-surgical treatment and the decision to proceed to surgical treatment. Additional variables that were routinely collected in our database at baseline included age, sex, type of work, symptom duration, treatment side and dominance (Table 1).

Table 1. Demographic characteristics

Variable	Demographic characteristics (N = 431)
Age, mean ± SD	38.2 ± 13
Female sex, %	80%
Symptom duration in months, mean ±SD	16.4 ± 24.9
Treatment Side, %	
- Left	40%
- Right	60%
Dominance, %	
- Left	6%
- Right	91%
- Both	3%
Type of work, %	
- Unemployed	18%
- Light physical labor	32%
- Moderate physical labor	36%
- Heavy physical labor	14%
Second opinion, %	9%

Study size

Power analysis for a repeated measures design with two primary outcomes using a conventional medium effect size of 0.15 (defined by Cohen[33]), a = 0.025 and a power of 0.80 showed that a total sample of 87 participants was needed, which was well below the sample of 435 participants that we were able to include.

Statistical methods

At baseline, 62-72% of the primary outcomes were available. If there was missing data, we checked whether it could be retrieved from patient charts. Missing value analysis for outcomes at three months demonstrated a non-significant Little's test (p=0.771), which suggested that missing values were missing completely at random.[34-36] To further evaluate missing data at three months, significance testing on demographic characteristics and baseline primary outcomes was performed to compare participants with the presence of a primary outcome at three months with participants without the presence of a primary outcome at three months. No significant differences between participants with and without the presence of a

primary outcome at three months were found (Supplementary Table 1). Because the data were missing completely at random and no differences between participants with and without the presence of a primary outcome at three months were present, we used multiple imputation to obtain missing data for continuous variables with <75% missing.[34,37,38]

Treatment outcomes were analyzed using univariate linear mixed model analyses, using the outcome of interest as a dependent variable and timepoint as a fixed factor. Assumptions were checked using residual plots and normal probability plots. The threshold for significance is lowered to 0.025 from a conventional 0.05 to correct for multiple testing.

In addition to the overall treatment effect in the entire sample, we performed subgroup analysis for the patients that eventually converted to surgery, again using linear mixed model analyses.

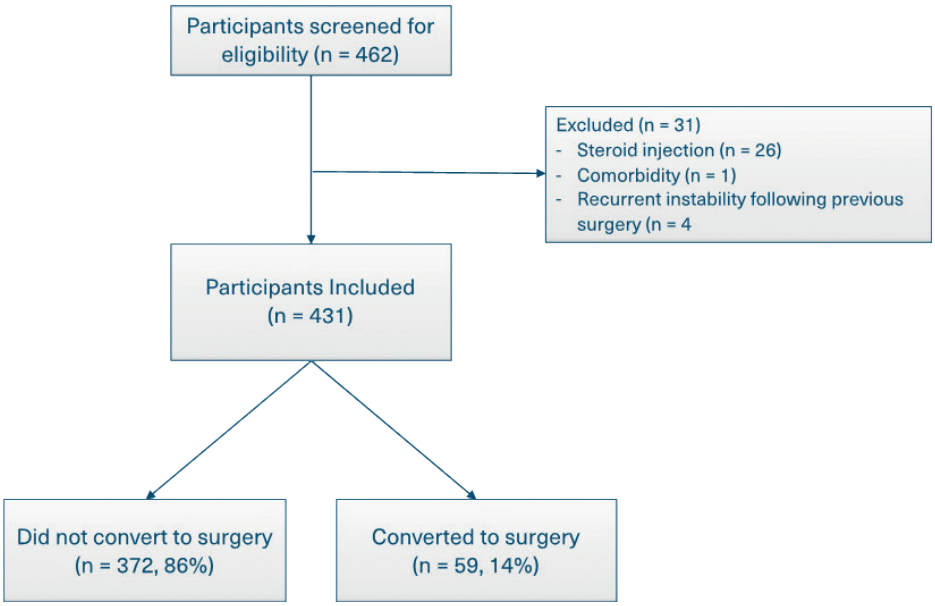

Figure 1. Flowchart of the study

RESULTS

Pain, hand function and satisfaction with treatment result

A total of 462 participants was screened for eligibility and 431 participants were included after applying the eligibility criteria. From the excluded participants, 26 participants received an injection, 1 had comorbidity (de Quervain's tenosynovitis) and 4 had recurrent CMC-1 instability following previous surgery (Figure 1). VAS scores for pain during the last week, pain at rest and pain during physical load improved with mean differences at 3 months of 17 [97.5% Confidence interval: 9:25], 13 [9:18] and 19 [12:27] points respectively (p<0.001, Figure 2).

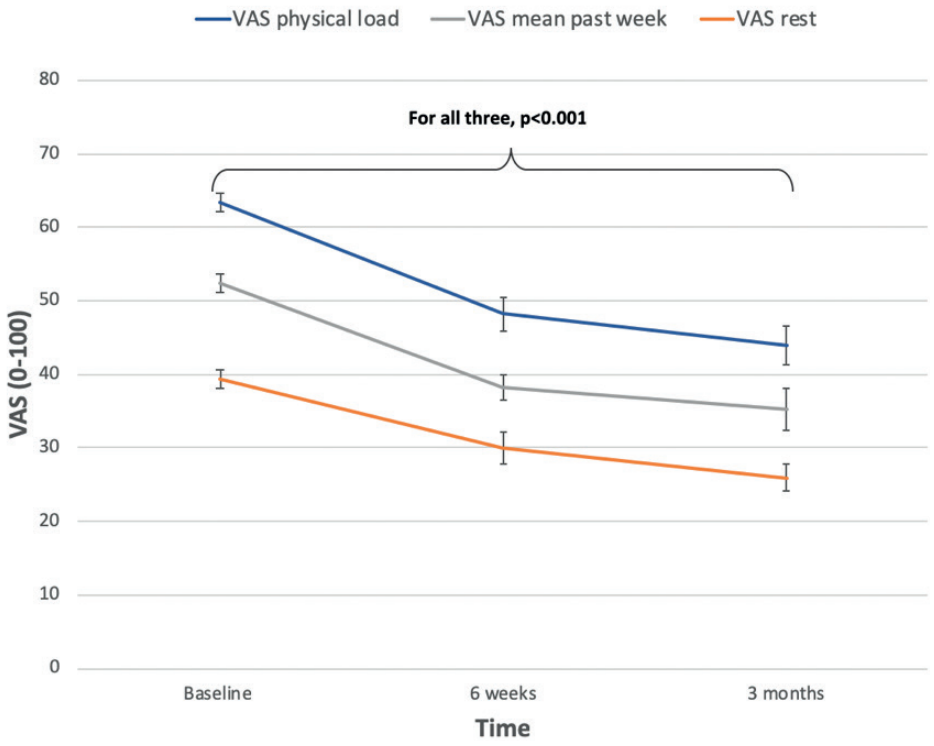

Figure 2. Visual Analogue Scale (VAS, 0-100, higher scores represent more pain) scores for pain physical load, mean pain last week and pain at rest at baseline, 6 weeks and 3 months. Linear mixed model analysis demonstrated that pain during physical load, mean pain last week and pain at rest decreased at 3 months compared to baseline (p<0.001). Group means and standard errors are plotted.

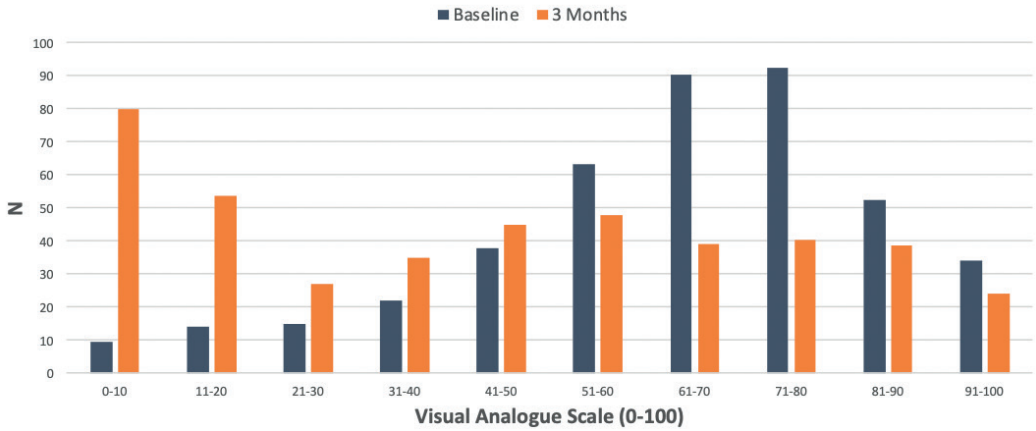

Figure 3. Overall distribution of the entire sample for Visual Analogue Scale (VAS, 0-100, higher scores represent more pain) at baseline and 3 months after non-surgical treatment, displaying the number of patients per 10-point intervals in VAS score.

Figure 3 demonstrates the distribution of VAS pain during physical load at baseline and 3 months, indicating large variability in pain levels both prior to and after treatment. However, Figure 4 shows the course of VAS pain during physical load over time for four quartiles of baseline pain levels, indicating that higher baseline pain during physical load not necessarily leads to more pain at follow-up.

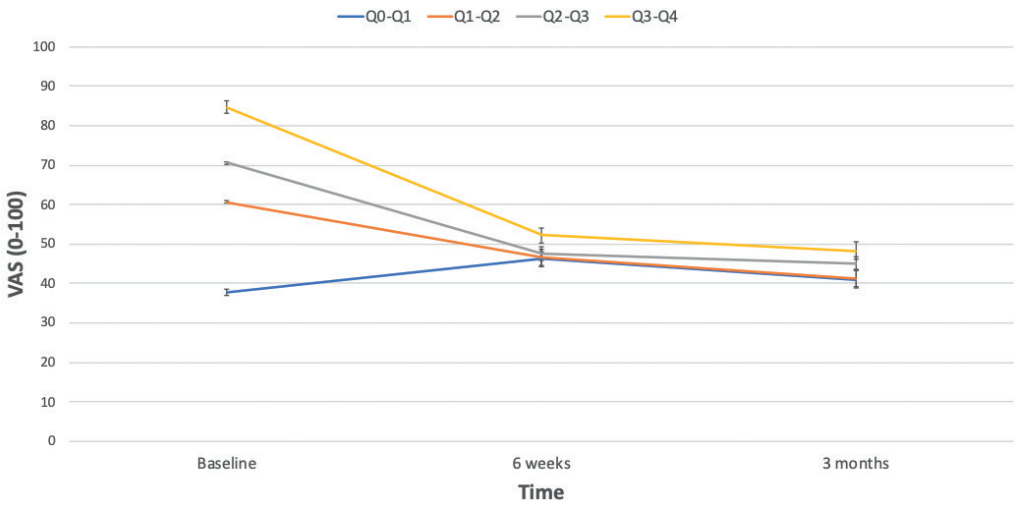

Figure 4. Course over time for Visual Analogue Scale (VAS, 0-100, higher scores represent more pain), categorized by quartiles for baseline pain during physical load, indicating that patients with higher baseline pain demonstrate the largest improvement and patients with lower baseline pain demonstrate little improvement.

For the MHQ total score, no significant difference was present at 3 months, but the MHQ subscales ADL, work performance, pain and satisfaction with hand function improved compared to baseline (p<0.001-0.007, Table 2). No significant changes were found in the MHQ subscales overall hand function and aesthetics. At 3 months, 83% of the participants would consider to undergo the non-surgical treatment again under similar circumstances (Table 2).

Table 2. Outcomes for Michigan Hand outcomes Questionnaire (MHQ, score range 0-100, higher scores indicate better performance except for the pain subscale) at baseline and 3 months and patient satisfaction at three months following non-surgical treatment. Significance testing for mean differences in MHQ at 3 months was performed using linear mixed model analysis.

Variable	Baseline	3 months	Mean difference baseline - 3 months [97.5% CI]	p-value
Total MHQ, mean (SD)	60.7 (14.1)	64.8 (18.9)	4.2 [-2:11]	0.036
MHQ Subscales:				
- Overall hand function	57.6 (17.7)	60.2 (25.6)	2.6 [-2:8]	0.154
- ADL	62.3 (23)	69.7 (26.7)	7.4 [1:14]	**<0.001**
- Work performance	53.3 (26)	63.1 (23.8)	9.8 [4:16]	**<0.001**
- Pain (higher scores indicate more pain)	36.9 (24.2)	31.6 (14.5)	5.2 [2:9]	**0.007**
- Aesthetics	81.9 (19.2)	72 (28.9)	9.9 [-5:25]	0.096
- Satisfaction with hand function	43.3 (20.5)	55.7 (34.3)	12.4 [2:22]	**<0.001**
Satisfaction with treatment result, %				
- Excellent		10%		
- Good		38%		
- Fair		23%		
- Moderate		21%		
- Poor		8%		
Participants that would undergo treatment again, %		83%		

Conversion to surgery

Figure 5 shows the survival curve for conversion to surgery, indicating that after a median follow-up of 2.8 years, 59 (14%) participants converted to surgical treatment. For the participants that converted to surgical treatment, median time to make the decision to convert to surgery was 3.4 months (range: 1-37 months) after the start of the non-surgical treatment.

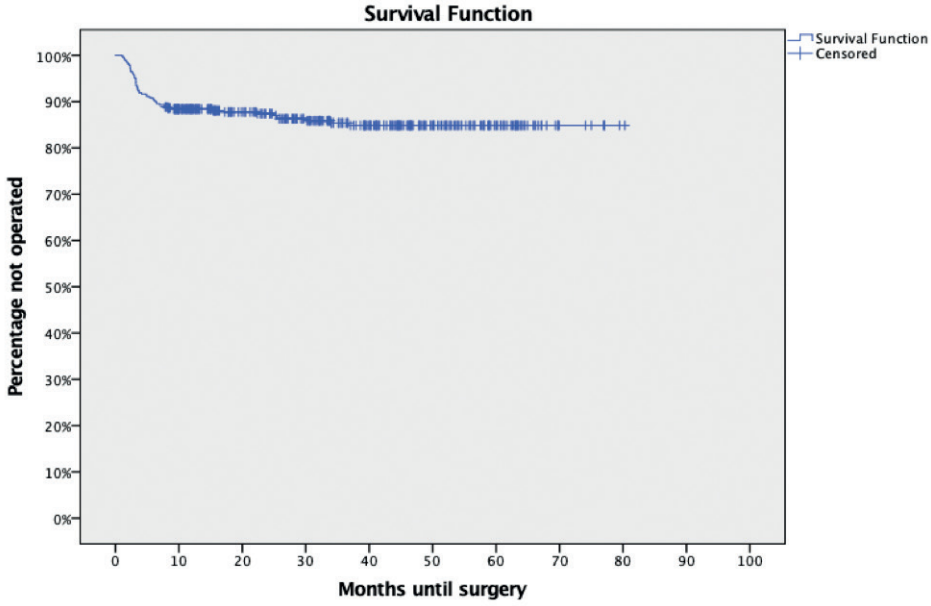

Figure 5. Survival curve displaying the number of patients that converted to surgery over time. The y-axis represents the percentage of patients not converting to surgery and the x-axis the time in months after start of treatment. After a median time of 3.4 months after the start of the non-surgical treatment (range of conversion: 1-37 months), 14% decided to convert to surgery.

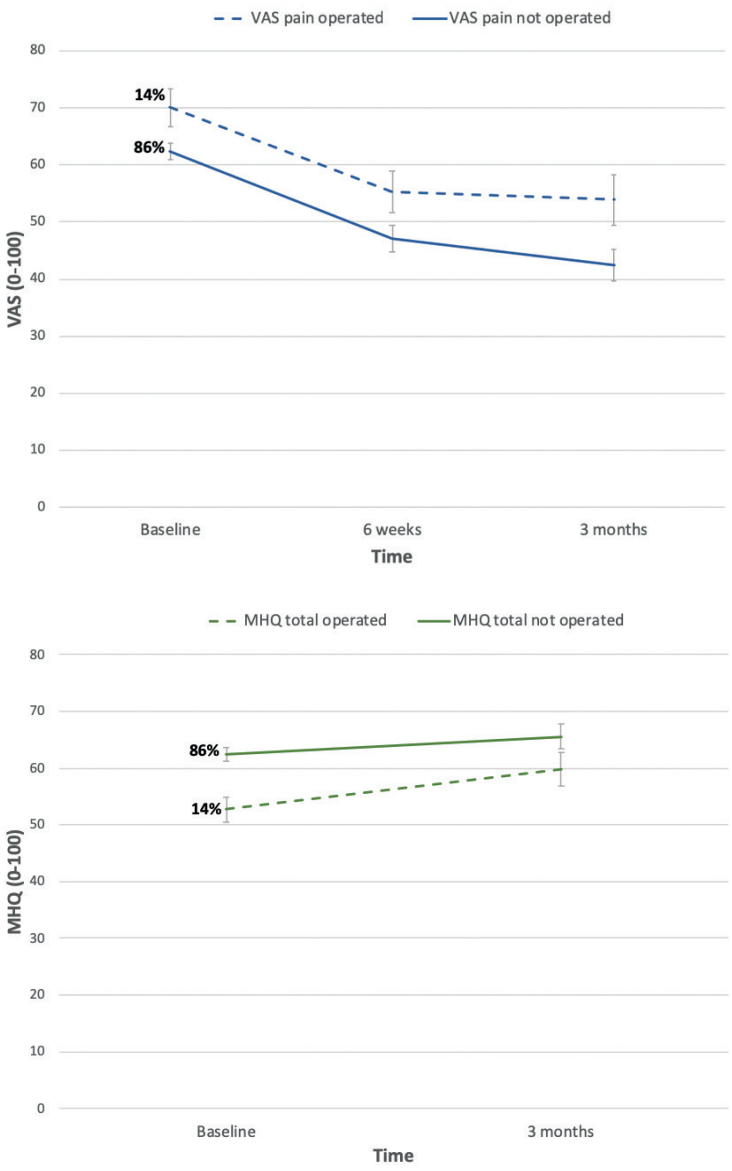

Figure 6A-B: Visual Analogue Scale (VAS 0-100, higher scores represent more pain, Figure 6A) score for pain during physical load and Michigan Hand outcome Questionnaire (MHQ, 0-100, higher scores represent better function, Figure 6B) separately for participants that converted to surgery (n=59, 14%) and participants that did not convert to surgery (n=372, 86%). Linear mixed model analysis demonstrated that pain during physical load decreased in both participants that did (p=0.010) or did not convert to surgery at 3 months compared to baseline (p<0.001). For MHQ total score, no significant improvement was achieved in both subgroups (p=0.046-0.152). However, both pain and hand function levels were worse for patients that eventually converted to surgery (p<0.001). Moreover, there was an interaction between subgroup and change in pain or hand function scores over time (p<0.001). VAS scores during rest and VAS last week demonstrated the same pattern as VAS during physical load. Group means and standard errors are plotted.

DISCUSSION

We found a clinically relevant decrease in pain for patients treated non-surgically for symptomatic CMC-1 instability. Furthermore, only 14% of the patients were surgically treated after a median follow-up of 2.8 years. In addition, improvements were found in secondary outcomes for ADL, work performance and satisfaction with hand function. Additionally, our subgroup analysis indicated that for patients who eventually converted to surgery, there still was a clinically relevant decrease in pain scores despite the decision to proceed to surgical treatment. However, both pain and hand function scores remained worse over time in the subgroup that converted to surgery compared to those who did not convert to surgery.

To our knowledge, this is the first study reporting outcomes for non-surgical treatment for symptomatic CMC-1 instability, hence we cannot compare our results with previous studies. Since our study indicates clinically relevant improvement in patient reported outcome measures and surgical treatment may lead to unsatisfactory results,[2,19] it is highly recommended that non-surgical treatment for symptomatic CMC-1 instability is considered as a primary treatment of choice in patients with CMC-1 instability. This is especially the case since non-surgical treatment for CMC-1 instability is aiming to improve lifestyle, joint mechanics and function and might therefore prevent or at least delay the development of CMC-1 OA in later life, since CMC-OA might be a result of CMC-1 instability.[5-10] However, since we did not evaluate the disease course over a longer period of time in this study, future studies should investigate if non-surgical treatment for CMC-1 instability has a preventive effect in CMC-1 OA development.

When analyzing the subgroup of patients with CMC-1 instability that eventually converted to surgery, we found a clinically relevant decrease in pain scores at three months compared to baseline scores. This decrease in pain levels over time is in contrast to findings by Tsehaie et al.[15], who found that in patients with CMC-1 OA that eventually converted to surgery, pain levels did not change over time. In another study[39], Tsehaie et al. found that the decision to undergo surgical treatment strongly depends on a change in pain levels during non-surgical treatment. Our findings suggest that in patients with CMC-1 instability this is not the case, and the decision to undergo surgery might depend on higher residual pain levels and not on change in pain score over time. This is supported by our finding that while pain levels decreased in the subgroup that converted

to surgery, pain levels and hand function scores remained worse compared to those of the subgroup of patients that did not convert to surgery. However, future studies using prediction models in patients with CMC-1 instability are needed to validate this hypothesis.

Another remarkable finding is that, in general in our sample, we found a relatively large variability in outcomes. For example, we found that while 83% of the patients would undergo the same treatment again, 17% would not. Further, we found large variation in pain levels both prior to treatment and 3 months after treatment. However, whereas some studies report that higher baseline pain predict higher residual pain in patients with CMC-1 OA[11,14], our study also indicates that this pattern might be otherwise in patients with CMC-1 instability. These findings indicate that while the majority of patients responds well to this non-surgical treatment, some patients do not. Hence, future studies need to investigate factors that contribute to this variability in outcome.

Study limitations

A strength of this study is that this is, to our knowledge, the first study reporting outcomes of non-surgical treatment for CMC-1 instability. Furthermore, we were able to evaluate a large group of 431 using standardized patient reported outcome measures. However, there are also a number of limitations. First, a limitation of this study is its observational character. Despite standardization of treatment using strict protocols and standardized procedures for data collection, inherent to observational studies, the actual provided treatment might have deviated from the treatment protocols. For example, the exercises and orthotics might not have been applied in every patient. However, in contrast to a randomized controlled trial setting, an advantage of our observational study design is that the results are highly representative for actual daily practice.

An additional limitation of this study is that the present study does not allow evaluation of separate treatment effects of exercise therapy or the usage of orthoses in CMC-1 instability. While the exercise therapy aims to improve joint mechanics, active stability and strength and the orthosis aims to reduce subluxation and inflammation, it is unknown if combining this treatment with orthoses is useful. Hence, future studies should investigate the long-term outcomes for these different non-surgical treatments for CMC-1 instability separately in a more standardized setting.

Another limitation of this study is the amount of missing data and the need for multiple imputation. However, our non-responder analyses and the non-significant Little's test give us confidence that our outcomes represent the target population.

Furthermore, a limitation of this study is that the percentage of conversion to surgery that we report might be an underestimation, since, despite our efforts to follow our patients over time, a patient might have been surgically treated elsewhere. Hence, this percentage of patients converting to surgery following non-surgical treatment for CMC-1 instability needs validation in future prospective research.

In conclusion, patients treated non-surgically for symptomatic CMC-1 instability showed a clinically relevant decrease in pain and improvement in secondary outcomes such as ADL, work performance and satisfaction with hand function. Furthermore, only 14% of all 431 patients converted to surgery after a median follow-up of 2.8 years, indicating this non-surgical treatment is a successful treatment of choice, although we found large variation in pain levels. Future studies should investigate predictive factors that contribute to this variability in outcome following non-surgical treatment for CMC-1 instability.

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Supplementary Table 1. Non-responder analysis, where participants with the presence of a primary outcome at three months were compared with participants without a primary outcome at three months using independent samples t-tests and Chi square tests. SD = standard deviation, VAS = Visual Analogue Scale, MHQ = Michigan Hand outcomes Questionnaire

Variable	*Primary outcome at three months present*	*Primary outcome at three months absent*	*p-value*
Participants, N (%)	153 (36%)	278 (64%)	-
Age, mean ±SD	37.2 ± 12.8	38.8 ± 13.1	0.232
Female sex, %	80%	79%	0.757
Symptom duration in months, mean ±SD	18.4 ± 29.1	15.3 ± 22.3	0.218
Treatment Side, %			0.932
- Left	40%	40%	
- Right	60%	60%	
Dominance, %			0.595
- Left	7%	5%	
- Right	90%	91%	
- Both	3%	4%	
Type of work, %			0.182
- Unemployed	14%	20%	
- Light physical labor	31%	33%	
- Moderate physical labor	42%	32%	
- Heavy physical labor	13%	15%	
Second opinion, %	12%	7%	0.080
VAS pain rest, mean (SD)	38.6 ± 24.3	39.4 ± 24.5	0.785
VAS pain physical load, mean (SD)	64.9 ± 20.1	63.2 ± 23.6	0.503
MHQ total, mean (SD)	60.8 ± 14.8	60.3 ± 14.2	0.764

CHAPTER 5

PREDICTING OUTCOME AFTER HAND ORTHOSIS AND HAND THERAPY FOR THUMB CARPOMETACARPAL OSTEOARTHRITIS: A PROSPECTIVE STUDY

Jonathan Tsehaie
Kim R. Spekreijse
Robbert M. Wouters
Reinier Feitz
Steven E.R. Hovius
Harm P. Slijper
Ruud W. Selles

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ABSTRACT

Objective: 1) to identify predictive factors for outcome after splinting and hand therapy for CMC OA and to identify predictive factors for conversion to surgical treatment, and 2) to determine how many patients that have not improved in outcome within six weeks after start of treatment will eventually improve after three months.

Methods: In this observational prospective multi-center cohort study, 809 patients with CMC OA received splinting and weekly hand therapy for three months between 2011 and 2014. Main outcome measures were pain and satisfaction measured with a visual analog scale, and function measured with the Michigan Hand Questionnaire at baseline, six weeks and three months post-treatment. Using regression analysis, patient demographics and pretreatment baseline scores were considered as predictors for the outcome of conservative treatment after three months and for conversion to surgery.

Results: Multivariable regression model explained 34-42% of the variance in outcome ($p<0.001$) with baseline satisfaction, pain and function as significant predictors. Cox regression analysis showed that baseline pain and function were significant predictors for conversion to surgery. Of patients with no clinically-relevant improvement in pain and function after six weeks, 73-83% also had no clinically-relevant improvement after three months.

Conclusion: This study showed that patients with either high pain or low function may benefit most from conservative treatment. We therefore recommend to always start with conservative treatment, regardless of symptom severity of functional loss at start of treatment. Furthermore, it seems valuable to consider changing the content of conservative treatment or to discuss surgery with patients after six weeks of therapy, when levels of improvement are still mainly unsatisfactory.

INTRODUCTION

Primary osteoarthritis (OA) of the carpometacarpal (CMC) joint is common among the elderly.[1] Multiple options are available to treat CMC OA[2-4] and various guidelines recommend to start with conservative treatment that can include: hand therapy, topical or oral non-steroidal anti-inflammatory drugs, intra-articular steroid injection, and splinting.[5-7]

Studies on outcome after non-operative treatment are mainly based on group level analysis and large variation is reported between individual patients, e.g. some were highly satisfied and almost/fully free of pain, while others were unsatisfied and/or had residual pain.[8-10] However, the quality of most of these studies was only weak to moderate. For example, although one systematic review showed that hand orthosis may help relieve pain, the sample size of the included studies ranged from only 10 to 37 patients and follow-up ranged from only 1 week to 6 months. [8] Another systematic review on comparative studies of hand orthosis or hand therapy for CMC OA, concluded that hand orthosis or hand therapy may provide some reduction in pain; however, the follow-up of these latter studies ranged from 2 weeks to 3 months and the study samples comprised only older individuals (aged 70-90 years).[9]

Whereas for various surgical techniques for CMC OA predictive factors for outcome have been described[11,12], no predictors are reported for the outcome of conservative treatment; thus, it remains unclear which patients might benefit from conservative treatment.

Therefore, this study aims to: 1) identify predictive factors for outcome after splinting/hand therapy for CMC OA and for conversion to surgical treatment, and 2) determine how many patients with no improvement in outcome within six weeks after start of treatment will improve after three months.

METHODS

This observational, prospective multi-center cohort study was conducted using data collected between January 2011and November 2014. All patients with symptomatic, clinically-diagnosed CMC OA were asked to participate and were included at Xpert Clinic in the Netherlands. This clinic comprises 15 locations in the Netherlands, with 16 European Board certified (FESSH) hand surgeons and

over 50 hand therapists. No remuneration was provided to any of the patients. The study was approved by the local institutional review board (MEC-2015-691) and written informed consent was obtained from all patients.

For the present study, patients diagnosed with primary, non-traumatic CMC OA by a hand surgeon were eligible for inclusion; patients were selected that were not previously surgically treated for CMC OA and did not have simultaneous treatment for any other hand condition(s). Excluded were patients who received intra-articular corticosteroid injection as part of their treatment, since this treatment may interact with the effectiveness of splinting and/or hand therapy.

Treatment

Treatment was based on the current treatment guideline in the Netherlands.[7] In general, treatment consisted of prescribing a custom-made or pre-fabricated orthosis (based on the preference of the surgeon, hand therapists, and medical insurance of the patient). The orthotic device was a butterfly thumb orthosis in which the CMC joint of the thumb was fixed in extension/abduction, and the metacarpophalangeal joint (MCP-1) of the thumb was fixed in mild flexion.

In addition, patients received two sessions of hand therapy per week of (on average) 25 min per session. All hand therapists received the same internal training on how to treat CMC OA with hand therapy. However, this was a pragmatic study in that the hand therapy was not strictly protocolled and controlled but was evaluated based on clinical practice. Therapy sessions were planned based on the judgment of the therapist, and the ability and availability of the patient. In a small minority of the cases, patients did not visit a hand therapist and only received a hand orthosis; however, the number of patients receiving only an orthosis was negligible.

The treatment was divided into two phases; phase one (weeks 0-6) included instructions to wear the splint (almost) 24 h/day, and consisted of hand therapy for optimizing thumb position (training pinch and grasping movements without hyperextension in the metacarpophalangeal thumb joint and without CMC adduction) and using a full thumb range of motion (i.e. training specific coordination of the intrinsic/extrinsic muscles of the thumb). The rationale for advising patients to wear the orthotic device 24 h/day was to give the thumb rest, reduce inflammation, and improve stability in the joint.[13,14] Another goal of the first phase of the study was to re-learn correct positioning of the thumb; to achieve

this patients should preferably be without pain. In phase two (weeks 7-12), the splint was slowly phased out: the patients were advised to use the splint only during heavy activities, depending on the pain level and the patient's ability to perform activities with a stable thumb position. During this phase, hand therapy focused on maintaining pain reduction, introducing the stability learned during daily activities, and improving thenar muscle strength. In addition, fewer hand therapy sessions were scheduled and patients performed more home exercises (up to 4-6 times a day). The number of prescribed home exercises ranged from 3-6 exercises per day, with 10-15 repetitions each, depending on the individual patient and the level of pain.

After this period of supervised therapy, patients were encouraged to continue doing the exercises and were allowed to use the splint when necessary. No corticosteroid injections were given for CMC OA during or after hand therapy, and no anti-inflammatory medication was prescribed by the surgeon.

Measures

At the start of treatment, baseline data of all patients were collected, including duration of complaints, hand dominance, sex, age, comorbidity and occupation. Outcome measures were recorded via our web-based conservative outcome registration at i) start of treatment (baseline), and at ii) six weeks and iii) three months after start of treatment.

Conservative treatment was evaluated at the follow-up appointment at three months. Surgical intervention was discussed when patients did not respond well to the splinting and hand therapy and had functional impairments and/or residual pain. All surgeries performed between January 2012 and February 2016, together with the time until surgery, were retrieved from the clinical records; this information was collected irrespective of whether or not patients responded to the study questionnaires.

Pain, function and satisfaction

Pain was measured using a Visual Analogue Scale (VAS, where 0=no pain and 100=the worst possible pain) during two situations: i) pain during physical load, and ii) pain intensity during the week prior to the follow-up measurement. The minimal clinically important difference (MCID) for VAS pain is 9.7.[15] In the present study, for convenience, the MCID for VAS pain was considered to be 10. Hand function was measured with the Michigan Hand Questionnaire (MHQ; Dutch

Language Version) where 0=poorest function and 100=ideal function).[16-18] The MHQ measures patient-rated, self-reported hand function based on 37 items, covering six domains (pain, esthetics, hand function, performance of activities of daily living, work performance, and satisfaction). For non-traumatic hand conditions, the MCID for the total MHQ ranges from 9-13 points.[19] In the present study, for convenience, the MCID for the total MHQ score was considered to be 10. Lastly, we asked patients to score overall satisfaction with their hand on a VAS where 0=completely dissatisfied and 100=completely satisfied.

Statistical analysis

Since data were collected during daily clinical practice, there was a substantial proportion of non-response during follow-up (Supplementary Table 1). Therefore, we performed an extensive responder/non-responder analysis (Supplementary Table 2) and missing data analysis and concluded that the outcome variables were missing at random. Therefore, we performed multiple imputation by chained equations (MICE) by fully conditional specification. Multiple imputation is an appropriate method to handle large amounts of missing data (up to 80%).[20]

To identify predictors for outcome, patient demographics and baseline measures of pain, function and satisfaction were examined. Outcome was defined as pain, function and self-reported satisfaction with the hand at six weeks and at three months after start of treatment, and conversion to surgery. First, the correlation between a possible predictor and each outcome parameter was studied using Pearson's correlation. Univariate Cox regression analysis was used to examine predictors at the time of conversion to surgery. All variables with a univariate association with a significance level of <0.10 were used for backward entered multivariable linear regression analysis, and backward entered conditional Cox regression. For all tests, a p-value ≤ 0.05 was considered statistically significant.

Secondly, in the absence of a clinically relevant improvement at six weeks, we examined how often there was a clinically-relevant improvement in pain and function at three months after start of treatment. This allowed to evaluate whether further conservative treatment after six weeks was beneficial. A clinically-relevant improvement was defined as an improvement of more than the MCID of 10 for pain and of 10 for the MHQ (as described above). The diagnostic value of the six-week outcome for the outcome at three months was further tested with a receiver operating characteristic (ROC) curve.

Based on the ROC curve the following were calculated: i) the sensitivity (i.e. the proportion of patients with no clinically-relevant improvement at 0-3 months that also had no clinically-relevant improvement at 0-6 weeks), ii) the specificity (i.e. the proportion of patients with a clinically-relevant improvement at 0-3 months that also had a clinically-relevant improvement at 0-6 weeks), iii) the positive predictive value (i.e. the proportion of patients with a clinically-relevant improvement at 0-3 months that had no clinically-relevant improvement at 0-6 weeks), and iv) the false-positive rate (i.e. the proportion of patients with no clinically-relevant improvement at 0-3 months that had a clinically-relevant improvement at 0-6 weeks).

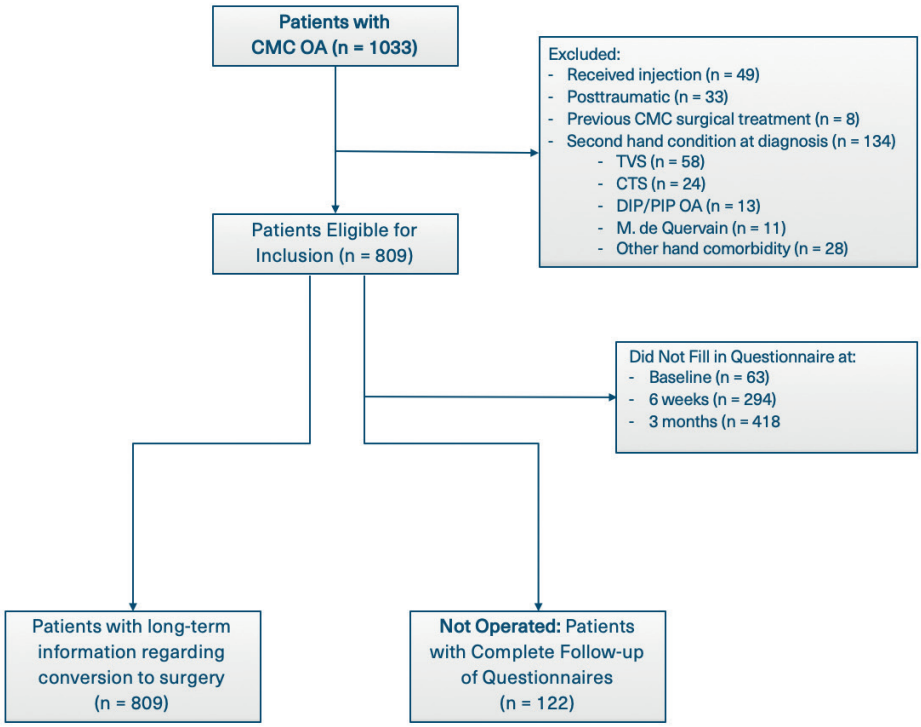

Figure 1. Flowchart of the study

RESULTS

Study population and outcome of conservative treatment

The study included 809 patients who were treated for complaints due to CMC OA between January 2011 and November 2014: Figure 1 presents an overview

of the study population. Table 1 lists the baseline characteristics of the patients, and outcome at six weeks and three months after start of treatment. There was a significant improvement in satisfaction (from 41± 22 at baseline to 56 ± 23 at three months), a significant decrease in pain (from 49 ± 20 at baseline to 40 ± 21 at three months) and a significant improvement in hand function (from 66 ± 14 at baseline to 72 ± 11 at three months). After a mean follow-up of 2.2 years, 15% of the patients underwent surgery.

Table 1. Baseline characteristics and outcome of treatment with splinting and hand therapy at 6 weeks and at 3 months.

Variables		**Baseline (% or mean ±SD)**	**6 weeks (mean ± SD)**	**3 months (mean ± SD)**
Sex	*Female*	76		
Treated hand	*Right*	50		
Workload	*No work*	43		
	Light physical work	23		
	Moderate physical work	23		
	Heavy physical work	11		
Dominance	*Left*	9		
	Right	87		
	Both	4		
Age (years)		60 ± 9		
Duration of symptoms (months)		34 ± 62		
Pain during activities (VAS 0-100)*		61 ± 22	49 ± 23	48 ± 23
Pain intensity during the week prior to follow-up (VAS 0-100)*		49 ± 20	40 ± 21	40 ± 21
MHQ (0-100)	*Total¥*	66 ± 14	70 ± 9	72 ± 11
	Daily Activities¥	77 ± 22	82 ± 15	80 ± 18
	Function¥	66 ± 16	67 ± 14	68 ± 15
	Esthetics¥	85 ± 17	86 ± 15	86 ± 17
	Satisfaction¥	61 ± 26	70 ± 19	71 ± 21
	*Pain**	54 ± 25	46 ± 19	42 ± 21
	Work performance¥	61 ± 23	63 ± 20	68 ± 20
Hand satisfaction (VAS 0-100)¥		41 ± 22	54 ± 24	56 ± 23

*: High scores indicate worse outcome
¥: High scores indicate good outcome
Abbreviations: MHQ, Michigan Hand Questionnaire; VAS, Visual analog scale; SD, Standard Deviation

Predictive factors

Univariate analysis showed that pre-treatment baseline scores, sex, age, workload and treated hand side correlated with the outcome measures (Table 2). Results of the multivariable regression analysis are given in Table 3. For change in pain after three months (VAS), the multivariable regression model explained 34% of the variance in outcome ($p<0.001$), with one significant predictor i.e. pain intensity during the week prior to the baseline measurement. For change in patient satisfaction (VAS) after three months, the multivariable regression analysis model explained 38% of the variance in outcome ($p<0.001$), with baseline patient satisfaction with their hand as significant predictor. For change in function (MHQ) after three months, the multivariable regression analysis model explained 42% of the variance in outcome ($p<0.001$), with baseline function and baseline patient satisfaction with their hand as significant predictors.

Table 2. Results of univariate analysis. Correlation coefficients are displayed.

Baseline Variables	Outcome at 6 weeks			Outcome at 3 months			Conversion to surgery
	Δ in overall pain‡ (VAS)	*Δ in hand satisfaction (VAS)*	*Δ in hand function (total MHQ)*	*Δ in overall pain‡ (VAS)*	*Δ in hand satisfaction (VAS)*	*Δ in hand function (total MHQ)*	*hazard ratio B per 10*
Sex			0.129*			0.070*	
Age				0.109*			
Dominance					-0.07**		
Treated hand		0.073**	0.302*			0.209*	
Duration of complaints							
Workload			-0.064**				
Hand function (MHQ Total)	0.170*	-0.134*	-0.796*	0.156*	-0.169*	-0.648*	0.72*
Hand Satisfaction (VAS)	0.179*	-0.558*	-0.188*	0.206*	-0.616*	-0.122*	0.82*
Pain during activities (VAS)	-0.419*	0.195*	0.233*	-0.440*	0.244*	0.245*	1.23*
Pain intensity during the week prior to follow-up (VAS)	-0.581*	0.213*	0.216*	-0.581*	0.235*	0.220*	1.32*

‡ Pain refers to pain intensity during the week prior to follow-up
*Association significant at p-value <0.05.
** Association significant at p-value <0.10.
Empty cells indicate a non-significant correlation at p-value >0.10
Abbreviations: MHQ, Michigan Hand outcomes Questionnaire; VAS, Visual Analogue Scale

For the probability of converting to surgery, Cox regression analysis resulted in two significant predictors: function (MHQ) at baseline and pain intensity during the week prior to the baseline measurement. For every 10 points of improvement in MHQ at baseline, the probability of a patient undergoing surgery decreased by 19%. For every 10 points of improvement in pain intensity during the week prior to the baseline measurement, the probability of a patient undergoing surgery decreased by 26%.

Table 3. Multivariable regression analysis: beta-coefficients related to different outcome measures.

Baseline variables	**Outcome at 6 weeks**			**Outcome at 3 months**			**Conversion to surgery**
	Δ in overall pain‡ (VAS)	*Δ in hand satisfaction (VAS)*	*Δ in hand function (total MHQ)*	*Δ in overall pain‡ (VAS)*	*Δ in hand satisfaction (VAS)*	*Δ in hand function (total MHQ)*	*Δ in overall pain‡ (VAS)*
R^2 (% explained variance)	**35%**	**31%**	**63%**	**34%**	**38%**	**42%**	
Hand function (MHQ Total)		-0.780*			-0.648		0.81*
Hand satisfaction (VAS)	-0.126*	-0.697*			-0.808*	0.039	
Pain intensity during the week prior to follow-up (VAS)	-0.770*			-0.741*			1.26*

‡ Pain refers to pain intensity during the week prior to follow-up
*Association significant at p-value <0.05
Empty cells indicate a nonsignificant correlation at p-value >0.05

Abbreviations: MHQ, Michigan Hand outcomes Questionnaire; VAS, Visual Analogue Scale

Sensitivity analysis

After three months of conservative treatment, 380 patients showed a clinically-relevant improvement on pain scores (VAS). Using the ROC curve, we calculated a sensitivity of 0.765 (95% CI 0.721-0.803) and a specificity of 0.676 (95% CI 0.626-0.722). This resulted in a positive predicted value of 73% (95% CI 68-77%) (Table 4), indicating that 73% of the patients that had no clinically-relevant improvement in pain after six weeks also had no clinically-relevant improvement in pain after three months.

After three months, 259 patients showed a clinically-relevant improvement in function (MHQ). Again, using the ROC curve, we calculated a sensitivity of 0.896 (95% CI 0.867-0.920) and a specificity of 0.618 (95% CI 0.555-0.677). This resulted in a positive predicted value of 83% (95% CI 80-86%) (Table 4), indicating that 83% of the patients who had no clinically-relevant improvement in function after six weeks also had no clinically-relevant improvement in function after three months of conservative treatment. We redid the sensitivity analysis using the dataset with only complete cases and observed very similar outcome (Supplementary Table 3).

Table 4. Positive predictive values for pain and function at six weeks, i.e. the percentage of patients that did not show a clinically-relevant improvement at three months and did not show a clinically-relevant improvement at six weeks.

		Clinically-relevant improvement at 0 to 3 months[Þ]				
Pain (VAS)		*Yes*	*No*	*Total*	*Positive predictive value (95% CI)*	*Negative likelihood ratio (95% CI)*
Clinically-relevant improvement 0 to 6 weeks[‡]	*No[†]*	123	328	451	0.73 (0.67-0.79)	0.35 (0.29-0.41)
	Yes	257	101	358		
	Total	380	429	809		
		Clinically-relevant improvement at 0 to 3 months[‡]				
Hand function (MHQ)		*Yes*	*No*	*Total*	*Positive predictive value (95% CI)*	*Negative likelihood ratio (95% CI)*
Clinically-relevant improvement at 0 to 6 weeks[‡]	*No[†]*	99	492	592	0.83 (0.80-0.86)	0.17 (0.13-0.22)
	Yes	160	57	217		
	Total	259	550	809		

[Þ] Clinically-relevant improvement defined as an improvement of 10 or more on the 0-100 VAS scale[15]

‡ Clinically-relevant improvement defined as an improvement of 10 or more on the 0-100 MHQ scale[16-18]

Abbreviations: MHQ, Michigan Hand outcomes Questionnaire; VAS, Visual Analogue Scale

DISCUSSION

This study had two main aims. The first was to identify predictive factors for outcome of conservative treatment and predictive factors for conversion to surgical treatment. The multivariable regression model explained 34-42% of the variance in satisfaction, pain and function (MHQ) after three months, with baseline satisfaction with the hand, baseline pain and baseline function (MHQ) as predictive factors. In addition, every 10 points of improvement in baseline pain led to a 26% decrease in the risk of conversion to surgery of 26% and every 10 points of improvement in baseline MHQ score led to a 19% decrease in the risk of conversion to surgery.

The second aim was to determine how many patients that showed no improvement in pain within six weeks after start of conservative treatment also showed no improvement after three months of treatment. A negative predictive value of 73% was found for pain and 83% for function (MHQ). This indicates that, in the absence of a clinically-relevant improvement after six weeks, 73% of the patients show no clinically-relevant improvement on the VAS pain score after three months, and 83% of the patients show no clinically-relevant improvement on the MHQ score after three months.

To our knowledge, the present study is the first to identify baseline predictive factors for conservative treatment of CMC OA. For surgery, a study on predictive factors for outcome showed that patients with CMC OA with hyperextension of the MCP joint or a restricted thumb web had a worse outcome after surgery; however, that study did not report the percentage of explained variance.[11] In daily practice, patients with considerable pain often undergo surgical treatment without first receiving hand therapy. The present study shows that patients with the most pain and the lowest level of function may benefit most from hand orthosis and hand therapy. Therefore, we recommend to always start with conservative treatment, irrespective of symptom severity or functional loss at start of treatment.

Since the present study found only moderate levels of explained variances, we can only partially predict which patients will have a greater chance of benefitting from conservative treatment. The predictors for conversion to surgery indicate which patients are more likely to undergo surgery and which will not. For example: in our patients with a baseline pain score of >75, 31% will undergo

surgery, whereas in patients with a baseline pain score of <25, only 5% will undergo surgery. Overall, at baseline we could not identify subgroups of patients with such a high probability of undergoing surgery after conservative treatment that this warranted selection for immediate surgery, without prior conservative treatment.

Although the baseline factors we found have only moderate predictive value, we did establish that a lack of clinical improvement in outcome after six weeks is a good indicator for a lack of clinical improvement in pain and function after three months. Only 17-27% of our patients that showed no clinically-relevant improvement in pain and function after six weeks showed a clinically-relevant improvement in these parameters after three months. In daily practice, surgeons tend to prescribe hand therapy for an arbitrary number of weeks/months, without knowing exactly when to evaluate treatment. Our findings indicate that, when the outcome is still unsatisfactory at six weeks, it may be worthwhile to evaluate treatment, potentially adjust the content of hand therapy or to discuss surgery with patients at that time. Future studies will hopefully elucidate whether changing the content of hand therapy or early termination of unsuccessful conservative treatment and conversion to surgery will lead to more efficient and cost-effective healthcare.

Study limitations

This study has both strengths and limitations. The main strength is the large sample size and another is the study's observational design, i.e. recording how conservative treatment is performed in actual clinical practice, rather than within the stricter and potentially less-natural setting of a randomized controlled trial. However, this was also a limitation since the measurements took place in multiple locations with the risk of large variation in treatment; this precluded the possibility of completely standardizing the treatment protocol. Also, unfortunately, from our database we were unable to retrieve the total number of therapy sessions for each patient and adjust outcomes based on these sessions. Future research could investigate to what extent the number of therapy sessions received might influence outcome.

One limitation is the lack of a control group. Therefore, the predictors found for outcome after three months of conservative treatment provide no information on the effectiveness of conservative treatment compared to no treatment, or compared to direct surgical treatment.

Secondly, there was a substantial amount of missing data. Since a small number of patients had failed conservative treatment before three months and received surgical treatment, their outcome measurements at three months were missing. However, the data missing for patients at three months were missing completely at random and no underlying mechanisms could be identified.

Another limitation is that, after being treated conservatively in our clinic, patients may have been treated surgically elsewhere, which may lead to underreporting of the rate of surgery. However, since our clinic specializes in treating hand and wrist conditions, we assume that the number of patients treated elsewhere is negligible.

Future research

Since we found only moderate baseline predictors for outcome after conservative treatment, future studies could focus on other predictive factors, e.g. psychosocial factors. For example, a recent systematic review[2121] found that depression and anxiety were highly prevalent in patients with osteoarthritis and that patients with these symptoms experienced more pain and had less optimal outcomes. Another study found that patients seeking care for CMC OA had more catastrophic thinking and higher rates of depression compared to patients that did not seek treatment for CMC OA.[22] Moreover, according to a report describing predictors for outcome after surgical treatment for osteoarthritis[12], future research could also focus on other objective measures, such as range of motion (hyperextension of MCP and narrow first web) and strength of thumb.

CONCLUSIONS

In these patients with CMC OA, the present study found that: 1) satisfaction, pain and function measured at baseline explained 32-42% of the outcome of these parameters after three months of conservative treatment and the probability of undergoing surgery, and 2) a lack of improvement after six weeks resulted in a 73-83% negative predictive value for a lack of improvement in pain and function after three months. Therefore, for all patients with CMC OA, we recommend to start with hand orthosis and hand therapy irrespective of symptom severity. In addition, it may be beneficial to evaluate treatment after a relatively short period of conservative treatment (e.g. six weeks) when there has been no demonstrable clinically-relevant improvement during that period.

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Supplementary Table 1. Number of complete cases per variable

Variable	Number of cases
Sex	809 (100%)
Treated hand	809 (100%)
Workload	806 (100%)
Dominance	806 (100%)
Age (years)	809 (100%)
Duration of symptoms (months)	806 (100%)
Pain during activities at baseline	746 (92%)
Pain during previous week at baseline	746 (92%)
Satisfaction with hand at baseline	746 (92%)
Pain during activities at 6 weeks	515 (64%)
Pain during previous week at 6 weeks	515 (64%)
Satisfaction with hand at 6 weeks	515 (64%)
Pain during activities at 3 months	391 (48%)
Pain during previous week at 3 months	391 (48%)
Satisfaction with hand at 3 months	391 (48%)
MHQ at baseline	610 (75%)
MHQ at 6 weeks	290 (36%)
MHQ at 3 months	380 (47%)

Abbreviations: MHQ, Michigan Hand outcomes Questionnaire

Supplementary Table 2. Baseline characteristics and responder/non-responder analysis.

Baseline characteristics		**Total (n=809)** *% or mean ± SD*	**Responders at 3 months (n=391)** *% or mean ± SD*	**Non-responders at 3 months (n=418)** *% or mean ± SD*	***p-value†***
Sex	*Female*	76	75	77	*0.735*
Treated hand	*Right*	50	48	51	*0.445*
Workload	*No work*	45	47	44	*0.141*
	Light physical work	23	19	24	
	Moderate physical work	23	27	22	
	Heavy physical work	9	6	10	
Dominance	*Left*	9	11	8	*0.359*
	Right	87	83	88	
	Both	4	5	4	
Age (years)		60 ± 9	60 ± 8	60 ± 9	*0.630*
Duration of symptoms (weeks)		34 ± 62	45 ± 92	32 ± 50	*0.070*
Pain during activities (VAS 0-100)*		61 ± 22	61 ± 21	61 ± 23	*0.985*
Pain intensity during the week prior to follow-up (VAS 0-100)*		49 ± 21	50 ± 20	49 ± 21	*0.856*
MHQ (0-100)	*Total¥*	64 ± 15	63 ± 16	64 ± 15	*0.443*
	Daily Activities¥	77 ± 23	76 ± 24	78 ± 23	*0.408*
	Function¥	66 ± 18	67 ± 17	66 ± 18	*0.640*
	Esthetics¥	85 ± 18	85 ± 19	85 ± 18	*0.753*
	Satisfaction¥	60 ± 28	58 ± 27	60 ± 29	*0.539*
	*Pain**	63 ± 27	62 ± 25	63 ± 28	*0.589*
	Work performance¥	61 ± 25	57 ± 23	62 ± 25	*0.016*
Hand satisfaction (VAS 0-100)¥		41 ± 22	42 ± 21	40 ± 23	*0.387*

† Significance of comparison between baseline characteristics of the responders and non-responders at 3-month measurement.
* High scores indicate worse outcome

¥ High scores indicate good outcome

Supplementary Table 3. Positive predictive values for pain and function at six weeks, i.e. the percentage of patients that did not show a clinically-relevant improvement at three months and did not show a clinically-relevant improvement at six weeks using the dataset with only complete cases. No differences in outcome between the imputed dataset (Table 4) and the dataset with only complete cases were seen.

		Clinically-relevant improvement at 0 to 3 months[þ]				
Pain (VAS)		*Yes*	*No*	*Total*	*Positive predictive value (95% CI)*	*Negative likelihood ratio (95% CI)*
Clinically-relevant improvement 0 to 6 weeks[‡]	*No[†]*	39	119	158	0.75 (0.68-0.82)	0.35 (0.27-0.45)
	Yes	122	43	165		
	Total	161	162	323		

		Clinically-relevant improvement at 0 to 3 months[‡]				
Hand function (MHQ)		*Yes*	*No*	*Total*	*Positive predictive value (95% CI)*	*Negative likelihood ratio (95% CI)*
Clinically-relevant improvement at 0 to 6 weeks[‡]	*No[†]*	28	87	115	0.76 (0.67-0.83)	0.17 (0.09-0.33)
	Yes	34	9	43		
	Total	62	96	158		

[þ] Clinically-relevant improvement defined as an improvement of 10 or more on the 0-100 VAS scale[15,16]

‡ Clinically-relevant improvement defined as an improvement of 10 or more on the 0-100 MHQ scale[10]

Abbreviations: MHQ, Michigan Hand outcomes Questionnaire; VAS, Visual Analogue Scale.

CHAPTER 6

PATIENTS WITH THUMB BASE OSTEOARTHRITIS SCHEDULED FOR SURGERY HAVE MORE SYMPTOMS, WORSE PSYCHOLOGICAL PROFILE AND HIGHER EXPECTATIONS COMPARED TO NON-SURGICAL COUNTERPARTS: A LARGE COHORT ANALYSIS

Robbert M. Wouters
Ana-Maria Vranceanu
Harm P. Slijper
Guus M. Vermeulen
Mark J. W. van der Oest
Ruud W. Selles
Jarry T. Porsius
for the Hand-Wrist study Group

2019; Clinical Orthopaedics and Related Research

ABSTRACT

Background: Psychological characteristics, such as depression, anxiety or negative illness perception are highly prevalent in patients with several types of OA. It is unclear whether there are differences in the clinical and psychological characteristics of patients with thumb carpometacarpal (CMC-1) osteoarthritis (OA) scheduled for non-surgical treatment and those with surgical treatment.

Questions/purposes: (1) What are the differences in baseline sociodemographic characteristics and clinical characteristics (including pain, hand function, and health-related quality of life) between patients with thumb CMC-1 OA scheduled for surgery and those treated non-operatively? (2) What are the differences in psychological characteristics between patients scheduled for surgery and those treated non-surgically, for treatment credibility, expectations, illness perception, pain catastrophizing, and anxiety and depression? (3) What is the relative contribution of baseline sociodemographic, clinical, and psychological characteristics to the probability of being scheduled for surgery?

Methods: This was a cross-sectional study using observational data. Patients with CMC-1 OA completed outcome measures before undergoing either non-surgical or surgical treatment. Between September 2017 and June 2018, 1273 patients were screened for eligibility. In total, 584 participants were included: 208 in the surgery group and 376 in the nonsurgery group. Baseline sociodemographic, clinical, and psychological characteristics were compared between groups, and a hierarchical logistic regression analysis was used to investigate the relative contribution of psychological characteristics to being scheduled for surgery, over and above clinical and sociodemographic variables. Baseline measures included pain, hand function, satisfaction with the patient's hand, health-related quality of life, treatment credibility and expectations, illness perception, pain catastrophizing, and anxiety and depression.

Results: Patients in the surgery group had longer symptom duration, more often a second opinion, higher pain, treatment credibility and expectations and worse hand function, satisfaction, HRQoL, illness perception and pain catastrophizing compared with the non-surgery group (effect sizes ranged from 0.20 to 1.20; p values ranged from < 0.001 to 0.044). After adjusting for sociodemographic, clinical, and psychological factors, we found that the following increased the probability of being scheduled for surgery: longer symptom duration (standardized

odds ratio [SOR], 1.86; p = 0.004), second-opinion visit (SOR, 3.81; p = 0.027), lower satisfaction with the hand (SOR, 0.65; p = 0.004), higher treatment expectations (SOR, 5.04; p < 0.001), shorter perceived timeline (SOR, 0.70; p = 0.011), worse personal control (SOR, 0.57; p < 0.001) and emotional response (SOR, 1.40; p = 0.040). The hierarchical logistic regression analysis including sociodemographic, clinical, and psychological factors provided the highest area under the curve (sociodemographics alone: 0.663 [95% confidence interval 0.618 to 0.709]; sociodemographics and clinical: 0.750 [95% CI 0.708 to 0.791]; sociodemographics, clinical and psychological: 0.900 [95% CI 0.875 to 0.925]).

Conclusions: Patients scheduled to undergo surgery for CMC-1 OA have a worse psychological profile than those scheduled for non-surgical treatment. Our findings suggest that psychological characteristics should be considered during shared decision-making, and they might indicate if psychological interventions, training in coping strategies, and patient education are needed. Future studies should prospectively investigate the influence of psychological characteristics on the outcomes of patients with CMC-1 OA.

INTRODUCTION

Thumb carpometacarpal (CMC-1) osteoarthritis (OA) is common, with a symptomatic prevalence of 7% and 2% among women and men aged at least 50 years, respectively [1-3]. Patients with CMC-1 OA often have thumb pain and limitations to activities of daily life and present with clinical features such as thenar muscle wasting or a thumb deformity [1,4]. Usually, initial treatment is non-surgical (for example, hand therapy), including exercises, orthotics, or both [5-12]. Increasing evidence shows that non-operative treatment decreases pain and improves hand function and patient satisfaction [5,7,8,10,13,14]. When non-surgical treatment does not alleviate symptoms, surgery may be considered [15,16]. Tsehaie et al. [14] reported that after non-surgical treatment, 15% of the patients eventually underwent surgical treatment after a mean period of 2.2 years, indicating that most patients with CMC-1 OA respond well to non-surgical treatment. In another study, Tsehaie et al. [17] found that baseline sociodemographic and clinical variables (such as pain intensity or hand function) account for 31% to 42% of the variance in outcome when predicting the results of non-surgical treatment and subsequent surgery, indicating that not all relevant covariates were covered.

During the past decade, studies have demonstrated that psychological characteristics such as depression, anxiety, negative illness perception, and pain catastrophizing are highly prevalent in patients with several types of OA [18-27]. However, little is known about differences in psychological characteristics and treatment expectations between patients with CMC-1 OA who have non-surgical treatment and those with surgical treatment. Hypothetically, when a non-surgical treatment fails (perhaps repeatedly), this suggests that a different psychological profile may be present at the start of surgical treatment. Only one study, by Lozano-Calderon et al. [28], evaluated differences between patients electing to undergo surgical and those choosing to undergo non-surgical treatment, using a relatively small sample of 72 participants and evaluating DASH scores, pain anxiety, catastrophizing, and depression. However, important domains such as illness perception, treatment credibility and expectations, and health-related quality of life were not studied, and the study might have been underpowered to determine between-group differences or predictors of whether a patient would elect to undergo surgery. More insight into the psychological profiles and treatment expectations of patients with CMC-1 OA treated non-surgically and those treated surgically is needed. This would provide clinicians and patients with valuable information for shared decision-making; decrease the number of surgeries performed; improve

the outcomes of surgery; or indicate if psychological interventions, training in coping strategies, and patient education are needed.

Therefore, we formulated the following research questions: (1) What are the differences in baseline sociodemographic characteristics and clinical characteristics (including pain, hand function, and health-related quality of life) between patients with thumb CMC-1 OA scheduled for surgery and those treated non-operatively? (2) What are the differences in psychological characteristics between patients scheduled for surgery and those treated non-surgically, for treatment credibility, expectations, illness perception, pain catastrophizing, and anxiety and depression? (3) What is the relative contribution of baseline sociodemographic, clinical, and psychological characteristics to the probability of being scheduled for surgery?

PATIENTS AND METHODS

Study Design

This was a cross-sectional study using baseline data collected before non-surgical or surgical treatment in a large observational cohort, following the STROBE statement [29].

Setting

Data were collected as part of routine outcome measurements using GemsTracker electronic data capture tools (Erasmus MC and Equipe Zorgbedrijven, Rotterdam/Eindhoven, The Netherlands) [30]. GemsTracker is a secure web-based application for distributing questionnaires and documents during clinical research and quality registration [31,32]. Data were collected at 18 outpatient hand surgery and therapy clinics in the Netherlands between September 2017 and June 2018. The study was approved by the local medical research ethical committee. Following the Dutch treatment guideline [33], all patients with CMC-1 OA diagnosed by a certified hand surgeon were initially referred for hand therapy and non-surgical treatment. Follow-up with the hand surgeon occurred after approximately 3 months, after which the decision to proceed to further (surgical) treatment could be made, based on persistent symptoms and patient preference. We classified patients who started with the non-surgical, hand therapy treatment as the nonsurgery group, and patients who proceeded to surgical treatment were classified as the surgery group.

Participants

Participants were eligible for inclusion if they were adults with CMC-1 OA diagnosed by a Federation of European Societies for Surgery of the Hand (FESSH)-certified hand surgeon and if they were scheduled for either non-surgical or surgical treatment. Non-surgical treatment included an orthosis combined with exercise therapy, which consisted hand therapy sessions (guided by an physical/occupational hand therapist, nationally certified in most cases) and exercises performed at home by the patient to improve active stability of the CMC-1 [9,11,13,14,34]. Surgical procedures included ligament reconstruction and tendon interposition as described by Burton and Pellegrini [35] and Weilby [36] (using either the flexor carpi radialis or abductor pollicis longus tendon) [36], simple trapeziectomy, and arthrodesis. Participants were excluded from this study if they had a comorbidity (such as de Quervain's tenosynovitis) that interfered with the treatment or outcome, prior surgery of the CMC-1 in the same hand, steroid injection in the affected hand or wrist within 6 weeks, surgery that targeted multiple pathologies (for example, an additional carpal tunnel release in the same session), or missing data for any measure being studied. Additionally, 13 patients were excluded because they completed the same measures both before their non-surgical and their subsequent surgical treatment. After applying the eligibility criteria, 584 participants were included: 208 in the surgery group and 376 in the nonsurgery group (Fig. 1).

Variables, Data Sources, and Measurement

Similar to other studies [37-39], we classified variables into three categories: sociodemographic, clinical, and psychological. All data represented baseline values before non-surgical or surgical treatment. Sociodemographic characteristics included age, sex, symptom duration, treatment side, dominance, type of work, whether the patient was seen for a second opinion, and type of surgery (for the surgery group).

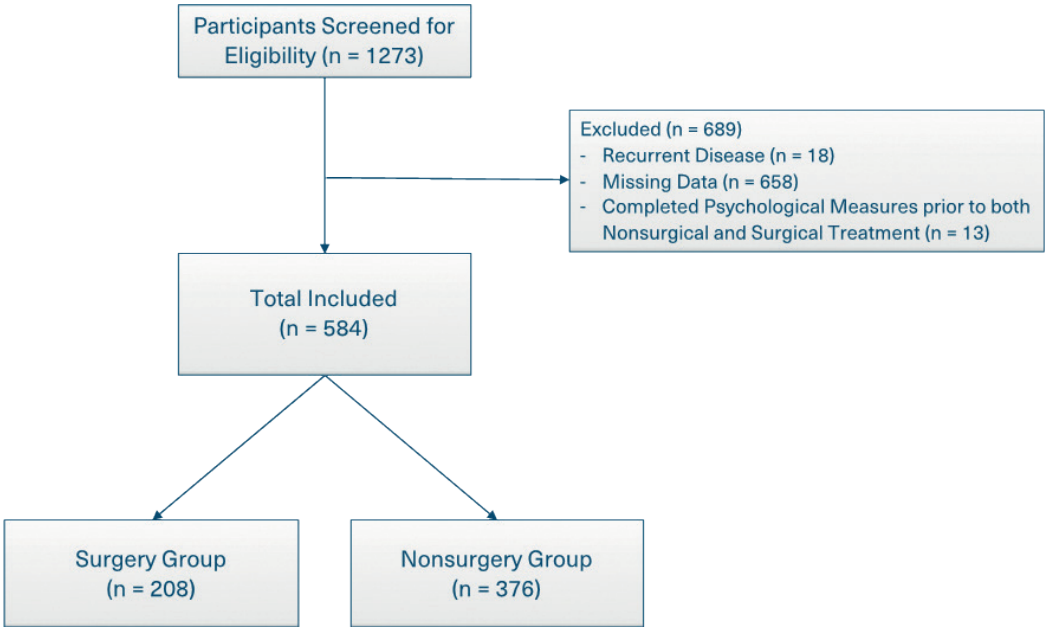

Figure 1. This flowchart illustrates the exclusions criteria for this study.

Clinical characteristics included pain, hand function, satisfaction, and health-related quality of life. We used the VAS [40] to measure pain (VAS score ranges from 0 to 100; higher scores indicate more pain) and the patients' satisfaction with their hand (exact question: "How satisfied are you with your hand at this moment?"; higher scores indicate better satisfaction). To assess hand function, we used the Michigan Hand outcomes Questionnaire (MHQ, range 0 to 100; higher scores indicate better performance, except for the subscale of pain), which is particularly applicable to patients with OA of the hand [41]. Health-related quality of life was measured using the EuroQol-5D-5L (EQ-5D-5L) [42].

Psychological characteristics included treatment credibility, treatment expectations, illness perception, pain catastrophizing, and anxiety and depression. Treatment credibility and expectations were measured using the Credibility/Expectancy Questionnaire (CEQ), consisting of a credibility and expectancy subscale (score range is 3 to 27; higher scores indicate higher credibility or expectations) [43]. Illness perception was measured using the brief Illness Perception Questionnaire ([IPQ]; item scores range from 0 to 10; higher scores indicate worse illness perception) [44]. Pain catastrophizing was measured with the Pain Catastrophizing Scale ([PCS]; score range is 0 to 52; higher scores indicate

more catastrophizing) [45]. Furthermore, anxiety and depression were measured with the Patient Health Questionnaire for anxiety and depression ([PHQ-4]; score range: 0 to 6 for the subscales of anxiety and depression; higher scores indicate more anxiety and depression), which is a tool for detecting depressive disorders [46]. Scores of 3 or higher for the subscales indicate a potential anxiety or depression disorder [46].

Study Size

A power analysis using an independent sample t-test (the primary analysis) with a conventional effect size [47] of 0.25 and power of 0.80 (a = 0.05) and an allocation ratio of 0.57 showed that 546 participants were needed, which was well below the sample of 584 participants we were able to include.

Statistical Methods

We compared baseline sociodemographic, clinical, and psychological characteristics between patients with CMC-1 OA scheduled for non-surgical treatment and those with surgical treatment, using independent sample t-tests and chi-square tests. Additionally, to more specifically investigate the relative contribution of sociodemographic, clinical, and psychological characteristics to the probability of being scheduled for surgery, we used a hierarchical logistic regression analysis with the treatment group as a dependent variable. Using this method, the relative contribution of psychological characteristics can be studied in more detail after adjusting for sociodemographic characteristics (for example, symptom duration) and clinical characteristics (such as VAS pain levels). Variables were added to this hierarchical model in separate steps. To illustrate the fit of the different models, we determined the area under the curve, Nagelkerke's r^2, and receiver operating characteristic curves for these different models. In this analysis, we carefully selected each variable for inclusion in every step based on the construct it measures. This means that not all variables from the primary analysis were used in the hierarchical model; we excluded variables for which there was overlap in the measured construct (for example, the EQ-5D-5L anxiety/depression index and PHQ-4). All available variables are reported in the primary analyses to provide an overview of both groups that was as clear as possible.

In the first step of the hierarchical model, only sociodemographic characteristics including age, sex, symptom duration, treatment side, dominance, type of work, and second-opinion visit were added. In the second step, we added clinical characteristics, including VAS scores for pain at rest and during physical

loading; VAS satisfaction; MHQ subscales of hand function, activities of daily life, work, and aesthetics; and the EQ-5D-5L index score. In the third step, we added psychological characteristics, including the CEQ subscales of credibility and expectancy; IPQ items of consequences, timeline, personal control, identity, concern, coherence, and emotional response; the PCS; and the PHQ anxiety and depression subscales.

We evaluated multicollinearity using correlation coefficients and the variance inflation factor. A variance inflation factor greater than 10 was considered an indication of multicollinearity [48].

Table 1. Final model following hierarchical logistic regression analyses (n = 584) using sociodemographic, clinical and psychological characteristics explaining the relative contribution of being in the surgery group. Unstandardized and standardized odds ratios (SOR), 95% confidence intervals for the unstandardized ORs are displayed, along with the area under the curve (AUC) and Nagelkerke R2 for the model. *Significant at < 0.05 level. MHQ = Michigan Hand outcomes Questionnaire, CEQ = Credibility and Expectancy Questionnaire, IPQ = brief Illness Perception Questionnaire, PCS = Pain Catastrophizing Scale, PHQ = Patient Health Questionnaire.

	Final model	
Variables	**Unstandardized OR (95% CI)**	**Standardized OR**
Step 1: Sociodemographic characteristics		
Treatment side	0.84 (0.54 to 1.30)	0.84
Dominance	1.01 (0.50 to 2.05)	1.01
Gender	0.77 (0.42 to 1.43)	0.77
Age onset	1.01 (0.97 to 1.05)	1.05
Symptom duration	1.01* (1.00 to 1.02)	1.86
Second opinion	3.81* (1.17 to 12.4)	3.81
Type of work category		
Type of work category (1)	1.07 (0.54 to 2.14)	1.07
Type of work category (2)	0.73 (0.37 to 1.42)	0.73
Type of work category (3)	1.31 (0.55 to 3.13)	1.31
Step 2: Clinical characteristics		
VAS pain at rest	1.00 (0.99 to 1.01)	1.01
VAS pain during physical load	1.01 (1.00 to 1.03)	1.34
VAS satisfaction with the patient's hand	0.98* (0.97 to 0.99)	0.65
MHQ hand function	1.00 (0.99 to 1.02)	1.01
MHQ activities of daily living	1.00 (0.99 to 1.01)	0.87

Table 1. Continued

Variables	Final model	
	Unstandardized OR (95% CI)	**Standardized OR**
MHQ work	0.99 (0.98 to 1.01)	0.86
MHQ aesthetics	0.99 (0.98 to 1.01)	0.86
EQ-5D-5L index score	0.40 (0.05 to 3.58)	0.87
Step 3: Psychological characteristics		
CEQ credibility	1.04 (0.94 to 1.15)	1.18
CEQ expectancy	1.42* (1.29 to 1.56)	5.04
IPQ consequences	1.04 (0.88 to 1.23)	1.09
IPQ timeline	0.86* (0.77 to 0.97)	0.70
IPQ personal control	0.78* (0.70 to 0.87)	0.57
IPQ symptoms due to illness	1.00 (0.89 to 1.13)	1.01
IPQ concern	1.00 (0.88 to 1.14)	1.00
IPQ understanding	1.02 (0.90 to 1.16)	1.03
IPQ emotional response	1.12* (1.01 to 1.25)	1.40
PCS	1.01 (0.97 to 1.04)	1.05
PHQ anxiety subscale	0.92 (0.71 to 1.19)	0.89
PHQ depression subscale	0.89 (0.65 to 1.22)	0.87
AUC (95% CI; p value)	0.900 (0.875 to 0.925; p < 0.001)	
Nagelkerke R^2	0.56	

RESULTS

After adjusting for sociodemographic, clinical, and psychological factors, we found that longer symptom duration (standardized odds ratio [SOR], 1.86; p = 0.004), second-opinion visit (SOR, 3.81; p = 0.027), lower satisfaction with the hand (SOR, 0.65; p = 0.004), higher treatment expectations (SOR, 5.04; p < 0.001), shorter perceived timeline (SOR, 0.70; p = 0.011), worse personal control (SOR, 0.57; p < 0.001) and emotional response (SOR, 1.40; p = 0.040) increased the probability of being scheduled for surgery to an area under the curve (AUC) of 0.900 (Table 1).

In an examination of sociodemographics alone, we found that patients in the surgery group reported a longer symptom duration (36 months) than did those in the nonsurgery group (23 months; p = 0.001) and visited our center more often for a

second opinion (7% versus 2%; p = 0.001). There were no other between-group differences in sociodemographic characteristics (Table 2).

Table 2. Sociodemographic characteristics for the surgery group (N=208) and the non-surgery group (N=376).

Variable	Surgery group (N=208)	Non-surgery group (N=376)	p-value
Age, mean ±SD	60.7 ± 7.9	60.3 ± 7.6	*0.532*
Female gender, %	78.8%	77.7%	*0.740*
Symptom duration in months, mean ±SD	36.3 ± 36.5	22.7 ± 57.1	***0.001***
Treatment Side*, %			*0.893*
- Left	48.6%	46%	
- Right	51.4%	47.6%	
- Both	-	6.4%	
*statistics are used to test left/right only, since bilateral surgical treatment is not employed			
Dominance, %			*0.854*
- Left	7.2%	6.6%	
- Right	89.4%	90.7%	
- Both	3.4%	2.7%	
Type of surgery, %:			*NA*
- LRTI (Burton-Pellegrini)	23.1%	-	
- LRTI (Weilby-FCR)	57.7%	-	
- LRTI (Weilby-APL)	7.7%	-	
- Simple trapeziectomy	10.1%	-	
- Arthrodesis	1.4%	-	
Type of work, %			*0.079*
- Unemployed	45.7%	41.2%	
- Light physical labor	16.8%	22.9%	
- Moderate physical labor	23.1%	26.6%	
- Heavy physical labor	14.4%	9.3%	
Second opinion, %	7.2%	1.9%	***0.001***

Abbreviations: LRTI = Ligament Reconstruction and Tendon Interposition, FCR = Flexor Carpi Radialis, APL = Abductor Pollicis Longus

Considering clinical characteristics, patients in the surgical treatment group reported worse symptom severity scores for the VAS and MHQ (except for the subscale of aesthetics) than did those in the non-surgical treatment group (p < 0.001 to 0.006; absolute effect sizes ranging from 0.24 to 0.67) (Table 3). Additionally, patients in the surgery group reported worse scores for the EQ-5D-5L domains of self-care, daily activities, pain and discomfort indexes, and total index score (p < 0.001 to 0.016; absolute effect sizes ranging from 0.22 to 0.46) (Table 3).

Table 3. Baseline mean ±SD values for clinical characteristics and symptom severity for the Visual Analogue Scales (VAS, score range: 0–100), the Michigan Hand outcomes Questionnaire (MHQ, score range: 0–100) and EQ-5D-5L (score range: 0–100 for self-rated health, 1–5 for subscales and -0.33–1.0 for the index score).

Variable	Surgery group (N=208)	Non-surgery group (N=376)	Effect size (Cohen's d)	p-value
VAS past week	67.2 ± 17.3	54.6 ± 21.5	0.65	***<0.001***
VAS rest	51.4 ± 22.7	40.2 ± 25.9	0.46	***<0.001***
VAS physical load	75.6 ± 17.4	63.3 ± 22.4	0.61	***<0.001***
VAS satisfaction with the patient's hand ("How satisfied are you with your hand at this moment?")	25.3 ± 20.4	37.2 ± 22.1	-0.56	***<0.001***
MHQ hand function	52.1 ± 17.9	57.9 ± 17.9	-0.32	***<0.001***
MHQ Activities of daily living	57.2 ± 27	69.1 ± 24.4	-0.46	***<0.001***
MHQ Work	49.1 ± 26.8	60.5 ± 25.8	-0.43	***<0.001***
MHQ Pain	64.5 ± 14.8	53.8 ± 17.1	0.67	***<0.001***
MHQ Aesthetics	78.9 ± 19.6	81.5 ± 19.6	-0.13	*0.124*
MHQ Satisfaction	42.2 ± 27.6	48.5 ± 24.9	-0.24	***0.006***
MHQ Total	50.1 ± 14.3	58.4 ± 14.7	-0.58	***<0.001***
EQ-5D-5L Self-rated health	75.6 ± 18.3	75.8 ± 18.4	0.00	*0.859*
EQ-5D-5L Mobility	1.36 ± 0.69	1.48 ± 0.82	-0.16	*0.054*
EQ-5D-5L Self care	1.44 ± 0.68	1.30 ± 0.61	0.22	***0.016***
EQ-5D-5L Daily activities	2.56 ± 0.97	2.30 ± 0.91	0.28	***0.002***
EQ-5D-5L Pain and discomfort	3.18 ± 0.72	2.85 ± 0.73	0.46	***<0.001***
EQ-5D-5L Anxiety	1.38 ± 0.73	1.32 ± 0.67	0.09	*0.360*
EQ-5D-5L index value	0.68 ± 0.16	0.73 ± 0.15	-0.31	***0.001***

When we compared the groups in terms of psychological characteristics, patients in the surgery group reported higher credibility and expectancy of their treatment than did those in the nonsurgery group ($p < 0.001$), with effect sizes of 0.81 and 1.20, respectively (Table 4). For the IPQ, patients in the surgery group reported having worse consequences, identity, concern, and emotional response because of their illness and a shorter expected timeline of their illness than did those in the nonsurgery group ($p < 0.001$ to 0.018; absolute effect sizes ranging from 0.20 to 0.47). Additionally, patients in the surgery group reported less personal control but more treatment control than did those in the nonsurgery group, suggesting a more external locus of control ($p < 0.001$; absolute effect sizes 0.46 and 0.90, respectively). Furthermore, patients in the surgery group reported more pain catastrophizing on the PCS ($p < 0.001$; effect size = 0.31) than did those in the non-surgical treatment group. No differences were found in PHQ scores (Table 4).

Table 4. Baseline mean ± SD scores on psychological questionnaires for treatment expectations, illness perception, pain catastrophizing and anxiety and depression. CEQ = Credibility and Expectancy Questionnaire (score range: 3–27), IPQ = brief Illness Perception Questionnaire (score range 0–10), PCS = Pain Catastrophizing Scale (score range: 0–52) PHQ = Patient Health Questionnaire-4 (PHQ, score range: 0-6 for the subscales)

Variable	Surgery group (n = 208)	Nonsurgery group (n = 376)	Effect size (Cohen's d)	p value
CEQ credibility	23.5 ± 2.8	20.8 ± 3.8	0.81	***<0.001***
CEQ expectancy	22.3 ± 3.1	17.6 ± 4.6	1.20	***<0.001***
IPQ consequences: How much does your illness affect your life? (10 = severely affects my life)	7.4 ± 1.8	6.4 ± 2.3	0.47	***<0.001***
IPQ timeline: How long do you think your illness will continue? (10 = forever)	6.7 ± 2.5	7.7 ± 2.3	-0.42	***<0.001***
IPQ personal control: How much control do you feel you have over your illness? (0 = absolutely no control)	4.3 ± 2.5	5.3 ± 2.1	-0.46	***<0.001***
IPQ treatment control: How much do you think your treatment can help your illness? (10 = extremely helpful)	8.3 ± 1.4	6.8 ± 1.8	0.90	***<0.001***
IPQ identity: How much do you experience symptoms from your illness? (10 = many severe symptoms)	6.9 ± 2.4	6 ± 2.5	0.38	***<0.001***
IPQ concern: How concerned are you about your illness? (10 = extremely concerned)	6.5 ± 2.5	5.9 ± 2.7	0.20	***0.018***
IPQ coherence: How well do you feel you understand your illness? (10 = understand very clearly)	8.4 ± 2	8.4 ± 1.8	0.00	*0.974*
IPQ emotional response: How much does your illness affect you emotionally? (for example, does it make you angry, scared, upset or depressed? (10 = extremely affected emotionally)	5.2 ± 3	4.2 ± 2.9	0.37	***<0.001***
PCS	14.4 ± 10.3	11.4 ± 9.1	0.31	***<0.001***
PHQ subscale anxiety	0.80 ± 1.35	0.77 ± 1.31	0.02	*0.765*
PHQ subscale depression	0.67 ± 1.28	0.55 ± 1.09	0.10	*0.252*
PHQ anxiety cutoff (score 3 or higher), n (%)	25 (12%)	32 (8.5%)	NA	*0.171*
PHQ depression cutoff (score 3 or higher), n (%)	17 (8.2%)	20 (5.3%)	NA	*0.175*
PHQ total	1.47 ± 2.44	1.32 ± 2.22	0.06	*0.437*

When analyzing the different models resulting from our hierarchical regression, the model including sociodemographic, clinical, and psychological factors

provided the highest areas under the curve (sociodemographics alone: 0.663 [95% CI 0.618 to 0.709]; sociodemographics and clinical: 0.750 [95% CI 0.708 to 0.791]; sociodemographics, clinical and psychological: 0.900 [95% CI 0.875 to 0.925], Supplementary Table 1). The ROC curve indicates that the probability of being scheduled for surgery is for the largest part explained by the last model, including sociodemographic, clinical, and psychological characteristics (Fig. 2).

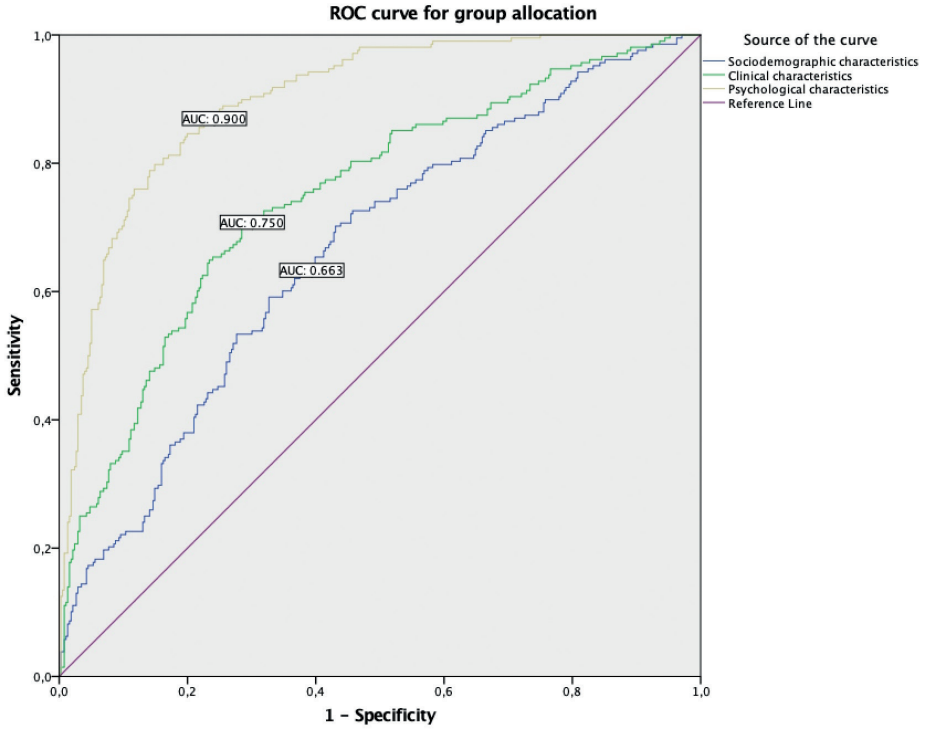

Figure 2. Receiver operating characteristic curve for the hierarchical models, with AUCs of 0.663, 0.750, and 0.900 for sociodemographic, plus clinical and plus psychological characteristics, respectively, indicating that the probability of being in the surgery group is for the largest part of explained by the model with sociodemographic, clinical and psychological characteristics. ROC = receiver operating characteristic; AUC = area under the curve.

DISCUSSION

Psychological characteristics, such as depression, anxiety or negative illness perception are highly prevalent in patients with OA. Before our study, it was unclear whether there are differences in the clinical and psychological characteristics of patients with CMC-1 OA scheduled for non-surgical or surgical

treatment. More insight in psychological profile of these patients would provide clinicians and patients with valuable information for shared decision-making and indicate if psychological interventions, training in coping strategies, and patient education are needed. We found that patients with CMC-1 OA scheduled for surgery have a worse psychological profile than do those undergoing non-surgical treatment. Additionally, the probability of being scheduled for surgery is best explained by our model, including sociodemographic, clinical, and psychological characteristics.

Limitations

The results of these between-group comparisons should be interpreted with caution because patients undergoing surgical treatment usually receive non-surgical treatment first but do not improve. In the present study, we do not know whether between-group differences occurred because of deterioration in clinical and psychological characteristics over time after initiating non-surgical treatment or if these differences were predetermined and predictors of conversion to surgery. Furthermore, the amount of missing data that lead to our final sample (n = 584 patients) and surgeon's preferences may have resulted in selection bias. Hence, our sample may be a different representation compared with the target population of patients with CMC-1 OA. Another limitation is that although we reported effect sizes, which allow comparisons across populations and measurement instruments, the between-group differences in this study should be interpreted in light of minimal clinical important difference values established in other disease populations, such as for the VAS and the MHQ [40,49,50].

Differences in Baseline Characteristics between Patients Treated Surgically and Those Treated Non-operatively

We found that patients scheduled for surgical treatment had longer symptom duration, more often sought a second opinion, had higher pain, treatment credibility and expectations and worse hand function, satisfaction, HRQoL, illness perception, and pain catastrophizing compared with those scheduled for non-surgical treatment. We did not find between-group differences in anxiety or depression.

Although several studies investigated the psychological profiles of patients with OA [18-27], only one other study [28] specifically compared the psychological profiles of patients with CMC-1 OA scheduled for surgical or non-surgical treatment. However, the study by Lozano-Calderon et al. [28] had a sample that was too

small to find any between-group differences, and many different measurement tools were used compared with our study (that is, the DASH versus the MHQ for evaluating hand function), making it difficult to compare findings. Our study confirms prior reports [18-27], which showed that psychological characteristics are of major importance in patients with chronic musculoskeletal diseases such as OA, and these characteristics influence clinical decision-making, although perhaps unconsciously [18,20-27]. Because the underlying pathology of OA of the CMC-1 is chronic, our study results might be generalizable to patients scheduled to undergo surgical or non-surgical treatment of other chronic diseases or body regions; for example, hip or knee OA. Therefore, future research should address other chronic diseases or body regions.

In the present study, we did not find between-group differences in anxiety or depression. However, Becker et al. [22] found differences in depression between patients visiting a clinician for CMC-1 OA and patients with coincidentally diagnosed CMC-1 OA. Becker et al. [22] used the nine-item version of the PHQ, which is a more extensive screening tool than the four-item tool used in the present study. However, a score of 5 or higher on the nine-item version of the PHQ indicates mild depression [51], and in the study by Becker et al. [22], a mean score of 4.5 was found in the group visiting a clinician for CMC-1 OA. This indicates that on average, no depression was present, which is comparable to our results.

Factors Contributing to the Probability of Being Scheduled for Surgery

Our findings suggest that patients with CMC-1 OA scheduled for surgical treatment have a worse psychological profile compared with patients scheduled for non-surgical treatment. The decision to undergo surgery might be influenced by potentially modifiable psychological characteristics, and addressing these factors may decrease the number of surgeries performed or improve the outcomes of surgery. Psychological interventions, training in coping strategies, and more extensive patient education may be indicated before surgical treatment is performed. However, although the correlation of psychological characteristics with the outcome of non-surgical or surgical treatment of CMC-1 OA is currently unknown, this correlation is known in patients who undergo surgery for carpal tunnel syndrome or trigger finger [52]. Future longitudinal studies should address the correlation of psychological characteristics with the outcomes of both non-surgical and surgical treatment of CMC-1 OA.

We found that patients in the nonsurgery group expected to have a longer illness duration and had more personal control, less treatment control (IPQ scores), and lower treatment expectations (CEQ scores) than did those in the surgical group. Patients scheduled for non-surgical treatment may cope with chronic disease differently than those with surgical treatment, implying that they are more willing to accept aging processes and adapt to daily life than patients who undergo surgery. Furthermore, the participants in the surgery group reported having higher treatment credibility and expectations but worse clinical and other psychological characteristics, suggesting that more research on how to manage treatment credibility and expectations is needed, especially in this population.

In the final model, we found a relatively large OR for whether a second opinion contributed to the probability of surgery. This finding may be explained by the theory that patients seeking a second opinion already had a relatively long clinical course, and they may have postponed surgery for a longer time period. However, this hypothesis cannot be confirmed with the present cross-sectional study design and should be investigated in a longitudinal setting.

CONCLUSIONS

In conclusion, we found worse clinical and psychological characteristics in patients scheduled for surgical treatment of CMC-1 OA than in patients at the initiation of non-surgical treatment. Furthermore, the probability of being scheduled for surgery was mostly explained by the model including sociodemographic, clinical, and psychological characteristics. A more thorough psychological evaluation might be considered before surgery is performed, especially in patients with high expectations, worse illness perception, and pain catastrophizing. Additionally, addressing these factors might decrease the number of surgeries performed, improve the outcomes of surgery or indicate if psychological interventions, training in coping strategies, and patient education might be indicated before converting to surgery. Future studies should investigate the influence of psychological characteristics on the outcomes of patients with CMC-1 OA.

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Supplementary Table 1. Entire hierarchical logistic regression analysis (n = 594) explaining the relative contribution of being in the surgery group using socio-demographic characteristics (model 1), clinical characteristics (model 2) and psychological characteristics (model 3). Unstandardized and standardized odds ratios (OR), the 95% confidence intervals (CI) for the unstandardized ORs, along with the area under the curve (AUC), the significance of the change of the AUC, and Nagelkerke R^2 for the different models. *Significance at < 0.05 level. MHQ = Michigan Hand outcomes Questionnaire, CEQ = Credibility and Expectancy Questionnaire, IPQ = brief Illness Perception Questionnaire, PCS = Pain Catastrophizing Scale, PHQ = Patient Health Questionnaire.

	Model 1		**Model 2**		**Model 3**	
Variables	*Unstandardized OR (95% CI)*	*Standardized OR*	*Unstandardized OR (95% CI)*	*Standardized OR*	*Unstandardized OR (95% CI)*	*Standardized OR*
Step 1: Sociodemographic characteristics						
Treatment side	0.74 (0.55 to 1.01)	0.74	0.72 (0.51 to 1.00)	0.72	0.84 (0.54 to 1.30)	0.84
Dominance	0.91 (0.52 to 1.59)	0.91	1.00 (0.55 to 1.83)	1.00	1.01 (0.50 to 2.05)	1.01
Gender	1.13 (0.72 to 1.76)	1.13	0.79 (0.49 to 1.29)	0.79	0.77 (0.42 to 1.43)	0.77
Age onset	1.01 (0.98 to 1.03)	1.05	1.02 (0.99 to 1.05)	1.15	1.01 (0.97 to 1.05)	1.05
Symptom duration	1.01* (1.00 to 1.01)	1.53	1.01* (1.00 to 1.01)	1.33	1.01* (1.00 to 1.02)	1.86
Second opinion	4.03* (1.57 to 10.31)	4.03	4.06* (1.47 to 11.22)	4.06	3.81* (1.17 to 12.4)	3.81
Type of work category						
Type of work category (1)	0.69 (0.41 to 1.17)	0.69	0.83 (0.47 to 1.46)	0.83	1.07 (0.54 to 2.14)	1.07
Type of work category (2)	0.81 (0.49 to 1.34)	0.81	1.01 (0.59 to 1.74)	1.01	0.73 (0.37 to 1.42)	0.73
Type of work category (3)	1.56 (0.84 to 2.89)	1.56	1.85 (0.96 to 3.59)	1.85	1.31 (0.55 to 3.13)	1.31
Step 2: Clinical characteristics						
VAS pain at rest			1.01 (1.00 to 1.01)	1.13	1.00 (0.99 to 1.01)	1.01
VAS pain during physical load			1.02* (1.00 to 1.03)	1.44	1.01 (1.00 to 1.03)	1.34
VAS patient satisfaction with their hand			0.98* (0.97 to 0.99)	0.67	0.98* (0.97 to 0.99)	0.65
MHQ hand function			1.00 (0.99 to 1.01)	0.98	1.00 (0.99 to 1.02)	1.01

MHQ activities of daily living		0.99* (0.98 to 1.00)	0.77	1.00 (0.99 to 1.01)	0.87
MHQ work		0.99 (0.99 to 1.00)	0.83	0.99 (0.98 to 1.01)	0.86
MHQ aesthetics		1.00 (0.99 to 1.01)	1.06	0.99 (0.98 to 1.01)	0.86
EQ-5D-5L index score		2.43 (0.53 to 11.10)	1.15	0.40 (0.05 to 3.58)	0.87
Step 3: psychological characteristics					
CEQ credibility				1.04 (0.94 to 1.15)	1.18
CEQ expectancy				1.42* (1.29 to 1.56)	5.04
IPQ consequences				1.04 (0.88 to 1.23)	1.09
IPQ timeline				0.86* (0.77 to 0.97)	0.70
IPQ personal control				0.78* (0.70 to 0.87)	0.57
IPQ symptoms due to illness				1.00 (0.89 to 1.13)	1.01
IPQ concern				1.00 (0.88 to 1.14)	1.00
IPQ understanding				1.02 (0.90 to 1.16)	1.03
IPQ emotional response				1.12* (1.01 to 1.25)	1.40
PCS				1.01 (0.97 to 1.04)	1.05
PHQ anxiety subscale				0.92 (0.71 to 1.19)	0.89
PHQ depression subscale				0.89 (0.65 to 1.22)	0.87
AUC (95% CI; p value)	0.663 (0.618 to 0.709; p < 0.001)	0.750 (0.708 to 0.791; p < 0.001)		0.900 (0.875 to 0.925; p < 0.001)	
Nagelkerke R^2	0.07	0.22		0.56	

PART 2

POSTOPERATIVE TREATMENT

CHAPTER 7

POSTOPERATIVE REHABILITATION FOLLOWING THUMB BASE SURGERY: A SYSTEMATIC REVIEW OF THE LITERATURE

Robbert M. Wouters
Jonathan Tsehaie
Steven E.R. Hovius
Burcu Dilek
Ruud W. Selles

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ABSTRACT

Objective: When conservative treatment fails to alleviate symptoms in patients with thumb base (CMC-1) osteoarthritis (OA), CMC-1 arthroplasty is indicated. However, there is no consensus regarding the components of postoperative rehabilitation for patients who underwent CMC-1 arthroplasty. This systematic review provides an overview of rehabilitation for patients who underwent CMC-1 arthroplasty, with emphasis on early active mobilization.

Data sources/study selection: PubMed/MEDLINE, Embase, CINAHL and Cochrane were searched for articles written in English that described postoperative regime (including immobilization period/method and/or description of exercises/physical therapy, follow-up ≥six weeks) on CMC-1 arthroplasty.

Data extraction: The PRISMA statement was used as guidance in this review and methodological quality was assessed using the Effective Public Health Practice Project quality assessment tool. Randomized studies were additionally scored using the Physiotherapy Evidence Database scale.

Data synthesis: Twenty-seven studies were included, concerning 1015 participants in whom 1118 surgical procedures were performed. A summary on the components of postoperative rehabilitation used in the included studies on CMC-1 OA is presented for different surgical interventions. We found that early active recovery (including short immobilization, early initiation of ROM and strength exercises) provides positive outcomes on pain, limitations in ADL and grip & pinch strength, but comparative studies are lacking. Furthermore, three postoperative exercises/therapy phases were identified in the literature: the 'acute phase', the 'unloaded phase' and the 'functional phase', but again comparative studies are lacking.

Conclusions: Early active recovery is used more often in the literature and does not lead to worse outcomes or more complications. This systematic review provides guidance for clinicians in the content of postoperative rehabilitation on CMC-1 arthroplasty. The review also clearly identifies the almost complete lack of high quality, comparative studies on postoperative rehabilitation after CMC-1 arthroplasty.

INTRODUCTION

Osteoarthritis (OA) of the thumb base joint (CMC-1) is a common disorder in the elderly.[1] The prevalence of radiologically diagnosed CMC-1 OA amongst females aged ≥50 years is 33-36%.[2,3] The number of patients with CMC-1 OA is expected to increase because of the ageing population.[4] Patients with CMC-1 OA often experience pain, have reduced pinch- and/or grip strength and report limitations in activities of daily life (ADL).[5]

When conservative treatment fails to reduce pain and limitations in ADL, CMC-1 arthroplasty may be indicated.[6] In the past decades, a variety of surgical techniques are described.[7,8] When CMC-1 OA is treated surgically, usually a trapeziectomy is performed, with or without ligament reconstruction and/or tendon interposition.[6-8] CMC-1 arthrodesis and implants are also used, but the usage of these techniques has been associated with a higher risk of complications (i.e. non-union or dislocation).[6-8]

Some studies emphasize the importance of postoperative rehabilitation for patients who underwent CMC-1 arthroplasty in order to improve pain intensity, limitations in ADL and improve range of motion (ROM) and grip & pinch strength.[6,8] However, the lack of consensus on the content of postoperative rehabilitation for patients who underwent CMC-1 arthroplasty is mentioned as well.[6,8]

A systematic review by Wolfe et al. in 2014 on postoperative rehabilitation following CMC-1 arthroplasty concluded that no recommendations on postoperative rehabilitation could be made, due to a large reported variation regarding type and duration of postoperative immobilization, postoperative exercises, and duration before patients returned to full activities.[9] Furthermore, no overview of postoperative rehabilitation and variations as used in literature (i.e. differences in immobilization period) is presented for different types of surgery. Additionally, their search in 2013 was limited to PubMed and Cochrane and limited information on the search strings and the inclusion and exclusion criteria is provided.[9] Therefore, an overview of the postoperative rehabilitation as used in the literature on CMC-1 arthroplasty remains desirable.

Aims and research questions

The aim of this systematic review is to describe and to create an overview on the different components and phases of postoperative rehabilitation protocols for

patients who underwent CMC-1 arthroplasty and to quantify how often these are used. Furthermore, we investigated several specific components or variations in postoperative rehabilitation protocols that are presently discussed. Since tensile strength of scar tissue is at 80% of normal tissue at 6 weeks and at 50% at 4 weeks, we specifically studied these time frames.[10] We formulated the following research questions:

1. What type of postoperative rehabilitation (including immobilization period and initiation of ROM & strengthening exercises) is used in literature for different types of surgery, categorized by used tendon plasty?

2. What are the outcomes of short immobilization (4-6 weeks or ≤4 weeks) with regard to pain intensity, limitations in ADL, grip & pinch strength and complications?

3. What are the outcomes of ROM and strengthening exercises in an early phase (≤4 weeks) with regard to pain intensity, limitations in ADL and grip & pinch strength and complications?

METHODS

Design

This systematic review was conducted using the PRISMA statement as guidance.[11]

The inclusion of eligible articles was conducted by 2 reviewers (RW & BD), disagreements were resolved in a consensus meeting between the two raters.

Search strategy

The electronic databases MEDLINE (PubMed, from 1950), Embase (Elsevier, from 1974), CINAHL (EBSCO, from 1961) and the Cochrane Library (time limit unknown) were searched for eligible articles (search date: June 15th 2017). The references of the included articles were scanned for eligibility after primary and secondary screening.

The following MeSH terms and keywords (and their synonyms) were employed: 'carpometacarpal joint', 'thumb', 'arthroplasty', 'trapeziectomy', 'ligament reconstruction and tendon interposition', 'rehabilitation' and 'hand therapy'. The

complete search strategy can be found in Appendix 1. We considered each tendon plasty as ligament reconstruction and tendon interposition (LRTI), except if authors specifically stated that only ligament reconstruction or tendon interposition was used.

Eligibility criteria

Articles were eligible for inclusion if they (1) concern patients who underwent CMC-1 arthroplasty due to symptomatic CMC-1 OA; (2) concern human males/females aged ≥18 years; (3) describe an intervention with a follow-up of ≥six weeks postoperatively; (4) Provide an adequate description of postoperative regime, including immobilization period, immobilization method or description of exercises/physical therapy treatment; (5) provide a description of the type of surgery performed; (6) describe a comparison of results over time (i.e. preoperative vs. postoperative); (7) included pain intensity and/or limitations in ADL and/or grip & pinch strength as outcome measures and (8) were written in English.

Articles were excluded when they (1) provide an abstract only, clinical commentary, research letter, editorial note, review presented at meetings, preliminary study, case reports with complications/exceptions or when full-texts was unavailable; (2) concern revision arthroplasty, external fixation, implant/prosthesis, arthrodesis, osteotomy, structural involvement of the first metacarpophalangeal (MCP-1) joint (i.e. volar capsulodesis) or other procedures; (3) are (systematic) reviews or (4) are long-term follow-up studies with already included study populations.

Study selection

Initially, articles were screened for eligibility on title and abstract. When titles and abstracts implied that an article was potentially eligible for inclusion, a full-text copy of the report was obtained. Additionally, reference tracking was performed in all included articles (see Figure 1: Flow chart).

Data extraction

Two reviewers (RW and JT) extracted data using a standard extraction form, disagreements were resolved in a consensus meeting between the two. Data extracted from the included articles were: (1) authors, publication year, and study location; (2) study design; (3) study population; (4) surgical intervention; (5) immobilization period; (6) therapy/exercises (7) outcome measurements; and (8) outcomes. If data were missing or further information was required, serious

attempts were made to contact the first two authors to request the required information. The rehabilitation protocol of the included studies was identified and summarized.

Assessment of methodological quality (risk of bias)

Two reviewers (RW and JT) independently assessed the methodological validity of the included articles. The methodological quality (risk of bias) was scored using the Effective Public Health Practice Project quality assessment tool (EPHPP),[12] randomized studies were scored using the Physiotherapy Evidence Database (PEDro) scale as well.[13] Disagreements were resolved in a consensus meeting between the two raters. The strength of inter-rater agreement was measured by Cohen`s κ coefficient.[14]

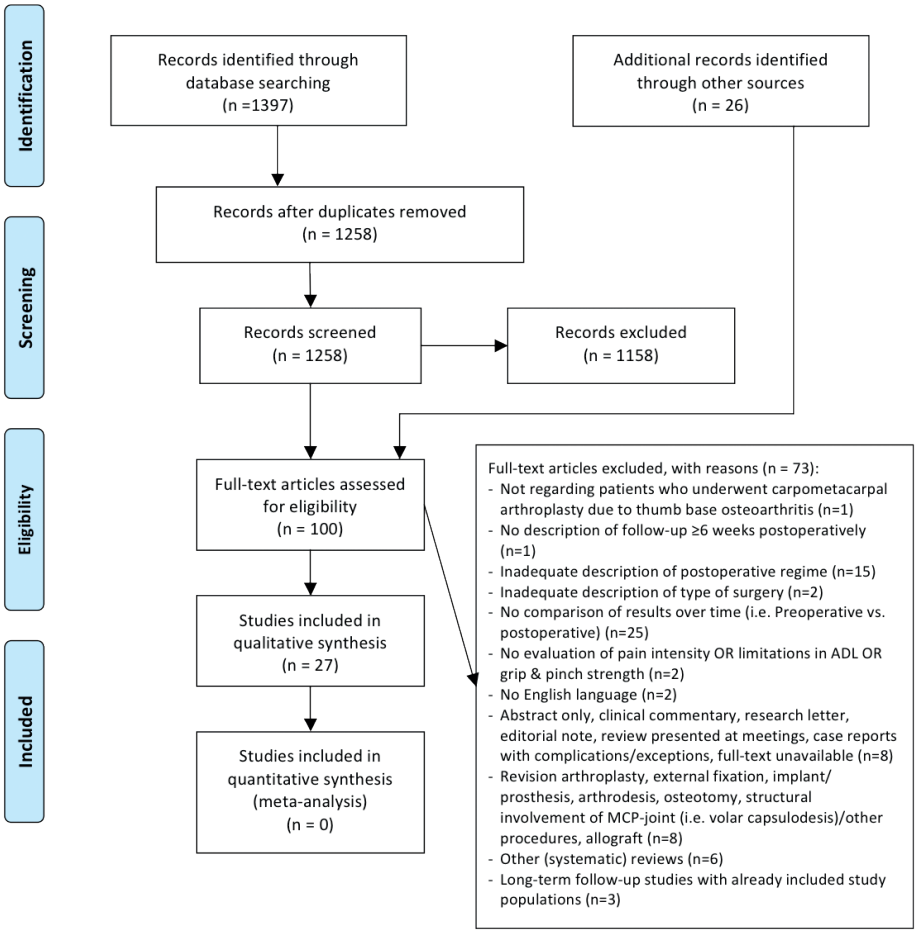

Figure 1. Flowchart of the search process (derived from PRISMA[11])

Synthesis of results and data analysis

Effect sizes were calculated for comparative studies included in this review when means and standard deviations for pre and posttest outcomes were provided. If data were missing or further information was required, we contacted the first two authors to request the required information. When standard deviations were obtained, the pretest standard deviations were pooled to calculate effect sizes.[15,16] Cohen[16] defined conventional values for effect sizes, where a value of 0.20 reflects a small, 0.50 a medium and 0.80 reflects a large effect size. Results of individual studies were not statistically pooled due to a limited number of comparative studies per research question and large heterogeneity.

RESULTS

Study selection and study characteristics

The initial search identified 1397 articles. After applying the inclusion and exclusion criteria, 27 studies were included in this systematic review (see Figure 1).

An overview of the included studies, their characteristics, measurements and outcomes are shown in Table 1. In the 27 selected studies, a total of 1015 participants were included in which 1118 procedures were performed. Twelve different surgical procedures were performed in the 27 included studies (Table 2). In eight studies, eleven surgical co-interventions were performed (Supplementary Table 1, Appendix 2). Six studies[17-22] described that no other co-interventions were performed and it is unclear if other co-interventions were performed in the thirteen remaining studies.[23-35]

On methodological quality (risk of bias), a Kappa score of 0.84 and 0.82 was found between the reviewers (RW & JT) with regard to the EPHPP and the PEDro scale respectively; both scores representing very good agreement.[14] Supplementary Table 2 (Appendix 2) gives an overview of the methodological quality of the included studies.

Table 1. Overview of the characteristics, measurements and outcomes of the included studies.

Author, year	Study design	Study population (N, F/M, age (mean, range/±SD), right/left, dominance)	Surgical intervention	Co-interventions	Postoperative rehabilitation - immobilization period
Abbas et al.[23] 2012	Case series	N = 10 F/M = 10/0 Age = 50-60 (N=4), 61-70 (N=3), 71-80 (N=2), 81-90) N=1) Dominance: 7	Modified LRTI using PL for interposition and FCR for ligament re-construction	Unknown/not described	0-6 weeks: short arm thumb spica cast, K-wire excision after six weeks
Ataker et al.[36] 2012	Retrospective Cohort	N = 23 consecutive patients, 27 thumbs F/M = 21/2 Age = 63.5 years (range: 30-83 years) Dominance: 13/27	Modified LRTI according to Burton-Pellegrini using FCR	CTR (n=3), trigger release (n=3), de Quervain tenosynovitis surgery (n=2), and extensor pollicis brevis tenodesis for MCP-1 joint reconstruction (n=1).	0-2 weeks: spica plaster cast (wrist in 20° extension, thumb in midway between extension and abduction, and the IP joint of the thumb is free) 2-6 weeks: CMC butterfly (24h/day), 6-8 weeks: CMC butterfly (only at night)

	Postoperative rehabilitation - Exercises	Measurements (instruments, follow-up)	Outcomes
	6 weeks: Range of motion exercises were begun with gradual progression to resistive pinch and grip strengthening by 12 weeks postoperatively	Limitations in ADL (Quick DASH). Measures at: T0 (pre-operative), T1 (3 months), T2 (6 months)	Quick DASH Score at T0: 58.8, T1: 40.5, T2: 31.3 (p=0.005)
	Mean of 16.8 therapy sessions 0-4 weeks: ROM exercises for the unaffected fingers, IP 1, elbow, and shoulder; and flexor and extensor tendon gliding exercises as a home-based program. The home exercise program includes 1. Fist/extension, 2. Finger abduction and adduction exercises (dig 2-5). 4x day 10 reps. 4-6 weeks: AROM exercises for CMC-1 and MCP1 supervised by a PT, no CMC-1 flexion/adduction, opposition. Scar management. 6-8 weeks: progressive ROM and strengthening: isometric abduction, extension, and adduction. If patient can perform opposition to Kapandji 6 with no pain, complete flexion can be attempted gradually. AROM IP, MP, CMC1, and thumb opposition added to the home exercise program 4xday 10 reps. 8-10 weeks: Isotonic strength, gentle pinch, grip using putties, and power webs; and the resistance is increased gradually. 10-12 weeks: Strengthening exercises with putty + discharge. 12+ weeks: no restrictions	Pain intensity (VAS 0-10), Limitations in ADL (DASH), ROM, Grip & pinch strength, joint imaging (SMD) Measures at: T0 (pre-operative): T1 (12 weeks): and T2 (31.5 months, range: 12-57 months)	VAS at T0: 8, T1: 3, T2: 3 (p<0.001). DASH at T0: 56, T1: 29, T2: 24 (p<0.001). Increase in palmar and radial abduction, Kapandji score (p<0.001). Grip strength (kg) at T0: 12, T1: 18 (p<0.001), T2: 13, Lateral pinch at T0: 3, T1: 5, T2: 4 (p<0.001). Joint imaging at T0: 11 mm, T1: 5 mm, T2: 3 mm

Table 1. Overview of the characteristics, measurements and outcomes of the included studies.

Author, year	Study design	Study population (N, F/M, age (mean, range/±SD), right/left, dominance)	Surgical intervention	Co-interventions	Postoperative rehabilitation - immobilization period
Başar et al.[22] 2012	Retrospective Cohort	N =19 F/M = 18/1 Age = 55 (±5,7 years) Dominance: 18/19	Modified LRTI using full-thickness FCR	None	0-4 weeks: thumb spica 4-8 weeks: removable splint 8 weeks: splint removed
Burton et al.[24] 1986	Retrospective Cohort	N = 24 patients, 25 thumbs (4 revisions, 1 bilateral), F/M = 21/3, Age = 55.4. Dominance = 3/24	Partial (6 cases) or complete trapeziectomy (19 cases) with LRTI using FCR, all with K-wire	Unknown/not described	0-4 weeks: thumb spica cast immobilization followed by pin removal 4-6 weeks: isoprene thumb Spica splint support, worn constantly except for hand exercises and washing. Splinting is stopped when full ROM is attained and thenar strength is improved to a functional level, usually 8 to 12 weeks after surgery
Davis et al.[37] 2004	Randomized controlled trial investigating different surgical procedures	N = 162 patients, 183 thumbs (Trapeziectomy group: 62, PL group: 59, FCR group: 62) F/M = 162/0 Age = Trapeziectomy group: 58 (range: 44-82), PL group: 60 (range: 41-74), LRTI group: 59 (range: 40-75) (3 groups) Dominance: Trapeziectomy group: 34/58, PL group: 38/60, LRTI group: 36/59	Trapeziectomy, trapeziectomy with PL interposition, trapeziectomy with LRTI with 50% FCR.	Total group: CTR (n=42), MCP K-wire (n=9), MCP capsulodesis (n=9), MCP arthrodesis (n=4), Quervain release (n=4), trigger thumb release (n=5), Trigger finger release (n=2)	0-6 weeks: plaster of Paris splint, wrist neutral & thumb abduction 4 weeks: K-wire excision if applicable

	Postoperative rehabilitation - Exercises	Measurements (instruments, follow-up)	Outcomes
	4-8 weeks: MCP & IP joint exercises and isometric thenar abduction amplification exercises 8 weeks - 3 months: CMC-1 joint mobilization allowed. Easy grasping exercises and progressive thenar abduction amplification exercises against resistance were started. + 3 months: resistive grasping and gripping exercises were started and increased progressively	Pain intensity (VAS 0-10 + other), ROM (Buck-Gramcko score, Kapandji), grip & pinch (tip pinch & lateral pinch) strength, joint imaging (SMD) Measures at: T0 (pre-operative) and T1 (60 months ± 15)	Pain intensity T0: 7(±0.9), T1: 0.9 (±1.4) ROM: Grip & pinch strength: Grip T0: 13.15, T1: 19.28, tip pinch T0: 2.78, T1: 4.45, lateral pinch T0: 4.13, T1: 5.60, all strength measures significant ($p<0.0001$) At T1, 0.2 mm height, not significant.
	4-6 weeks: 1). AROM CMC-1 abduction and extension while avoiding flexion adduction position, 2) AROM flexion of the MCP and IP joints with MC1 supported in abduction by the patient's opposite hand. 6 weeks, continued to 4-6 months: Thenar strengthening is emphasized. 8 weeks: grip and pinch strengthening is begun	Grip & pinch strength, Pain relief (self designed), joint imaging (method not described) Measures at: T0 (pre-operative) and T1 (postoperative follow-up at 2 years, range 1-4,5 years). Pain relief only measured at T1	Pain relief: 92% of patients enjoyed excellent pain relief and were satisfied with the thumb. T1 showed an overall improvement in grip and pinch strength of 19% compared with T0 values (no significance mentioned). Average loss of 11% of the initial postoperative arthroplasty space
	6 weeks: Physiotherapy was not arranged routinely but when the thumb plaster was discarded each patient was shown a series of exercises to mobilize and strengthen her thumb.	Pain intensity, stiffness, weakness and restriction of ADL (measured at once in categorical scores, self-designed), grip & pinch strength, ROM. Measures at: T0 (pre-operative), T1 (3 months), T2 (12 months)	Pain intensity, stiffness, weakness and restriction of ADL improved 'markedly' at T1 and further at T2 (no significance described). There was no significant difference between the different types of surgery ROM improved at T2 compared to T0 (no significance mentioned), there was no significant difference between different types of surgery. Thumb key and tip-pinch and grip strength in the whole study group at T1 were not different from T0. However, thumb key- and tip- pinch and grip strength in the whole group at the T2 were all significantly stronger compared to T0 ($p<0.001$ for all 3 types of surgery)

Table 1. Overview of the characteristics, measurements and outcomes of the included studies.

Author, year	Study design	Study population (N, F/M, age (mean, range/±SD), right/left, dominance)	Surgical intervention	Co-interventions	Postoperative rehabilitation - immobilization period
Eaton et al.[38] 1985	Retrospective cohort	N = 21 patients, 25 thumbs (4 bilateral) F/M = 14/7 men. Age = 57.3 years (range: 31-72). Dominance of the 17 patients with unilateral involvement = 12/17	Partial trapeziectomy with LRTI using FCR.	Stabilization of the MP joint for MP hyperextension >30° (n=5). Advancement or plication of a somewhat lax APL tendon (n=6).	0-4 weeks: plaster shell immobilizing CMC-1 and MCP1, along with K-wire. 4 weeks: K-wire excision
Horlock et al.[25] 2002	Randomized controlled trial investigating short vs. long immobilization	N = 39 patients, 40 thumbs (Early group: 20, Late group: 20) F/M = 30/10 (Early group: 14/6, Late group: 16/4) Age = Early group: 58 ± 7 years, Late group: 59 ± 9 years Dominance: 20/40	Trapeziectomy	Unknown/not described	Early group: 0-1 week: Scotch-cast application 1-6 weeks: Custom made Spica only during physical load and night Late group: 0-2 week: Scotch-cast application 2-4 weeks: Custom made Spica 24/7 4-6 weeks: gentle motion aloud out of splint
Kriegs-Au et al.[21] 2004	Randomized controlled trial investigating different surgical procedures	N = 43 patients, 52 thumbs. Finally 31 participants/thumbs were followed-up (LR group: 15, LRTI group: 16) F/M = 25/6 (LR group: 13/2, LRTI group: 12/4) Age = LR group: 58.4 / LRTI group: 59 years range/±SD: unknown Dominance: 20/31 (LR group: 9/15, LRTI group: 11/16)	Trapeziectomy with LR with FCR vs. Trapeziectomy with LRTI with FCR	None	Both groups: 0-3 week: Spica cast immobilization 3-6 weeks: Individually fitted thumb spica splint that was worn constantly, except during bathing

	Postoperative rehabilitation - Exercises	Measurements (instruments, follow-up)	Outcomes
	4-6 weeks: extension and circumduction of the CMC joint emphasized. 6-8 weeks: thumb is progressively opposed beginning with kapandji 3 gradually extended to kapandji 10. Pinch strengthening is emphasized once full ROM has been achieved.	Pinch strength, clinical results were graded as excellent, good, fair or failure Measures at: T0 (pre-operative) and T1 (follow-up 37,5 months, range 14-60 months).	Pinch strength at T0: 5.5 kg, T1: 6.1 kg (no significance reported) All patients had 'relief of pain' at T1. 55% reported no pain whatsoever, and 44% described 'an occasional twinge or rare mild ache'. No patient had postoperative pain, even those whose clinical results were graded as fair. According to the grading system, 41.7% of the cases were graded as excellent, 50% were good, and 8.3% were fair
	Early group: 1+ week: Light use allowed of the hand and were taught active exercises for the thumb Late group: 4-6 weeks: Gentle use and mobilization were then allowed out of the splint	Pain intensity, hand function, opinion about rehabilitation regimen, satisfaction with operation (VAS 0-100), ROM, grip & pinch strength and joint imaging (SMD & TMD). Measures at: T0 (preoperative), T1 (6-8 months)	No significant difference in pain intensity decrease. The early group experienced more convenience compared to the late group ($p<0.05$). Significant decrease in MCP-1 ROM was found in the late mobilization group but not in de early group (within group $p<0.02$). No significant difference in grip & pinch strength, although the early group performed slightly better when pooling effect sizes of grip, pulp pinch and key pinch strength. Complications were observed in 15% of the participants in the early group compared to 5% in the late group. No differences between groups in median SDM, 2 mm larger decrease in TM within the early group, but not significant
	Both groups: 6 weeks: Active and active-assisted range-of- motion and thenar muscle-strengthening exercises were performed	Grip & pinch strength, Buck-Gramcko score, ROM, self-administered questionnaire (pain, strength, daily function, dexterity, cosmetic appearance, willingness to undergo surgery again, overall satisfaction with result), current and past employment status and activity levels, joint imaging (SMD). Measures at: T0 (preoperative), T1 (48.2 months, range 32-64 months)	All outcomes: Significant improvements, although no differences for different types of surgery mentioned. Proximal migration of the first metacarpal was 37-42%.

Table 1. Overview of the characteristics, measurements and outcomes of the included studies.

Author, year	Study design	Study population (N, F/M, age (mean, range/±SD), right/left, dominance)	Surgical intervention	Co-interventions	Postoperative rehabilitation - immobilization period
Kuhns et al.[39] 2003	Prospective, Single-Surgeon Study	N = 26 F/M = 19/7 Age = 65 years range: 52-82 years Dominance: unknown	Trapeziectomy with k-wire immobilization	MCP-1 volar plate capsulodesis to correct hyperextension (n=7), CTR (n=4), trigger digit release (n=4 digits in 2 patients), ganglion excision (n=1), lipoma excision (n=1).	0-10 days: short-arm thumb spica splint 10 days - 5-6 weeks: thumb spica cast 5-6 weeks: K-wire removal +5-6 weeks: elastic roller bandage then was used to protect the thumb from extreme movements (each patient was encouraged to wean their use of the elastic bandage during the first week after K-wire removal)
Lee et al.[26] 2015	Retrospective Cohort	N = 19 F/M = 13/6 Age = 62 years range 43-82 years Dominance: 11/19	Trapeziectomy with APL sling	Unknown/not described	0-4 week: thumb spica cast in abduction
Lins et al.[40] 1996	Retrospective Cohort	N = 27 patients, 30 thumbs F/M = 25/2 Age = 64 years range 43-77 years Dominance: 19/30	LRTI with (partial N=20/whole N=10) FCR and k-wire.	CTR (n=4), IP-1 joint arthrodesis (n=1)	0-4 weeks: Thumb spica cast followed by Kirschner pin removal. Removable thumb spica splint at 4 weeks until 12 weeks

	Postoperative rehabilitation - Exercises	Measurements (instruments, follow-up)	Outcomes
	5 weeks: warm water soaks with range-of-motion exercises were initiated. 7 weeks: those who were not adducting their thumb fully into the plane of the palm and opposing it to the fifth metacarpal head (N=8) were referred for hand therapy for recovery of motion, instructed not to initiate strengthening exercises	Jebsen subtests II and III dexterity tests, AIMS2, pain relief, ROM opposition, Grip & pinch strength, joint imaging (SMD) Measures at: T0 (preoperative), T1 (6 months), T2 (24 months)	At final follow-up, 92% was pain free. Significant improvements in 3 subscales of the AIMS 2 At T1, 92% adducted fully into the plane of the palm and 96% opposed to the fifth metacarpal head Significant improvements in grip (+47%), key pinch (+33%), and tip pinch (+23%) strength at T2. SMD decreased with 51% at T1 compared to T0, no correlation between proximal migration and functional outcomes.
	4 weeks +: activity of the thumb was encouraged	Pain intensity (VAS 0-10), limitations in ADL (DASH) patient satisfaction (self designed), returning to work (self designed), ROM, grip & pinch strength, joint imaging (SMD) Measures at: T0 (preoperative), T1 (36 months, range 19 to 73.7 months)	VAS at T0: 7.2, T1: 1.7 ($p<0.05$) DASH at T0: 41, T1: 18, ($p<0.05$) Significant improvements in al ROM measurements at T1. Of the working participants, 77% returned to their work or activities without any difficulty or occupation modification, in 23% modifications were required. "All patients expressed their satisfaction for improved postoperative appearance of the hand." Increase of 1.1 kg in power pinch ($p<0.05$) at T1, no difference in tip pinch and grip strength at T1. SMD decreased 34.3% ($p<0.05$)
	4 weeks: gentle ROM exercises 12 weeks: unrestricted thumb movement allowed	Pain intensity (self designed), functional status / satisfaction (self designed), grip & pinch strength, web space, joint imaging (SMD). Measures at: T0 (preoperative), T1 (42-43 months, range 14-88 months)	At T1, 85% patients considered the frequency of pain 'improved a lot or resolved completely' compared to T0 and 89% considered the duration and severity as 'improved a lot or completely' at T1, compared to T0. At T1, 89% of the patients were satisfied with the 'relief of pain' Web space increased with 1.09 cm ($p<0.02$) Grip strength increased with 5.9 kg ($p<0.001$) and pinch strength increased with 1.4 kg ($p<0.01$) SMD decreased with 30% ($p<0.05$)

Table 1. Overview of the characteristics, measurements and outcomes of the included studies.

Author, year	Study design	Study population (N, F/M, age (mean, range/±SD), right/left, dominance)	Surgical intervention	Co-interventions	Postoperative rehabilitation - immobilization period
Mo et al.[27] 2004	Case series	N = 14 patients, 14 thumbs F/M = 11/3 Age = 59.6 years range 31-79 years Dominance: 5/11	LRTI with FCR (sometimes scaphotrapeziotrapezoid joint excision) & K-wire	Unknown/not described	0-4 weeks: thumb spica cast followed by pin removal at 4 weeks 4-8 weeks: removable spica
Nylen et al.[41] 1993	Prospective cohort	N = 93 patients, 102 thumbs F/M = 89/11 Age = 59 years range 40-78 Dominance: 56%	LRTI with FCR without K-wire	MCP arthrodesis (n=6) MCP-1 temporary pinned (n=13). 4 other procedures were performed in the similar hand (procedure unknown)	0-5 weeks: plaster spica with thumb in RAB/PAB. An abduction splint was sometimes used intermittently for a few weeks thereafter.
Poole et al.[28] 2011	Randomized controlled trial investigating the added value of postoperative exercises/ therapy	N = 9 participants (splint/HT group: 4, splint/HP group: 5) F/M = 8/1 (splint/HT group: 3/1, splint/HP group: 5/0) Age = 58.0 (splint/HT group: 59.3 (range 49–68) splint/HP group: 58.4 (range 52–64)) Dominance: 4/9	Partial trapeziectomy with LRTI using PL and The joint was pinned in 1 cm of distraction with K-wires	Unknown/ not described (first stated excluded, later included)	0-4 weeks: bulky dressing and a splint was applied 3-4 weeks: K-wire removal. Both groups: 4 weeks: thumb spica or c-bar splint, no description of discontinuation

	Postoperative rehabilitation - Exercises	Measurements (instruments, follow-up)	Outcomes
	4 weeks: exercises with emphasis on extension/ abduction, on maintaining MCP joint flexion and avoiding hyperextension 8 weeks: strengthening exercises	Limitations in ADL (DASH), ROM, grip & pinch strength. Joint imaging (SMD) Measures at: T0 (preoperative), T1 (20 months, range 12-44 months)	DASH outcomes associated with strength, no results over time reported The distance from thumb tip to the base of the small finger during maximum flexion decreased with 0.4 cm (p=0.02) Grip strength improved with 26% at T1 compared to T0 (p=0.01), pinch strength improved 11% (p=0.11). SMD improved with 2.5%, no correlation between proximal migration and functional outcomes.
	5 weeks: physiotherapy was started (therapy content unknown)	Pain intensity (self designed), limitations in ADL (self designed) Adduction contracture (self designed: severe, moderate, slight, none), ROM, grip & pinch strength, satisfaction. Return to work, joint imaging (SMD) Measures at: T0 (preoperative), T1 (36 months, range 24-54 months)	At T1, 49% was 'pain free' and 51% had 'some pain' Of the patients with limitations in ADL preoperatively, 73% reported no limitations at T1. Adduction contracture 'diminished' in 57% of the patients, decrease was not significant Significant improvements in pinch strength, no significant difference in grip strength. At T1, 88% was satisfied. Average SMD at T1 was 4 mm.
	The splint/HP group: 4 weeks postoperatively: 1 consult, which included thumb spica or c-bar splint, and home program (included information regarding splint wear, methods to control edema, AROM exercises, and massage of the hand). The splint/HT group: 4 weeks postoperatively: receive a thumb spica or c-bar splint followed by outpatient occupational therapy 1 hour, one time a week for approximately 4 weeks. Therapy included: application of a thumb spica or c-bar splint, reduction of edema, instructions in range of motion and strength exercises, and ADL	Pain intensity (Boston Questionnaire), Limitations in ADL (JHFT, AHFT), Grip & pinch strength, Quality of life (AIMS 2) Measures at: T0 (pre-op) and T1 (6 months postoperatively).	Improvements in pain intensity in both groups, although no significant within group differences due to small sample size. No significant differences between groups, although a larger decrease in symptom severity was found in the hand therapy group (ES = 0.53) Higher improvements in limitations in ADL in the hand therapy group for both the JHFT (ES = 0.52) as the AHFT (ES = 0.33), although not significant due to sample size. Improvements in grip (+13%) & 3-point pinch strength (+27%) were only found in the hand therapy group, while grip (-8%) & 3-point pinch strength (-6%) decreased in the home program group (ES grip strength = 0.77, ES 3-point pinch = 0.95). Significant improvements in several subscales of the Arthritis Impact Measurement Scales 2 for both groups, no between group differences.

Table 1. Overview of the characteristics, measurements and outcomes of the included studies.

Author, year	Study design	Study population (N, F/M, age (mean, range/±SD), right/left, dominance)	Surgical intervention	Co-interventions	Postoperative rehabilitation - immobilization period
Prosser et al.[29] 2014	Randomized Controlled Trial investigating partial vs. complete immobilization	N=56 (3 lost to follow-up, Rigid: 28, Semi-rigid: 28). F/M = 45/11 (Rigid: 23/28, Semi-rigid: 22/28) Age = 67.8 ±8.0 (Rigid 66.9 ±8.5, Semi-rigid 69.6 ±7.8) Dominance = 27/56 (Rigid: 14/28, Semi-rigid: 13/28)	Trapeziectomy & LRTI using FCR (N= 53), or trapeziectomy alone (N=3, (rigid N=1, semi-rigid N=2))	Unknown/not described	Both groups: 0-2 weeks: dorsal plaster back slab immobilizing wrist and thumb. Thereafter: randomization. Semi-rigid group: 2-6 weeks: custom made neoprene with a bonded thermoplastic piece from IP 1 to distal 2/3 of the forearm, with thermoplastic piece on radial aspect of thumb extending from mid proximal phalanx to just below the wrist and was bonded to the neoprene with thumb in maximal comfortable PAB. Rigid-group: 2-6 weeks: thermoplastic custom-made wrist-thumb splint

	Postoperative rehabilitation - Exercises	Measurements (instruments, follow-up)	Outcomes
	Both rigid/semi-rigid: 0-2 weeks: composite extension/flexion advised by surgeon Week 2-3: thumb IP flexion/extension, wrist flexion/extension 4x day 10 reps Week 3-4: isolated AROM MCP flexion/extension to neutral only (0) out of orthosis. Emphasis placed on flexion. 4-6 weeks: TMC AROM PAB, no opposition. 6 weeks: Wean splint, passive exercises, graded strengthening grip and pinch, scar management. Light activity at 6 weeks upgraded to moderate to heavy activity at 12 weeks. 0-4 weeks: scheduled for weekly visits, 4-10 weeks: fortnightly	Pain intensity and limitations in ADL (PRWHE, MHQ), and pinch strength. Measures at: T0 (pre-operative), T1 (6 weeks), T2 (3 months) and T3 (1 year)	No significant differences in pain intensity and limitations in ADL. No significant differences in pinch strength Complications were observed in 14% of the participants in the rigid group compared to 7% in the semi-rigid group.

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Author, year	Study design	Study population (N, F/M, age (mean, range/±SD), right/left, dominance)	Surgical intervention	Co-interventions	Postoperative rehabilitation - immobilization period
Roberts et al.[30] 2001	Retrospective Cohort	N = 23, 25 thumbs F/M = unknown Age = median 60 (Q1 = 53, Q3 =65), Dominance = unknown	Trapeziectomy with LRTI using FCR (N =7) or partial trapeziectomy with LRTI using FCR (N=18)	Unknown/not described	0-10 days: bivalve radial plaster thumb spica splint, and ulnar plaster gutter splint. Wrist in approximately 15° DF, thumb midway abduction & extension, and thumb IP free. 10 days: new radial gutter splint was fabricated 3 weeks: splint discontinued
Rocchi et al.[31] 2011	Retrospective Cohort	N=50, 8 lost to follow-up F/M = 34/8 Age = 60 ±9, range 49 - 79) Dominance = 31/50	Trapeziectomy with LRTI using APL	Unknown/not described	Week 0-1: plaster splint with wrist encompassed, MC1 in slight abduction. Week 1-4: thermoplastic splint with thumb in incremented abduction and opposition. Week 4-6: Splinting only at night

	Postoperative rehabilitation - Exercises	Measurements (instruments, follow-up)	Outcomes
	3 weeks: AROM wrist and thumb 3-4 times a day scar management initiated, Swelling and pain modalities (i.e. paraffin, Coban, gloves). 6 weeks: strengthening exercises begun for patients "who complained of weakness with pinch and grip." exercises consisted of isometrics and active motion against resistance. Education in joint protection, modification of pinch, and the use of adaptive equipment was provided	Pain intensity (VAS 0-10), limitations in ADL (self designed: 15-item daily living checklist). Preoperative pain intensity and limitations in ADL were measured retrospectively, Grip & pinch strength. Measures at: T0 (pre-operative), T1 (postop, median 1 year and 11 months, range 3 months-11 years, Q1 1 year, Q3 3 years 4 months).	Hemi-trapezium resections: VAS median improvement: 7.0 cm (p=0.001, N=12) ADL median improvement: 33% (p=0.001, N=13). Grip & pinch strength median improvements between T0-T1: grip 10.2 kg (p=0.01, N=12), lateral pinch 2.3 kg (p=0.01, N=13), tripod pinch 2.6 kg (p=0.01, N=8), and tip-to-tip pinch 1.6 kg (p=0.03, N=7) Full-trapezium resections: VAS median improvement: 8.0 cm (p = 0.04, N=5) ADL median improvement: 60% (p=0.4, N=5) Grip & pinch strength median improvements between T0-T1: grip 13.4 kg (p = 0.07, N=4), lateral pinch 0.9 kg (p=0.29, N=4), tripod pinch -0.4 kg (p = 1.0, N=3), and tip-to-tip pinch -0.4 kg (p =1.0, N=3)
	0-4 weeks: IP1 movements prescribed. 4+ weeks: exercises to regain full ability; i.e. opposition exercises which gradually progressed from aiming at the tip of the fifth finger, then towards reaching its base. Only for 8/42 patients a rehabilitation program was deemed necessary and exercises of passive, active-assisted and active range-of-motion were started.	Pain intensity (VAS mentioned, but results expressed as no pain and restriction, mild pain with use and some restriction, pain at rest and some restriction and pain at rest and severe restriction), satisfaction (VAS), limitations in ADL (DASH), Grip & key pinch strength, joint imaging (SMD). Measures at: T0 (pre-operative), T1 (3 months), T2 (6 months) and T3 (12 months)	N=42, 8 lost to follow-up At T3, zero patients had any pain at rest, only 1 occasional mild pain. No significance mentioned. Satisfaction 9.6, time point unknown. DASH at T0: 43.3, T1: 25.5, T2: 19.1 T3: 14.5, no significance mentioned. Grip strength at T0: 16.0 kg, at T3: 19.2 kg, key pinch at T0: 3.7 kg and at T3: 5.6 kg, no significance mentioned. At T3, SMD averaged 6.4 mm

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Saehle et al.[32] 2002	Retrospective Cohort	N = 47, 55 thumbs F/M = 44/3 Age = 58 years, range: 44-73 years Dominance: unknown	Trapeziectomy with LRTI using APL	Unknown/not described	0-4/5 weeks: Plaster of Paris
Sirotakova et al.[42] 2007	Case series	N = 74, 104 thumbs F/M = 59/15 Age = 59 years range 40-82 years Dominance: unknown	Trapeziectomy with APL sling (around FCR/ ECRL)	CTR (n=19 hands in 15 (20%) patients)	0-2 weeks: plaster of Paris splint. 2-4 weeks: thermo-plastic splint. 4+ weeks: Most remove the splint and only wear it at night. Sometimes during day
Soejima et al.[33] 2006	Prospective cohort	N = 18, 21 thumbs F/M = 16/2 Age = 63 years range: 52-77 years Dominance: unknown	Trapeziectomy with LRTI using APL	Unknown/not described	0-2 weeks: short arm spica splint.
Varitimidis et al.[43] 2000	Retrospective Cohort	N = 58, 62 thumbs F/M = 48/10 Age = 58.4 years range: 28-80 years Dominance: 31/58	Trapeziectomy with LRTI using entire FCR, partial trapeziodectomy in 32 cases	MCP-1 arthrodesis (n=3), CTR (n=4), trigger finger release (n=3), IP-1 arthrodesis (n=2).	0-4 weeks: Radial thumb spica splint. 4 weeks: Removable splint is applied. 6 weeks: weaning from splint begins. 3 months: free from immobilization

	Postoperative rehabilitation - Exercises	Measurements (instruments, follow-up)	Outcomes
	Unknown	Pain intensity (VAS 0-100, only at T1), Limitations in ADL (self-designed at T0 and T1 & DASH, only at T1), ROM (only at T1), Grip & pinch strength (compared with other hand, only at T1), Cosmetics (VAS 0-100, only at T1), joint imaging (SMD) Measures at: T0 (preoperative), T1 (41 months, range 16-60 months)	Median VAS pain intensity at T1: 11 ADL function measured with self-designed questionnaire improved in 51% of the patients at T1 compared to T0. Median DASH scores for the disability/symptom and work scales were both 28. The distal phalanx of the 5th finger could be reached by 52 of the 55 operated hands Average key pinch and grip strengths of the operated hands were reduced with 11% and 22% respectively compared to unaffected side. Median VAS score for the cosmetic result at T1: 5. SMD decreased with 55% at T1 compared to T0, no correlation between proximal migration and clinical results.
	The patient is seen weekly by the therapists 0-2 weeks: IP-1 joint flexion and extension exercises, which are performed 5 times on 3 occasions each day 2-6 weeks: opposition exercises.	Pain intensity, stiffness, weakness of the hand, functional disability (self designed), ROM, grip & pinch strength, joint imaging (SMD) Measures at: T0 (preoperative), T1 (6 months), T2 (12 months)	'Excellent' results in terms of pain relief were achieved in 91% Improvements in all ROM measures at T2 (not statistically tested) Grip & pinch strength improved in all measures at T2 (not statistically tested), SMD decreased with 29% at T2
	2 weeks: range-of-motion and grip-strengthening exercises were initiated.	Pain intensity (self designed), ROM, and grip & pinch strength, joint imaging (SMD) Measures at: T0 (preoperative), T1 (33 months, range 12-71 months)	At T1, 61% had no pain, 24% had mild pain with strenuous activities and 14% had mild pain with light work ROM radial and palmar abduction increased with 14° (p=0.09) and 8° (p=0.07) degrees respectively Grip and the pinch strength increased with 2 kg (p=0.18) and from 1.3 kg (p=0.23), respectively SMD decreased with 15% (p<0.05)
	4 weeks: Physical therapy is started if significant stiffness exists. 3 months: more intense strengthening exercises are started if necessary. Physical therapy usually is continued until the end of the fourth month, when satisfactory pinch and grip strength have been achieved	Pain intensity (self designed), ROM, grip & pinch strength, joint imaging (SMD) Measures at: T0 (preoperative), T1 (42.5 months, range 21-86 months)	T1: 95% had no pain, compared to 0% at T0. Increase of pain in 0% of participants 8% improvement in palmar abduction and a 10% improvement in radial abduction at T1 compared to T0 Significant improvement in strength at T1 in all measurements. SMD decreased with 10%

Table 1. Overview of the characteristics, measurements and outcomes of the included studies.

Author, year	Study design	Study population (N, F/M, age (mean, range/±SD), right/left, dominance)	Surgical intervention	Co-interventions	Postoperative rehabilitation - immobilization period
Vermeulen et al.[19] 2009	Prospective cohort	N = 19, 20 thumbs F/M = 17/2 Age = 58 years range: 51-80 years Dominance: unknown	Trapeziecto-my with LRTI (Weilby) using FCR	None	0-4 weeks: spica cast. 4 weeks: removable protective orthosis
Vermeulen et al.[20] 2014	Randomized controlled trial investigating different surgical procedures	N = 72 (BP group: 36, Weilby group: 36) F/M = 72/0 Age = BP Group: 64.7 ± 9.1, Weilby group: 63.5 ± 8.5 years Dominance: 36/72 (BP group: 18/36, Weilby group: 18/36)	Trapeziectomy with LRTI using FCR (BP) vs. Trapeziectomy with Weilby sling	None	0-4 weeks: spica cast. 4 weeks: removable protective orthosis
Werthel et al.[34] 2016	Prospective cohort	N = 43, 49 thumbs, 4 were lost to follow-up. F/M = unknown Age = 67 years range 53-85 years Dominance: 18/39	Trapeziectomy with LRTI using FCR	Unknown/not described	0-5 weeks: thumb and wrist immobi-lized in a cast

	Postoperative rehabilitation - Exercises	Measurements (instruments, follow-up)	Outcomes
	4 weeks: physiotherapy was started by a hand therapist (therapy content unknown)	Limitations in ADL (DASH, Specific Personal Questionnaire), grip & pinch strength, ROM. Measures at: T0 (preoperative), T1 (0 months), T2 (3 months), T3 (6 months), T4 (12 months)	DASH score: at T0: 51, T2: 36, T3: 30.5, T4: 30 (p<.001) Significant improvements in inter metacarpal distance, Kapandji score Significant improvements in 3-point pinch strength, and overall grip strength at final follow-up.
	4 weeks: a hand therapist started standardized hand therapy focused on reducing edema and regaining functionality by increasing mobility, stability, and strength of the thumb	Pain intensity and limitations in ADL (PRWHE, DASH), ROM, Grip & pinch strength, complications, joint imaging (SMD) Measures at: T0 (preoperative), T1 (3 months), T2 (12 months)	Pain intensity (PRWHE) decreased significantly for both types of surgery at T2 (Weilby: -17 points vs. Burton-Pellegrini: -18 points (score range 0-50)). DASH: significant improvements for both types of surgery (Weilby: -16 points vs. Burton-Pellegrini: -20 points (score range 0-100)). No differences between different types of surgery, except in CMC-1 extension (decrease in Burton-Pellegrini group) Increase in grip strength for both types of surgery (Weilby: +3 kg vs. Burton-Pellegrini: +4 kg). Key pinch decreased 0.1 kg for both types of surgery, Tip-pinch increased 0.4 kg for both types of surgery and 3-point pinch increased for both types of surgery (Weilby: +0.3 kg vs. Burton-Pellegrini: +0.5 kg). Statistical testing for group differences was not reported In total, complications were observed in 27,8% of the participants (Weilby: 23,1% vs. Burton-Pellegrini: 32,5%, difference not significant). SMD at T2 during rest in Weilby group decreased with 33%, in Burton-Pellegrini group with 48%, during pinch in Weilby group: 66%, Burton-Pellegrini group: 57%
	Physiotherapy was not required on a systematic basis postoperatively	Pain intensity (VAS), limitations in ADL (DASH) grip & pinch strength, ROM. Measures at: T0 (preoperative), T1 (37 months, range 29–72 months)	VAS during rest at T0: 2.3, at T1: 0.3 (p<0.05), VAS during key pinch at T0: 5.4, at T1: 1.3 (p<0.05) Quick DASH at T0: 49.4, at T1: 22.1 (p<0.05) Significant improvements in all ROM measures, except MCP-1 hyperextension. Pinch strength at T0: 3.3, T1: 5.1 (p<0.05), no change in grip strength.

Table 1. Overview of the characteristics, measurements and outcomes of the included studies.

Author, year	Study design	Study population (N, F/M, age (mean, range/±SD), right/left, dominance)	Surgical intervention	Co-interventions	Postoperative rehabilitation - immobilization period
Wong et al.[18] 2009	Retrospective Cohort	N = 22 patients, 22 thumbs F/M = 16/6 Age = 50 years range: 43-75 years Dominance: 13/22	Trapeziectomy with LRTI using FCR & PL	None	0-6 weeks: thermoplastic removable thumb spica splint
Yang et al.[19,20,28,35,39-41,43] 2014	Retrospective Cohort	N = 19, 21 thumbs F/M = 18/1 Age = 60 years range 52-75 years Dominance: unknown	Trapeziectomy with modified LRTI using FCR	Unknown/not described	0-2 weeks: volar plaster splint. 2-6 weeks: thumb spica cast with which the thumb is placed in an abducted position. 6-12 weeks: patient wears brace intermittently
J. Yao et al.[17] 2014	Case study	N = 1, F/M= 1/0 Age = 63 Dominance: unknown	Trapeziectomy with tightrope suspension	None	0-10 days: plaster thumb spica orthosis. 10-18 days: custom fabrication spica orthosis. 18 days-10 weeks: butterfly splint if needed, discontinued after 10 weeks

Note: N = number of participants, F/M = Females/Males, LRTI = Ligament Reconstruction and Tendon Interposition, FCR = Flexor carpi radialis, CMC-1 = thumb base joint, IP-1 = thumb interphalangeal joint, MCP-1 = thumb metacarpophalangeal joint, ROM = range of motion, AROM = active range of motion, VAS = Visual Analogue Scale, DASH = Disabilities of the Arm, Shoulder and Hand, APL = Abductor pollicis longus, PL = Palmaris longus, HT = Hand therapy, HP = Home program, ADL = Activities of daily life, PAB = Palmar abduction, CTR = carpal tunnel release, Dominance = number of treatments of dominant side, BP = Burton-Pellegrini, SMD = distance between base of first metacarpal and distal end of scaphoid, TMD = distance between base of first metacarpal and radial border of trapezoid

	Postoperative rehabilitation - Exercises	Measurements (instruments, follow-up)	Outcomes
	6 weeks: Gentle thumb and wrist mobilization exercise and control of the swelling immediately after removal of the splint. 8 weeks: Active thumb and wrist joint mobilization exercise (i.e. putty exercise and sandbag). 12 weeks: Passive thumb and wrist joint mobilization exercise together with vigorous strengthening exercise such as Dexter training, Theraband exercise were started	Pain intensity (self designed), grip & pinch strength, ROM, joint imaging (SMD) Measures at: T0 (preoperative) T1 (2 weeks) T2 (4 weeks), T3 (8 weeks), T4 (12 weeks), T5 (24 weeks) and T6 (52 weeks), T7 (final follow-up: average 48 months, range 12-72 months)	At final follow-up, 82% was 'pain free' Kapandji score increased from 4 at T0 to 6 at T7 (p=0.04) When comparing T0 with T7, differences were found in grip strength (+4 kg, p=0.03), tip pinch (+0.7 kg, p=0.04) and key pinch (+1.0 kg, p=0.03), at T7 SMD space ratio decreased with 9% and SMD in mm decreased with 13%
	6 weeks: range of motion and strengthening exercises are started	Pain intensity (VAS 0-10) ROM, grip & pinch strength, joint imaging (SMD) Measures at: T0 (preoperative), further examined at 2 weeks, 6 weeks and 3 months after surgery, then every 3 months for the first year, and every 6 months thereafter. Final follow-up analyzed: T1 (13.9 months, range 9-28 months))	VAS pain at T0: 6.6, T1: 0.5 ($p<0.05$), Improvement in ROM at T1 compared to T0 ($p<0.05$) Grip strength at T0: 18.6, T1: 20.5 ($p>0.05$), Tip pinch strength at T0: 4.4, T1: 4.5 ($p>0.05$). At T1 SMD space ratio decreased with 56% and SMD in mm decreased with 55%
	10-18 days: AROM exercises (unspecified). 18 days - 2 months +18 days: edema control, scar massage, isometric exercises lateral pinch strength, guidance regarding ADL	Limitations in ADL (DASH). Measures at: T0 (pre-operative), T1 (11 months)	DASH at T0: 63, at T1: 10

Table 2. Types of surgical interventions performed in included studies

Surgical intervention	N	Reference(s)
Trapeziectomy with LRTI using the FCR	448	19-22,29,30,34-36,41,43
Trapeziectomy with LRTI using the APL	249	26,31-33,42
Trapeziectomy with LRTI using the FCR and PL	32	18,23
Trapeziectomy with LRTI using the FCR and Kirschner-wire fixation	125	24,27,37,40
Trapeziectomy with tendon interposition using the PL and Kirschner-wire fixation	59	37
Trapeziectomy with ligament reconstruction using the FCR	15	21
Partial trapeziectomy with LRTI using the FCR	18	30
Partial trapeziectomy with LRTI using the FCR and Kirschner-wire fixation	31	24,38
Partial trapeziectomy with LRTI using the PL and Kirschner-wire fixation	9	28
Trapeziectomy	43	25,29
Trapeziectomy with Kirschner-wire fixation	88	37,39
Trapeziectomy with tightrope suspension	1	17
Total	1118	

NOTE: No distinction was made between half or complete tendon use or the presence or absence of a bone tunnel in this classification.
Abbreviations: APL, abductor pollicis longus; FCR, flexor carpi radialis; LRTI, ligament reconstruction and tendon interposition; N, number of interventions per hand (multiple interventions were performed in several cases because of bilateral disease); PL, palmaris longus.

Results of individual studies and synthesis of results

Six comparative studies were included, of which three investigated the research questions of the present study (the other three studies compared different surgical procedures). Given the low amount of comparative studies on the research questions, no statistical pooling was performed. A summary of the rehabilitation protocols as used in the included studies (including total immobilization period, initiation of ROM and strengthening exercises) is displayed per surgical intervention (categorized by used tendon plasty) in Figure 2. Figure 2 shows that the most progressive postoperative rehabilitation (including short immobilization and early initiation of ROM and strength exercises) is used in the literature for simple trapeziectomy or for LRTI with either a slip, a strip of or the entire Abductor Pollicis Longus (APL) tendon.

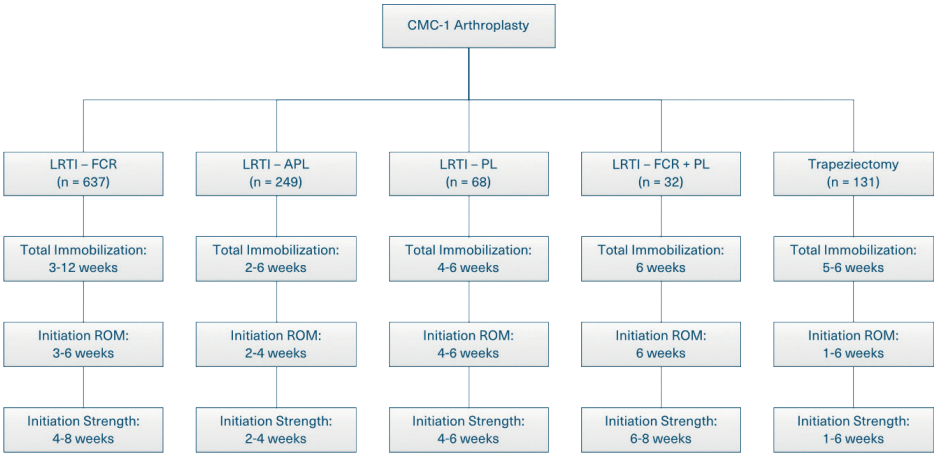


Figure 2. A summary of the rehabilitation protocols used in the included studies regarding total immobilization period and initiation of ROM and strengthening exercises is displayed per surgical intervention (categorized by the tendon used). The displayed time frames indicate the range (minimum to maximum period) of the used period in the literature. Abbreviations: APL, abductor pollicis longus; FCR, flexor carpi radialis; LRTI, ligament reconstruction and tendon interposition; PL, palmaris longus.

Postoperative immobilization

An overview of the immobilization periods and methods per study, sorted by year of publication in Table 3, shows that the total immobilization varied substantially, from 2 to 12 weeks. In most studies, emphasis was placed on immobilization in palmar abduction and extension of the CMC-1. Type of immobilization consisted of plaster cast immobilization only[18,23,26,32-34,37,38], plaster cast immobilization

followed by a removable splint which is gradually reduced[17,24,29,31,35,36,39,40,42,43] or completely discontinued at a certain moment.[21,22,25,27,30] Splint usage gradually reduced over time consisted of only night usage[31,36,42], the use of a butterfly splint if needed[17] or the splint is stopped when full ROM is attained and thenar strength is improved to a functional level.[24] The discontinuation criterion was not described clearly in eight studies.[19,20,28,35,39-41,43]

Table 3. Overview of the immobilization period per week for individual studies

YEAR	AUTHOR	N	TYPE SURGERY / TENDON PLASTY	WEEK 1	2	3	4	5	6	7	8	9	10	11	12	13	14
1985	Eaton et al.[38]	25	***FCR***														
1986	Burton et al.[24]	25	***FCR***														
1993	Nylen et al.[41]	102	***FCR***														
1996	Lins et al.[40]	30	***FCR***														
2000	Varitimidis et al.[43]	62	***FCR***														
2001	Roberts et al.[30]	25	***FCR***														
2002	Saehle et al.[32]	55	***APL***														
2002	Horlock et al.[25]	40															
	Late group	20	***Simple Trapeziectomy***														
	Early group	20	***Simple Trapeziectomy***														
2003	Kuhns et al.[39]	26	***Simple Trapeziectomy***														
2004	Mo et al.[27]	14	***FCR***														
2004	Kriegs-Au et al.[21]	52	***FCR***														
2004	Davis et al.[37]	62	***FCR***														
		59	***PL***														

Table 3. Continued

YEAR	AUTHOR	N	TYPE SURGERY / TENDON PLASTY	WEEK
		62	***Simple Trapeziectomy***	
2006	Soejima et al.[33]	21	***APL***	
2007	Sirotakova et al.[42]	104	***APL***	
2009	Vermeulen et al.[19]	20	***FCR***	
2009	Wong et al.[18]	22	***FCR + PL***	
2011	Rocchi et al.[31]	50	***APL***	
2011	Poole et al.[28]	9		
	Home program group	*5*	***PL***	
	Occupational therapy group	*4*	***PL***	
2012	Ataker et al.[36]	27	***FCR***	
2012	Başar et al.[22]	19	***FCR***	
2012	Abbas et al. [23]	10	***FCR + PL***	
2014	Prosser et al.[29]	53		
	Rigid group	*27*	***FCR***	
	*Semi-rigid group**	*26*	***FCR***	

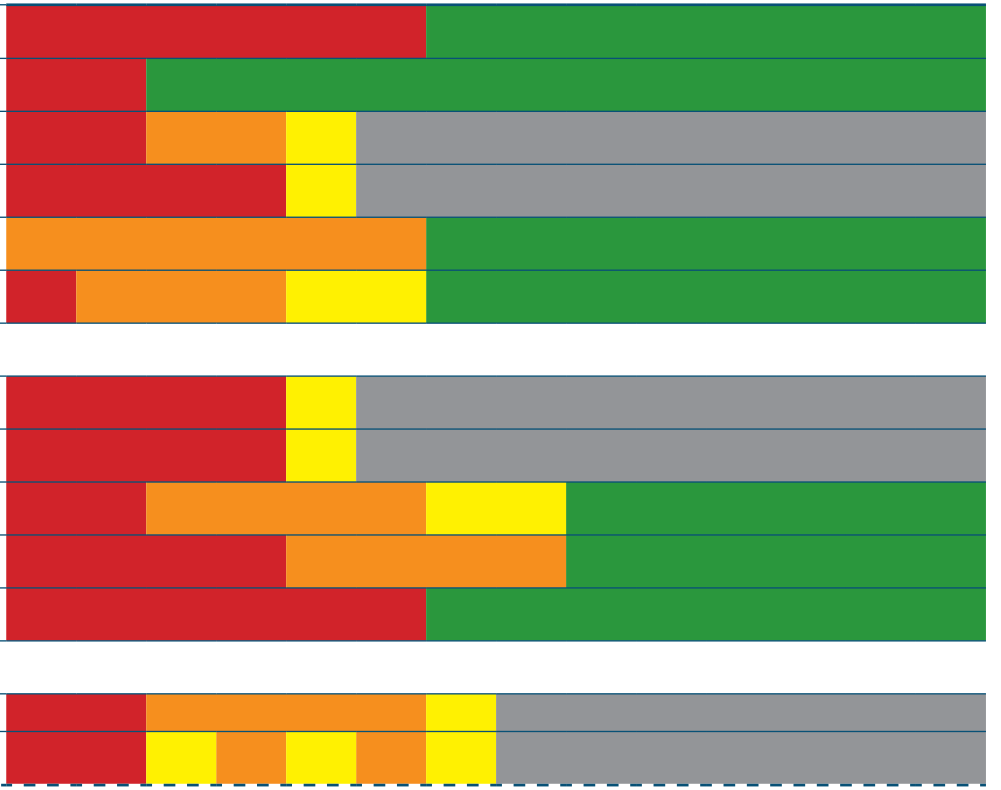
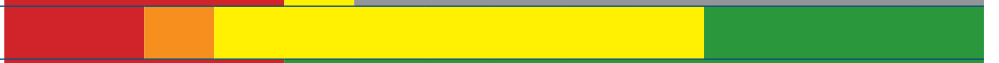


Table 3. Continued

YEAR	AUTHOR	N	TYPE SURGERY / TENDON PLASTY	WEEK
	Rigid group	*1*	***Simple Trapeziectomy***	
	*Semi-rigid group**	*2*	***Simple Trapeziectomy***	
2014	Yang et al.[35]	21	***FCR***	
2014	Vermeulen et al.[20]	72	***FCR***	
2014	Yao et al.[17]	1	***Tightrope***	
2015	Lee et al.[26]	19	***APL***	
2016	Werthel et al.[34]	49	***FCR***	

Note for Table 3: In case studies in which an orthosis was intermittently used from a certain moment but no endpoint of orthosis usage was described, the first week was considered as gradually reduced orthosis usage, and the rest is considered unknown.
Abbreviations: APL, abductor pollicis longus; FCR, flexor carpi radialis; PL, palmaris longus.
* After 2 weeks, the semirigid group in this study wore an orthosis 24h/d that partly immobilized the wrist, instead of complete immobilization (the rigid group). To demonstrate this difference, it is displayed as "orthosis gradually reduced."

Legend Table 3:
Cast immobilization 24h/day =
Splint immobilization 24h/day =
Splint gradually reduced =
Immobilization completely discontinued =
Immobilization content unknown =

Two comparative studies[25,29] on postoperative immobilization were found (Table 4). In these studies, partial immobilization until 6 weeks was compared with complete immobilization until 6 weeks. The authors did not find more complications or worse outcomes at six to twelve months postoperatively when partial immobilization was used; on the contrary, the same or better outcomes were found in the groups that used partial immobilization compared to complete immobilization. Insufficient data was provided by Prosser et al[29] to calculate effect sizes. In the study by Horlock et al. effect sizes on pain intensity, satisfaction, ROM and grip & pinch strength range from -0.66 to 0.66, where positive values indicate superior results for partial immobilization (Table 4).

Table 4 also provides the outcomes for studies using a total immobilization period 4-6 weeks or ≤4 weeks respectively. Fourteen studies[18-21,23,25,28,29,31,34,37,39,41,42] used a total immobilization period of 4-6 weeks and five studies[26,30,32,33,38] used a total immobilization period ≤4 weeks. We found similar complications and outcomes in studies using a total immobilization period of 4-6 or ≤4 weeks compared to studies that used an immobilization period ≥6 weeks.

Table 4. Overview of studies comparing different types of immobilization and of studies using a total immobilization period of 4-6 weeks or ≤4 weeks. Immobilization methods and outcomes per study are displayed.

Studies comparing immobilization	Immobilization methods	Measures at	Measurements & instruments
Horlock et al.[25] 2002	Late vs. early mobilization: Cast immobilization for two weeks followed by thermoplastic splint 24h/day until six weeks vs. cast immobilization for one week followed by thermoplastic splint only during physical load until six weeks.	T0 (preoperative) T1 (6-8 months)	1) Pain intensity, Hand function, Opinion about rehabilitation regimen, Satisfaction with operation (VAS 0-100) 2) ROM 3) Grip & pinch strength. 4) Complications 5) Joint imaging (SMD & TMD)
Prosser et al.[29] 2014	Rigid vs. semi-rigid immobilization: Thermoplastic splint until 6 weeks with full immobilization of the thumb and wrist vs. combined thermoplastic and neoprene splint until 6 weeks allowing thumb and wrist motion	T0 (preoperative) T1 (6 weeks) T2 (3 months) T3 (1 year)	1) Pain intensity and limitations in ADL (PRWHE, MHQ) 2) Pinch strength 3) Complications
Abbas et al.[23] 2012	Only plaster cast immobilization	T0 (preoperative) T1 (3 months) T2 (6 months)	1) Limitations in ADL (Quick DASH)
Davis et al.[37] 2004	Only plaster cast immobilization	T0 (preoperative) T1 (3 months) T2 (12 months)	1) Pain intensity, stiffness, weakness and restriction of ADL (measured at once in categorical scores, self-designed) 2) ROM 3) Grip & pinch strength
Horlock et al.[25] 2002	Late vs. early mobilization: Cast immobilization for two weeks followed by thermoplastic splint 24h/day until six weeks vs. cast immobilization for one week followed by thermoplastic splint only during physical load until six weeks.	T0 (preoperative) T1 (6-8 months)	1) Pain intensity, Hand function, Opinion about rehabilitation regimen, Satisfaction with operation (VAS 0-100) 2) ROM 3) Grip & pinch strength. 4) Complications 5) Joint imaging (SMD & TMD)

	Outcomes
	1) No significant difference in pain intensity decrease, although ES = -0.66 due to preoperative group differences, but VAS score at T1: Late group = 30, Early group = 28. The early group experienced more convenience compared to the late group (ES = 0.66, p<0.05). 2) Significant decrease in MCP-1 ROM was found in the late mobilization group but not in de early group (ES = 0.19, within group p<0.02). 3) No significant difference in grip & pinch strength, although the early group performed slightly better when pooling effect sizes of grip, pulp pinch and key pinch strength (ES = 0.05). 4) Complications were observed in 15% of the participants in the early group compared to 5% in the late group. 5) No differences between groups in median SDM, 2 mm larger decrease in TM within the early group, but not significant
	1) No significant differences in pain intensity and limitations in ADL. Insufficient data was provided to calculate ES. 2) No significant differences in pinch strength. Insufficient data was provided to calculate ES. 3) Complications were observed in 14% of the participants in the rigid group compared to 7% in the semi-rigid group.
	1) Quick DASH Score at T0: 58.8, T1: 40.5, T2: 31.3 (p=0.005)
	1) Pain intensity, stiffness, weakness and restriction of ADL improved 'markedly' at T1 and further at T2 (no significance described). There was no significant difference between the different types of surgery 2) ROM improved at T2 compared to T0 (no significance mentioned), there was no significant difference between different types of surgery. 3) Thumb key- and tip-pinch and grip strength in the whole study group at T1 were not different from T0. However, thumb key- and tip- pinch and grip strength in the whole group at the T2 were all significantly stronger compared to T0 (p<0.001 for all 3 types of surgery)
	1) No significant difference in pain intensity decrease, although ES = -0.66 due to preoperative group differences, but VAS score at T1: Late group = 30, Early group = 28. The early group experienced more convenience compared to the late group (ES = 0.66, p<0.05). 2) Significant decrease in MCP-1 ROM was found in the late mobilization group but not in de early group (ES = 0.19, within group p<0.02). 3) No significant difference in grip & pinch strength, although the early group performed slightly better when pooling effect sizes of grip, pulp pinch and key pinch strength (ES = 0.05). 4) Complications were observed in 15% of the participants in the early group compared to 5% in the late group. 5) No differences between groups in median SDM, 2 mm larger decrease in TM within the early group, but not significant

Table 4. Overview of studies comparing different types of immobilization and of studies using a total immobilizat

Studies with a total immobilization period 4-6 weeks	Immobilization methods	Measures at	Measurements & instruments
Kriegs-Au et al.[21] 2004	Plaster cast immobilization + removable splint	T0 (preoperative), T1 (48.2 months, range 32-64 months)	1) ROM 2) Grip & pinch strength 3) Buck-Gramcko score 4) Self-designed questionnaires: pain, strength, daily function, dexterity, cosmetic appearance, willingness to undergo surgery again, overall satisfaction with result, current and past employment status and activity levels. 5) Joint imaging (SMD)
Kuhns et al.[39] 2003	Plaster cast immobilization + removable splint gradually reduced	T0 (preoperative), T1 (6 months), T2 (24 months)	1) Pain relief (measurement instrument unclear) 2) Limitations in ADL (Jebsen subtests II and III dexterity tests, AIMS2) 3) ROM (descriptive only) 4) Grip & pinch strength. 5) Joint imaging
Nylen et al.[41] 1993	Plaster cast immobilization + removable splint	T0 (preoperative), T1 (36 months, range 24-54 months)	1) Pain intensity (self designed) 2) Limitations in ADL (self designed) 3) ROM: Adduction contracture (self designed: severe, moderate, slight, none) 4) Grip & pinch strength 5) Satisfaction, return to work (self-designed) 6) Joint imaging (SMD)
Poole et al.[28] 2011	Both groups: Plaster cast immobilization + removable splint	T0 (pre-op) and T1 (6 months postoperatively).	1) Pain intensity (Boston Questionnaire) 2) Limitations in ADL, (JHFT, AHFT) 3) Grip & pinch strength 4) Quality of life (AIMS 2)

tion period of 4-6 weeks or ≤4 weeks. Immobilization methods and outcomes per study are displayed.

	Outcomes
	All outcomes: Significant improvements, although no differences for different types of surgery mentioned. Proximal migration of the first metacarpal was 37-42%.
	1) At final follow-up, 92% was pain free. 2) Significant improvements in 3 subscales of the AIMS 2 3) At T1, 92% adducted fully into the plane of the palm and 96% opposed to the fifth metacarpal head 4) Significant improvements in grip (+47%), key pinch (+33%), and tip pinch (+23%) strength at T2 5) SMD decreased with 51% at T1 compared to T0, no correlation between proximal migration and functional outcomes.
	1) At T1, 49% was 'pain free' and 51% had 'some pain' 2) Of the patients with limitations in ADL preoperatively, 73% reported no limitations at T1. 3) Adduction contracture 'diminished' in 57% of the patients, decrease was not significant 4) Significant improvements in pinch strength, no significant difference in grip strength. 5) At T1, 88% was satisfied 6) Average SMD at T1 was 4 mm
	1) Improvements in pain intensity in both groups, although no significant within group differences due to small sample size. No significant differences between groups, although a larger decrease in symptom severity was found in the hand therapy group. 2) Higher improvements in limitations in ADL in the hand therapy group for both the JHFT as the AHFT, although not significant due to sample size. 3) Improvements in grip (+13%) & 3-point pinch strength (+27%) were only found in the hand therapy group, while grip (-8%) & 3-point pinch strength (-6%) decreased in the home program group 4) Significant improvements in several subscales of the Arthritis Impact Measurement Scales 2 for both groups, no between group differences.

Table 4. Overview of studies comparing different types of immobilization and of studies using a total immobilizat

Studies with a total immobilization period 4-6 weeks	Immobilization methods	Measures at	Measurements & instruments
Prosser et al.[29] 2014	Rigid vs. semi-rigid immobilization: Thermoplastic splint until 6 weeks with full immobilization of the thumb and wrist vs. combined thermoplastic and neoprene splint until 6 weeks allowing thumb and wrist motion	T0 (preoperative) T1 (6 weeks) T2 (3 months) T3 (1 year)	1) Pain intensity and limitations in ADL (PRWHE, MHQ) 2) Pinch strength 3) Complications
Rocchi et al.[31] 2011	Plaster cast immobilization + removable splint gradually reduced	T0 (preoperative) T1 (3 months) T2 (6 months) T3 (12 months)	1) Pain intensity (VAS mentioned, but results expressed as no pain and restriction, mild pain with use and some restriction, pain at rest and some restriction and pain at rest and severe restriction) 2) Satisfaction (VAS) 3) Limitations in ADL (DASH) 4) Grip & key pinch strength. 5) Joint imaging (SMD)
Sirotakova et al.[42] 2007	Plaster cast immobilization + removable splint gradually reduced	T0 (preoperative), T1 (6 months) T2 (12 months)	1) Pain intensity, stiffness, weakness of the hand, functional disability (self designed) 2) ROM 3) Grip & pinch strength 4) Joint imaging (SMD)
Vermeulen et al.[19] 2009	Plaster cast immobilization + removable splint	T0 (preoperative) T1 (0 months) T2 (3 months) T3 (6 months) T4 (12 months)	1) Limitations in ADL (DASH, Specific Personal Questionnaire) 2) ROM 3) Grip & pinch strength

tion period of 4-6 weeks or ≤4 weeks. Immobilization methods and outcomes per study are displayed.

	Outcomes
	1) No significant differences in pain intensity and limitations in ADL. Insufficient data was provided to calculate ES. 2) No significant differences in pinch strength. Insufficient data was provided to calculate ES. 3) Complications were observed in 14% of the participants in the rigid group compared to 7% in the semi-rigid group.
	1) At T3, zero patients had any pain at rest, only 1 occasional mild pain. No significance mentioned. 2) Satisfaction 9.6, time point unknown. 3) DASH at T0: 43.3, T1: 25.5, T2: 19.1 T3: 14.5, no significance mentioned. 4) Grip strength at T0: 16.0 kg, at T3: 19.2 kg, key pinch at T0: 3.7 kg and at T3: 5.6 kg, no significance mentioned. 5) At T3, SMD averaged 6.4 mm
	1) 'Excellent' results in terms of pain relief were achieved in 91% 2) Improvements in all ROM measures at T2 (not statistically tested) 3) Grip & pinch strength improved in all measures at T2 (not statistically tested) 4) SMD decreased with 29% at T2
	1) DASH score: at T0: 51, T2: 36, T3: 30.5, T4: 30 (p<.001) 2) Significant improvements in inter metacarpal distance, Kapandji score 3) Significant improvements in 3-point pinch strength, and overall grip strength at final follow-up.

Table 4. Overview of studies comparing different types of immobilization and of studies using a total immobilizat

Studies with a total immobilization period 4-6 weeks	**Immobilization methods**	**Measures at**	**Measurements & instruments**
Vermeulen et al.[20] 2014	Plaster cast immobilization + removable splint	T0 (preoperative) T1 (3 months) T2 (12 months)	1) Pain intensity and limitations in ADL (PRWHE, DASH) 2) ROM 3) Grip & pinch strength 4) Complications 5) Joint imaging (SMD)
Werthel et al.[34] 2016	Only plaster cast immobilization	T0 (preoperative) T1 (37 months, range: 29–72 months)	1) Pain intensity (VAS) 2) Limitations in ADL (DASH) 3) ROM 4) Grip & pinch strength
Wong et al.[18] 2009	Only plaster cast immobilization	T0 (preoperative) T1 (2 weeks) T2 (4 weeks) T3 (8 weeks) T4 (12 weeks) T5 (24 weeks) T6 (52 weeks) T7 (48 months, range 12-72 months)	1) Pain intensity (self designed) 2) ROM 3) Grip & pinch strength 4) Joint imaging (SMD)
Studies with a total immobilization period ≤4 weeks	**Immobilization methods**	**Measures at**	**Measurements & instruments**
Eaton et al.[38] 1985	Only plaster cast immobilization	T0 (preoperative) T1 (37,5 months, range 14-60 months)	1) Pinch strength 2) Clinical results were graded as excellent, good, fair or failure

tion period of 4-6 weeks or ≤4 weeks. Immobilization methods and outcomes per study are displayed.

	Outcomes
	1) Pain intensity (PRWHE) decreased significantly for both types of surgery at T2 (Weilby: -17 points vs. Burton-Pellegrini: -18 points (score range 0-50)). DASH: significant improvements for both types of surgery (Weilby: -16 points vs. Burton-Pellegrini: -20 points (score range 0-100)). 2) No differences between different types of surgery, except in CMC-1 extension (decrease in Burton-Pellegrini group) 3) Increase in grip strength for both types of surgery (Weilby: +3 kg vs. Burton-Pellegrini: +4 kg). Key pinch decreased 0.1 kg for both types of surgery, Tip-pinch increased 0.4 kg for both types of surgery and 3-point pinch increased for both types of surgery (Weilby: +0.3 kg vs. Burton-Pellegrini: +0.5 kg). Statistical testing for group differences was not reported 4) In total, complications were observed in 27,8% of the participants (Weilby: 23,1% vs. Burton-Pellegrini: 32,5%, difference not significant) 5) SMD at T2 during rest in Weilby group decreased with 33%, in Burton-Pellegrini group with 48%, during pinch in Weilby group: 66%, Burton-Pellegrini group: 57%
	1) VAS during rest at T0: 2.3, at T1: 0.3 ($p<0.05$), VAS during key pinch at T0: 5.4, at T1: 1.3 ($p<0.05$) 2) Quick DASH at T0: 49.4, at T1: 22.1 ($p<0.05$) 3) Significant improvements in all ROM measures, except MCP-1 hyperextension. 4) Pinch strength at T0: 3.3, T1: 5.1 ($p<0.05$), no change in grip strength.
	1) At final follow-up, 82% was 'pain free' 2) Kapandji score increased from 4 at T0 to 6 at T7 ($p=0.04$) 3) When comparing T0 with T7, differences were found in grip strength (+4 kg, $p=0.03$), tip pinch (+0.7 kg, $p=0.04$) and key pinch (+1.0 kg, $p=0.03$) 4) At T7 SMD space ratio decreased with 9% and SMD in mm decreased with 13%

	Outcomes
	1) Pinch strength at T0: 5.5 kg, T1: 6.1 kg (no significance reported) 2) All patients had 'relief of pain' at T1. 55% reported no pain whatsoever, and 44% described 'an occasional twinge or rare mild ache'. No patient had postoperative pain, even those whose clinical results were graded as fair. According to the grading system, 41.7% of the cases were graded as excellent, 50% were good, and 8.3% were fair

Table 4. Overview of studies comparing different types of immobilization and of studies using a total immobilizat

Studies with a total immobilization period ≤4 weeks	Immobilization methods	Measures at	Measurements & instruments
Lee et al.[26] 2015	Only plaster cast immobilization	T0 (preoperative) T1 (36 months, range 19 to 73.7 months)	1) Pain intensity (VAS) 2) Limitations in ADL (DASH) 3) ROM 4) Grip & pinch strength 5) Patient satisfaction (self designed) 6) Returning to work (self designed) 7) Joint imaging
Roberts et al.[30] 2001	Plaster cast immobilization + removable splint	T0 (preoperative) T1 (median 1 year and 11 months, range 3 months-11 years, Q1 1 year, Q3 3 years 4 months)	1) Pain intensity (VAS 0-10), measured retrospectively 2) Limitations in ADL (self designed: 15-item daily living checklist), measured retrospectively 3) Grip & pinch strength
Saehle et al.[32] 2002	Only plaster cast immobilization	T0 (preoperative) T1 (41 months, range 16-60 months)	1) Pain intensity (VAS 0-100, only at T1) 2) Limitations in ADL (self-designed at T0 and T1 & DASH, only at T1) 3) ROM (only at T1) 4) Grip & pinch strength (compared with other hand, only at T1) 5) Cosmetics (VAS 0-100, only at T1) 6) Joint imaging (SMD)
Soejima et al.[33] 2006	Only plaster cast immobilization	T0 (preoperative) T1 (33 months, range 12-71 months)	1) Pain intensity (self designed) 2) ROM 3) Grip & pinch strength 4) Joint imaging (SMD)

Note: VAS = Visual Analogue Scale, ROM = Range of Motion, ES = Effect Size (positive scores indicate better performance of experimental treatment compared to control treatment), MCP-1 = First Metacarpophalangeal joint, ADL = Activities of Daily Life, PRWHE = Patiënt Rated Wrist & Hand Evaluation, MHQ = Michigan Hand outcomes Questionnaire, DASH = Disabilities of Arm, Shoulder and Hand, AIMS2 = Arthritis Impact Measurement Scales 2, JHFT = Jebsen Hand Function Test, AHFT = Arthritis Hand Function Test, SMD = distance between base of first metacarpal and distal end of scaphoid, TMD = distance between base of first metacarpal and radial border of trapezoid

tion period of 4-6 weeks or ≤4 weeks. Immobilization methods and outcomes per study are displayed.

	Outcomes
	1) VAS at T0: 7.2, T1: 1.7 (p<0.05) 2) DASH at T0: 41, T1: 18, (p<0.05) 3) Significant improvements in al ROM measurements at T1 4) Increase of 1.1 kg in power pinch (p<0.05) at T1, no difference in tip pinch and grip strength at T1. 5) "All patients expressed their satisfaction for improved postoperative appearance of the hand." 6) Of the working participants, 77% returned to their work or activities without any difficulty or occupation modification, in 23% modifications were required 7) SMD decreased 34.3% (p<0.05)
	1) VAS scores decreased with 8 points (p=0.04) 2) Limitations in ADL showed 60% improvement (p=0.4) 3) Significant improvements in grip & pinch strength in group with hemi-resections, except in groups with full-trapezium resections
	1) Median VAS pain intensity at T1: 11 2) ADL function measured with self-designed questionnaire improved in 51% of the patients at T1 compared to T0. Median DASH scores for the disability/symptom and work scales were both 28. 3) The distal phalanx of the 5th finger could be reached by 52 of the 55 operated hands 4) Average key pinch and grip strengths of the operated hands were reduced with 11% and 22% respectively compared to unaffected side. 5) Median VAS score for the cosmetic result at T1: 5 6) SMD decreased with 55% at T1 compared to T0, no correlation between proximal migration and clinical results.
	1) At T1, 61% had no pain, 24% had mild pain with strenuous activities and 14% had mild pain with light work 2) ROM radial and palmar abduction increased with 14° (p=0.09) and 8° (p=0.07) degrees respectively 3) Grip and the pinch strength increased with 2 kg (p=0.18) and from 1.3 kg (p=0.23), respectively 4) SMD decreased with 15% (p<0.05)

Postoperative exercises/therapy

Large variations were observed in postoperative exercises/therapy regimens of the included studies. One comparative study[28] investigated the added value of hand therapy compared to a home program only in postoperative rehabilitation. No significant differences were found between the groups due to a small sample size, although higher improvements were found for pain intensity, limitations in ADL and grip & pinch six months postoperatively in the group that received hand therapy (Table 5). Effect sizes on pain intensity, limitations in ADL, grip & pinch strength and quality of life range from 0.33 to 0.95, indicating superior treatment effects of hand therapy compared to a home program only.

Five studies[19,26,32,34,41] did not describe the content of postoperative exercises/therapy. When the other 23 studies are summarized, three phases can be identified on postoperative exercises/therapy: (1) the 'acute postoperative phase' (range: zero to six weeks postoperatively); (2) the 'unloaded phase' (range: one to twelve weeks postoperatively) and (3) the 'functional phase' (range: three weeks to six months postoperatively).

Table 5. Overview of studies investigating benefits of postoperative exercises/therapy and of studies initiating thumb range of motion or strengthening exercises ≤4 weeks. Exercises of other joints (i.e. fingers, wrist) are not described.

Studies on benefits of postoperative exercises/therapy	Methods	Measures at	Measurements & instruments
Poole et al.[28] 2011	Home program group: 4 weeks: 1 consult initiating ROM exercises Hand therapy group: ROM exercises, one therapy session every week	T0 (pre-op) and T1 (6 months postoperatively).	5) Pain intensity (Boston Questionnaire) 6) Limitations in ADL, (JHFT, AHFT) 7) Grip & pinch strength 8) Quality of life (AIMS 2)
Ataker et al.[36] 2012	4 weeks: AROM exercises for CMC1 and MCP1 supervised by a PT, no CMC flexion/adduction, opposition	T0 (preoperative) T1 (12 weeks) T2 (31.5 months, range: 12-57 months)	1) Pain intensity (VAS) 2) Limitations in ADL (DASH) 3) ROM 4) Grip & pinch strength 5) Joint imaging (SMD)
Burton et al.[24] 1986	4 weeks: 1) Active abduction and extension while avoiding flexion and adduction, 2) AROM flexion of the MCP and IP joints with MC1 supported in abduction by the patient's opposite hand	T0 (preoperative) T1 (2 years, range 1-4.5 years).	1) Pain relief (self designed, only measured at T1) 2) Grip & pinch strength 3) Joint imaging
Eaton et al.[38] 1985	4 weeks: extension and circumduction of the CMC-1 joint is emphasized	T0 (preoperative) T1 (37,5 months, range 14-60 months)	1) Pinch strength 2) Clinical results were graded as excellent, good, fair or failure
Horlock et al.[25] 2002	Early group, 1 week: Light use of the hand allowed and active exercises for the thumb Late group, 2 weeks: Gentle use and mobilization were allowed out of the splint	T0 (preoperative) T1 (6-8 months)	6) Pain intensity, Hand function, Opinion about rehabilitation regimen, Satisfaction with operation (VAS 0-100) 7) ROM 8) Grip & pinch strength. 9) Complications 10) Joint imaging (SMD & TMD)

	Outcomes
	5) Improvements in pain intensity in both groups, although no significant within group differences due to small sample size. No significant differences between groups, although a larger decrease in symptom severity was found in the hand therapy group (ES = 0.53) 6) Higher improvements in limitations in ADL in the hand therapy group for both the JHFT (ES = 0.52) as the AHFT (ES = 0.33), although not significant due to sample size. 7) Improvements in grip (+13%) & 3-point pinch strength (+27%) were only found in the hand therapy group, while grip (-8%) & 3-point pinch strength (-6%) decreased in the home program group (ES grip strength = 0.77, ES 3-point pinch = 0.95). 8) Significant improvements in several subscales of the Arthritis Impact Measurement Scales 2 for both groups, no between group differences.
	1) VAS at T0: 8, T1: 3, T2: 3 ($p<0.001$). 2) DASH at T0: 56, T1: 29, T2: 24 ($p<0.001$). 3) Increase in palmar and radial abduction, Kapandji score ($p<0.001$). 4) Grip strength (kg) at T0: 12, T1: 18 ($p<0.001$), T2: 13, Lateral pinch at T0: 3, T1: 5, T2: 4 ($p<0.001$). 5) Joint imaging at T0: 11 mm, T1: 5 mm, T2: 3 mm
	1) Pain relief: 92% of patients enjoyed excellent pain relief and were satisfied with the thumb 2) T1 showed an overall improvement in grip and pinch strength of 19% compared with T0 values (no significance mentioned). 3) Average loss of 11% of the initial postoperative arthroplasty space
	3) Pinch strength at T0: 5.5 kg, T1: 6.1 kg (no significance reported) 4) All patients had 'relief of pain' at T1. 55% reported no pain whatsoever, and 44% described 'an occasional twinge or rare mild ache'. No patient had postoperative pain, even those whose clinical results were graded as fair. According to the grading system, 41.7% of the cases were graded as excellent, 50% were good, and 8.3% were fair
	6) No significant difference in pain intensity decrease, although ES = -0.66 due to preoperative group differences, but VAS score at T1: Late group = 30, Early group = 28. The early group experienced more convenience compared to the late group (ES = 0.66, $p<0.05$). 7) Significant decrease in MCP-1 ROM was found in the late mobilization group but not in de early group (ES = 0.19, within group $p<0.02$). 8) No significant difference in grip & pinch strength, although the early group performed slightly better when pooling effect sizes of grip, pulp pinch and key pinch strength (ES = 0.05). 9) Complications were observed in 15% of the participants in the early group compared to 5% in the late group. 10) No differences between groups in median SDM, 2 mm larger decrease in TM within the early group, but not significant

Table 5. Continued

Studies initiating CMC-1 ROM ≤4 weeks	Description of ROM exercises initiated ≤4 weeks	Measures at	Measurements & instruments
Lins et al.[40] 1996	4 weeks: gentle ROM exercises	T0 (preoperative) T1 (42-43 months, range 14-88 months)	1) Pain intensity (self designed) 2) Functional status / satisfaction (self designed) 3) ROM (web space) 4) Grip & pinch strength 5) Joint imaging (SMD)
Mo et al.[27] 2004	4 weeks: exercises with emphasis on extension/abduction, on maintaining MCP-1 joint flexion and avoiding hyperextension	T0 (preoperative) T1 (20 months, range 12-44 months	1) Limitations in ADL (DASH) 2) ROM 3) Grip & pinch strength 4) Joint imaging (SMD)
Poole et al.[28] 2011	Home program group, 4 weeks: 1 consult initiating ROM exercises Hand therapy group: ROM exercises, one therapy session every week	T0 (pre-op) and T1 (6 months postoperatively).	1) Pain intensity (Boston Questionnaire) 2) Limitations in ADL (JHFT, AHFT) 3) Grip & pinch strength 4) Quality of life (AIMS 2)
Prosser et al.[29] 2014	Rigid vs. Semi-rigid immobilization. Both groups at 4 weeks: abduction exercises	T0 (preoperative) T1 (6 weeks) T2 (3 months) T3 (1 year)	4) Pain intensity and limitations in ADL (PRWHE, MHQ) 5) Pinch strength 6) Complications
Roberts et al.[30] 2001	3 weeks: thumb ROM exercises	T0 (preoperative) T1 (median 1 year and 11 months, range 3 months-11 years, Q1 1 year, Q3 3 years 4 months)	1) Pain intensity (VAS 0-10), measured retrospectively 2) Limitations in ADL (self designed: 15-item daily living checklist), measured retrospectively 3) Grip & pinch strength

	Outcomes
	1) At T1, 85% patients considered the frequency of pain 'improved a lot or resolved completely' compared to T0 and 89% considered the duration and severity as 'improved a lot or completely' at T1, compared to T0. 2) At T1, 89% of the patients were satisfied with the 'relief of pain' 3) Web space increased with 1.09 cm ($p<0.02$) 4) Grip strength increased with 5.9 kg ($p<0.001$) and pinch strength increased with 1.4 kg ($p<0.01$) 5) SMD decreased with 30% ($p>0.05$)
	1) DASH outcomes associated with strength, no results over time reported 2) The distance from thumb tip to the base of the small finger during maximum flexion decreased with 0.4 cm ($p=0.02$) 3) Grip strength improved with 26% at T1 compared to T0 ($p=0.01$), pinch strength improved 11% ($p=0.11$). 4) SMD improved with 2.5%, no correlation between proximal migration and functional outcomes.
	1) Improvements in pain intensity in both groups, although no significant within group differences due to small sample size. No significant differences between groups, although a larger decrease in symptom severity was found in the hand therapy group (ES = 0.53) 2) Higher improvements in limitations in ADL in the hand therapy group for both the JHFT (ES = 0.52) as the AHFT (ES = 0.33), although not significant due to sample size. 3) Improvements in grip (+13%) & 3-point pinch strength (+27%) were only found in the hand therapy group, while grip (-8%) & 3-point pinch strength (-6%) decreased in the home program group (ES grip strength = 0.77, ES 3-point pinch = 0.95). 4) Significant improvements in several subscales of the Arthritis Impact Measurement Scales 2 for both groups, no between group differences.
	4) No significant differences in pain intensity and limitations in ADL. Insufficient data was provided to calculate ES. 5) No significant differences in pinch strength. Insufficient data was provided to calculate ES. 6) Complications were observed in 14% of the participants in the rigid group compared to 7% in the semi-rigid group.
	4) VAS scores decreased with 8 points ($p=0.04$) 5) Limitations in ADL showed 60% improvement ($p=0.4$) 6) Significant improvements in grip & pinch strength in group with hemi-resections, except in groups with full-trapezium resections

Table 5. Continued

Studies initiating CMC-1 ROM ≤4 weeks	Description of ROM exercises initiated ≤4 weeks	Measures at	Measurements & instruments
Rocchi et al.[31] 2011	4 weeks: exercises to regain full ability; i.e. opposition exercises which gradually progressed from aiming at the tip of the fifth finger, then towards reaching its base	T0 (preoperative) T1 (3 months) T2 (6 months) T3 (12 months)	6) Pain intensity (VAS mentioned, but results expressed as no pain and restriction, mild pain with use and some restriction, pain at rest and some restriction and pain at rest and severe restriction) 7) Satisfaction (VAS) 8) Limitations in ADL (DASH) 9) Grip & key pinch strength. 10) Joint imaging (SMD)
Sirotakova et al.[42] 2007	2 weeks: opposition exercises	T0 (preoperative), T1 (6 months) T2 (12 months)	1) Pain intensity, stiffness, weakness of the hand, functional disability (self designed) 2) ROM 3) Grip & pinch strength 4) Joint imaging (SMD)
Soejima et al.[33] 2006	2 weeks: ROM exercises were initiated	T0 (preoperative) T1 (33 months, range 12-71 months)	5) Pain intensity (self designed) 6) ROM 7) Grip & pinch strength 8) Joint imaging (SMD)
Vermeulen et al.[20] 2014	4 weeks: standardized hand therapy focused on regaining functionality by increasing mobility	T0 (preoperative) T1 (3 months) T2 (12 months)	1) Pain intensity and limitations in ADL (PRWHE, DASH) 2) ROM 3) Grip & pinch strength 4) Complications 5) Joint imaging (SMD)
Yao et al.[17] 2014	10 days: Active ROM exercises	T0 (preoperative) T1 (11 months)	1) Limitations in ADL (DASH)

	Outcomes
	6) At T3, zero patients had any pain at rest, only 1 occasional mild pain. No significance mentioned. 7) Satisfaction 9.6, time point unknown. 8) DASH at T0: 43.3, T1: 25.5, T2: 19.1 T3: 14.5, no significance mentioned. 9) Grip strength at T0: 16.0 kg, at T3: 19.2 kg, key pinch at T0: 3.7 kg and at T3: 5.6 kg, no significance mentioned. 10) At T3, SMD averaged 6.4 mm
	5) 'Excellent' results in terms of pain relief were achieved in 91% 6) Improvements in all ROM measures at T2 (not statistically tested) 7) Grip & pinch strength improved in all measures at T2 (not statistically tested) 8) SMD decreased with 29% at T2
	5) At T1, 61% had no pain, 24% had mild pain with strenuous activities and 14% had mild pain with light work 6) ROM radial and palmar abduction increased with 14° (p=0.09) and 8° (p=0.07) degrees respectively 7) Grip and the pinch strength increased with 2 kg (p=0.18) and from 1.3 kg (p=0.23), respectively 8) SMD decreased with 15% (p<0.05)
	6) Pain intensity (PRWHE) decreased significantly for both types of surgery at T2 (Weilby: -17 points vs. Burton-Pellegrini: -18 points (score range 0-50)). DASH: significant improvements for both types of surgery (Weilby: -16 points vs. Burton-Pellegrini: -20 points (score range 0-100)). 7) No differences between different types of surgery, except in CMC-1 extension (decrease in Burton-Pellegrini group) 8) Increase in grip strength for both types of surgery (Weilby: +3 kg vs. Burton-Pellegrini: +4 kg). Key pinch decreased 0.1 kg for both types of surgery, Tip-pinch increased 0.4 kg for both types of surgery and 3-point pinch increased for both types of surgery (Weilby: +0.3 kg vs. Burton-Pellegrini: +0.5 kg). Statistical testing for group differences was not reported 9) In total, complications were observed in 27,8% of the participants (Weilby: 23,1% vs. Burton-Pellegrini: 32,5%, difference not significant) 10) SMD at T2 during rest in Weilby group decreased with 33%, in Burton-Pellegrini group with 48%, during pinch in Weilby group: 66%, Burton-Pellegrini group: 57%
	1) DASH at T0: 63, at T1: 10 (single case)

Table 5. Continued

Studies initiating strengthening exercises ≤4 weeks	Description of strengthening exercises initiated ≤4 weeks	Measures at	Measurements & instruments
Poole et al.[28] 2011	Hand therapy group, 4 weeks: strength exercises	T0 (pre-op) and T1 (6 months postoperatively).	1) Pain intensity (Boston Questionnaire) 2) Limitations in ADL, (JHFT, AHFT) 3) Grip & pinch strength 4) Quality of life (AIMS 2)
Soejima et al.[33] 2006	2 weeks: strength exercises	T0 (preoperative) T1 (33 months, range 12-71 months)	1) Pain intensity (self designed) 2) ROM 3) Grip & pinch strength 4) Joint imaging (SMD)
Vermeulen et al.[20] 2014	4 weeks: standardized hand therapy focused on regaining functionality by increasing strength	T0 (preoperative) T1 (3 months) T2 (12 months)	1) Pain intensity and limitations in ADL (PRWHE, DASH) 2) ROM 3) Grip & pinch strength 4) Complications 5) Joint imaging (SMD)
J. Yao et al.[17] 2014	18 days: isometric exercises lateral pinch strength exercises	T0 (preoperative) T1 (11 months)	1) Limitations in ADL (DASH)

Note: VAS = Visual Analogue Scale, ROM = Range of Motion, ES = Effect Size (positive scores indicate better performance of experimental treatment compared to control treatment), MCP-1 = First Metacarpophalangeal joint, ADL = Activities of Daily Life, PRWHE = Patient Rated Wrist & Hand Evaluation, MHQ = Michigan Hand outcomes Questionnaire, DASH = Disabilities of Arm, Shoulder and Hand, AIMS2 = Arthritis Impact Measurement Scales 2, JHFT = Jebsen Hand Function Test, AHFT = Arthritis Hand Function Test, IP = Interphalangeal joint, SMD = distance between base of first metacarpal and distal end of scaphoid, TMD = distance between base of first metacarpal and radial border of trapezoid

	Outcomes
	1) Improvements in pain intensity in both groups, although no significant within group differences due to small sample size. No significant differences between groups, although a larger decrease in symptom severity was found in the hand therapy group (ES = 0.53) 2) Higher improvements in limitations in ADL in the hand therapy group for both the JHFT (ES = 0.52) as the AHFT (ES = 0.33), although not significant due to sample size. 3) Improvements in grip (+13%) & 3-point pinch strength (+27%) were only found in the hand therapy group, while grip (-8%) & 3-point pinch strength (-6%) decreased in the home program group (ES grip strength = 0.77, ES 3-point pinch = 0.95). 4) Significant improvements in several subscales of the Arthritis Impact Measurement Scales 2 for both groups, no between group differences.
	1) At T1, 61% had no pain, 24% had mild pain with strenuous activities and 14% had mild pain with light work 2) ROM radial and palmar abduction increased with 14° (p=0.09) and 8° (p=0.07) degrees respectively 3) Grip and the pinch strength increased with 2 kg (p=0.18) and from 1.3 kg (p=0.23), respectively 4) SMD decreased with 15% (p<0.05)
	1) Pain intensity (PRWHE) decreased significantly for both types of surgery at T2 (Weilby: -17 points vs. Burton-Pellegrini: -18 points (score range 0-50)). DASH: significant improvements for both types of surgery (Weilby: -16 points vs. Burton-Pellegrini: -20 points (score range 0-100)). 2) No differences between different types of surgery, except in CMC-1 extension (decrease in Burton-Pellegrini group) 3) Increase in grip strength for both types of surgery (Weilby: +3 kg vs. Burton-Pellegrini: +4 kg). Key pinch decreased 0.1 kg for both types of surgery, Tip-pinch increased 0.4 kg for both types of surgery and 3-point pinch increased for both types of surgery (Weilby: +0.3 kg vs. Burton-Pellegrini: +0.5 kg). Statistical testing for group differences was not reported 4) In total, complications were observed in 27,8% of the participants (Weilby: 23,1% vs. Burton-Pellegrini: 32,5%, difference not significant) 5) SMD at T2 during rest in Weilby group decreased with 33%, in Burton-Pellegrini group with 48%, during pinch in Weilby group: 66%, Burton-Pellegrini group: 57%
	1) DASH at T0: 63, at T1: 10 (single case)

Table 6 provides a summary of the phases and the physical therapy content per phase as used in the included studies and Table 7 provides an overview of the phases per study. In general in postoperative exercises/therapy, emphasis is placed on MCP-1 flexion and CMC palmar abduction and extension, while CMC flexion, adduction and opposition is avoided.

Table 5 provides the outcomes for studies initiating ROM or strengthening exercises respectively ≤4 weeks postoperatively. Thirteen studies[17,20,24,25,27-31,33,38,40,42] initiated ROM exercises and four studies[17,20,28,33] initiated strengthening exercises ≤4 weeks. No comparative studies on different regimens of ROM or strengthening exercises were found. We did not find more complications or worse outcomes in studies that initiated ROM or strengthening exercises ≤4 weeks compared to studies that initiated ROM or strengthening exercises ≥4 weeks.

Table 6. Summary of the phases and content of postoperative rehabilitation following thumb base arthroplasty as used in the literature. **Note:** The displayed time frames indicate the range from start to end (minimum – maximum period) of the used period in the literature. Abbreviation: IP-1, thumb interphalangeal joint.

Phase	Weeks postoperative	Physical therapy content
1. Acute	Range: 0 – 6wk	Composite finger flexion/extension, thumb IP-1 flexion/extension, wrist/elbow/shoulder movement is emphasized and no CMC-1 or MCP-1 movement is encouraged
2. Unloaded	Range: 1 – 12wk	ROM-exercises for MCP-1 and CMC-1 are initiated. In general, emphasis is placed on MCP-1 flexion and CMC palmar abduction and extension, while CMC flexion, adduction and opposition are avoided. The exercises are supplemented with scar management and edema control
3. Functional	Range: 3wk to 6mo	Progressive ROM of the CMC-1 and MCP-1 is allowed, and strength exercises are initiated.

Table 7. An overview of the phases on postoperative exercises/therapy per week for the individual studies.

YEAR	AUTHOR	N	TYPE SURGERY / TENDON PLASTY	WEEK 1	2	3	4	5	6	7	8	9	10	11	12	13	14
1985	Eaton et al.[38]	25	***FCR***														
1986	Burton et al.[24]	25	***FCR***														
1993	Nylen et al.[41]	102	***FCR***														
1996	Lins et al.[40]	30	***FCR***														
2000	Varitimidis et al.[43]	62	***FCR***														
2001	Roberts et al.[30]	25	***FCR***														
2002	Saehle et al.[32]	55	***APL***														
2002	Horlock et al.[25]	40															
	Late group	*20*	***Simple Trapeziectomy***														
	Early group	*20*	***Simple Trapeziectomy***														
2003	Kuhns et al.[39]	26	***Simple Trapeziectomy***														
2004	Mo et al.[27]	14	***FCR***														
2004	Kriegs-Au et al.[21]	52	***FCR***														
2004	Davis et al.[18,23,26,32-34,37,38]	62	***FCR***														

Table 7. An overview of the phases on postoperative exercises/therapy per week for the individual studies.

YEAR	AUTHOR	N	TYPE SURGERY / TENDON PLASTY	WEEK 1 2 3 4 5 6 7 8 9 10 11 12 13 14
		59	***PL***	
		62	***Simple Trapeziectomy***	
2006	Soejima et al.[33]	21	***APL***	
2007	Sirotakova et al.[42]	104	***APL***	
2009	Vermeulen et al.[19]	20	***FCR***	
2009	Wong et al.[18]	22	***FCR + PL***	
2011	Rocchi et al.[31]	50	***APL***	
2011	Poole et al.[28]	9		
	Home program group	*5*	***PL***	
	Occupational therapy group	*4*	***PL***	
2012	Ataker et al.[36]	27	***FCR***	
2012	Başar et al.[22]	19	***FCR***	
2012	Abbas et al. [23]	10	***FCR + PL***	
2014	Prosser et al.[29]	53		

Table 7. An overview of the phases on postoperative exercises/therapy per week for the individual studies.

YEAR	AUTHOR	N	TYPE SURGERY / TENDON PLASTY	WEEK 1	2	3	4	5	6	7	8	9	10	11	12	13	14
	Rigid group	*27*	***FCR***														
	*Semi-rigid group**	*26*	***FCR***														
	Rigid group	*1*	***Simple Trapeziectomy***														
	*Semi-rigid group**	*2*	***Simple Trapeziectomy***														
2014	Yang et al.[19,20,28,35,39-41,43]	21	***FCR***														
2014	Vermeulen et al.[20]	72	***FCR***														
2014	Yao et al.[17]	1	***Tightrope***														
2015	Lee et al.[26]	19	***APL***														
2016	Werthel et al.[34]	49	***FCR***														

Abbreviations Table 7: FCR = Flexor Carpi Radialis, APL = Abductor Pollicis Longus, PL = Palmaris Longus

Legend Table 7:

Acute phase =

Unloaded phase =

Functional phase =

Content unknown =

DISCUSSION

The aim of this systematic review was to describe the different components of postoperative rehabilitation protocols for patients who underwent CMC-1 arthroplasty and several components of rehabilitation protocols were specifically investigated. Twenty-seven studies were included with a total of 1015 participants in whom 1118 procedures were performed. This systematic review presents a summary of the used postoperative rehabilitation for different surgical interventions (Figure 2). We found positive outcomes of partial instead of complete immobilization until 6 weeks, a total immobilization period 4-6 or ≤4 weeks and the initiation of ROM or strengthening exercises ≤4 weeks, but too few comparative studies are available in order to draw firm conclusions on relative effectiveness. Additionally, we identified three phases on postoperative exercises/therapy as used in the included studies: the 'acute phase', the 'unloaded phase' and the 'functional phase' (Table 6-7).

In general in this review, postoperative exercises/therapy emphasizes on positioning the CMC-1 in extension and abduction, while flexion and adduction is avoided during rehabilitation.[44,45] Furthermore, MCP-1 hyperextension should be avoided while MCP-1 flexion is encouraged to prevent the development of a z-deformity.[44] Despite the fact that no conclusions regarding effectiveness can be drawn, the presented summary for different surgical interventions and the identification of the aforementioned phases may provide guidance in clinical decision making for hand therapists and surgeons in the postoperative rehabilitation for patients who underwent CMC-1 arthroplasty. However, there is considerable variation in time frames of the individual phases, possibly since the phases are carried out more quickly over the years in literature (Table 7). Hence, further exploration of these phases is needed in future research. Furthermore, these phases should be identified for different surgical procedures specifically.

Wolfe et al. concluded that there was too much variation in the literature in order to formulate recommendations on postoperative immobilization and exercises.[9] In the present systematic review, we also conclude that there are insufficient comparative studies to draw conclusions regarding the effectiveness of postoperative rehabilitation. However, we do present a more extensive overview of the postoperative rehabilitation as used in the literature compared to the results by Wolfe et al.[9] All the nineteen studies included by Wolfe et al.[9] were identified in the literature search of the present study, but only four were included in the

present review. For example, Wolfe et al. also included several types of joint prostheses while we excluded joint prostheses. The inclusion of other studies than included by Wolfe et al. may have resulted in a different representation of postoperative rehabilitation for patients who underwent CMC-1 arthroplasty.

Two comparative studies[25,29] on postoperative immobilization were included in this review (Table 4). Similar or better outcomes were found when partial instead of complete immobilization was used in the first six weeks postoperatively. Horlock et al., where partial instead of complete immobilization was used following simple trapeziectomy, found an effect size of -0.66 on pain intensity, indicating worse outcomes in the early mobilization group. However, the difference was not statistically significant and mostly due to a mean difference at baseline between both groups. Furthermore, Visual Analogue Scale score for pain intensity at follow-up were comparable with previously reported outcomes following simple trapeziectomy.[8] Therefore, the effect size of -0.66 on pain intensity should be interpreted with caution.

On MCP-1 flexion and experienced convenience by the participants, the early mobilization group performed significantly better than the late mobilization group with effect sizes 0.19 and 0.66 respectively, indicating small to large treatment effects[16]. Hence, these studies suggest that partial instead of complete immobilization demonstrates good outcomes but more randomized controlled trials on postoperative immobilization are needed to confirm this.

The study by Poole et al.[28] was the sole study that compared rehabilitation including a home program only with a more extensive rehabilitation program including hand therapy following CMC-1 arthroplasty. No significant between-group differences were found postoperatively, probably due to a small sample size (n=9) although more within-group improvements were found on pain intensity, limitations in ADL and grip & pinch strength in the group that received hand therapy with effect sizes between 0.33 and 0.95, indicating small to large treatment effects[16]. For example, improvements were found in postoperative grip strength (+13%) & pinch strength (+27%) in the hand therapy group, while a decrease in grip strength (-8%) and pinch strength (-6%) was found in the group that did not receive hand therapy. These findings suggest that additional hand therapy is beneficial in reducing pain intensity and limitations in ADL and improving grip & pinch strength after CMC-1 arthroplasty, but randomized controlled trials with larger sample sizes are needed.

Several studies investigated the concept of 'early active recovery', which includes short immobilization and allows patients to exercise in an early post-operative phase.[25,28,29] A trend is identifiable indicating that early active recovery (including short immobilization, early initiation of ROM and strength exercises) provides positive outcomes on pain, limitations in ADL and grip & pinch strength, but no conclusions on effectiveness can be drawn since comparative studies are lacking. Additionally, Table 7 indicates a trend that, over the years, early active rehabilitation is applied more often in literature. This accelerated type of rehabilitation does not lead to worse outcomes or more complications. Faster recovery may result in faster return to work, which could be beneficial for patients with CMC-1 OA considering the fact that ageing populations need to participate longer in working life. Hence, future high-quality studies are needed in order to determine the effectiveness of early active recovery.

Historically, determining of postoperative scaphometacarpal distance (SMD) by joint imaging has been a particular outcome of interest in many studies on CMC-1 arthroplasty, since the hypothesis is that maintenance of SMD after surgery results in better function and less pain.[8] The sole comparative study on evaluating SMD was by Horlock et al.[25], in which no difference in SMD was found between the early and late mobilization group. Additionally, Wajon et al.[8] reported that there is no clinically relevant correlation between SMD and pinch strength and all of the studies included in the present review did not find a correlation between SMD and clinical outcomes. Therefore, the influence of different types of postoperative rehabilitation on SMD and the predictive value of SMD on clinical outcomes remains unclear and should be addressed in future research.

Study limitations

A weakness of this systematic review is the large amount of low-quality studies included (Supplementary Table 2, Appendix 2). Despite that findings of the individual studies are in line with each other, no conclusions on effectiveness of postoperative rehabilitation following CMC-1 arthroplasty can be drawn since comparative studies are lacking and large heterogeneity in outcome measures and measurement instruments is present. Therefore, we recommend, predominantly in line with Vermeulen et al.[7] and Wajon et al.[8] that future studies report homogenous outcome measures, preferably measured with validated measurement instruments. Additionally, confounding may be present regarding the fulfillment of the different components of rehabilitation. The outcomes of studies without group comparisons are based on an interaction between type of surgery, immobilization type, immobilization period

and postoperative exercises/therapy. Hence, no conclusions can be drawn on the specific effects of one of the aforementioned components of treatment. Therefore, future research should explore different postoperative regimes within the same surgical procedure, which allows researchers to study the effectiveness of specific rehabilitation protocols for individual surgical techniques.

Another limitation is that many studies regarding CMC-1 arthroplasty provide very little or no information on postoperative rehabilitation.[6,8] This may have resulted in a biased reflection of the actual postoperative regime for CMC-1 arthroplasty. Therefore, it is strictly recommended that future studies on CMC-1 arthroplasty provide an adequate description of the postoperative regime, including an adequate description of postoperative immobilization and postoperative exercises/therapy.

CONCLUSIONS

In conclusion, this review presents an overview of postoperative rehabilitation for different surgical interventions on CMC-1 OA. Furthermore, three postoperative phases were identified with regard to postoperative exercises/therapy: the 'acute phase', the 'unloaded phase' and the 'functional phase'. In addition, we found that early active recovery (including short immobilization, early initiation of ROM and strength exercises) provides positive outcomes for patients who underwent CMC-1 arthroplasty and is used more often in literature, but more high-quality studies comparing different postoperative rehabilitation protocols are needed to get more insight in the effectiveness of postoperative rehabilitation. Additionally, it is strongly recommended that future studies regarding CMC-1 arthroplasty provide adequate descriptions of their postoperative regime.

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CHAPTER 8

SHORTER VERSUS LONGER IMMOBILIZATION AFTER SURGERY FOR THUMB CARPOMETACARPAL OSTEOARTHRITIS: A PROPENSITY SCORE MATCHED STUDY

Jonathan Tsehaie and Robbert M. Wouters**
Reinier Feitz
Steven E.R. Hovius
Harm P. Slijper
Ruud W. Selles
for the Hand-Wrist Study Group

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**Both authors contributed equally to this article*

ABSTRACT

Objective: To investigate if shorter immobilization is non-inferior to longer immobilization after Weilby procedure for thumb carpometacarpal osteoarthritis

Design: Prospective cohort study with propensity score matching (PSM)

Setting: Data collection took place in sixteen outpatient clinics for hand surgery and hand therapy

Intervention: Shorter immobilization (3-5 days plaster cast followed by a thumb spica orthosis including wrist until 4 weeks postoperatively) was compared with longer immobilization (10-14 days plaster cast followed by a thumb spica orthosis including wrist until 6 weeks postoperatively) after Weilby procedure for CMC-1 osteoarthritis. PSM was used to control for confounders.

Main outcome measures: Outcomes were pain measured with a Visual Analogue Scale (VAS) and hand function measured with the Michigan Hand outcomes Questionnaire (MHQ) at three and twelve months. Secondary outcomes were complications, range of motion, grip and pinch strength, satisfaction with treatment and return to work.

Results: We matched 131 participants with shorter immobilization and 131 participants with longer immobilization. No significant differences were found in VAS pain (effect size 0.03, 95% C.I. -0.21-0.27) or the MHQ (effect size 0.01, 95% C.I. -0.23-0.25) between the groups at three months or at twelve months. Furthermore, no differences were found in complication rate or in other secondary outcomes.

Conclusions: In conclusion, shorter immobilization of 3-5 days of a plaster cast after Weilby procedure is equal compared to longer immobilization for outcomes on pain, hand function and our secondary outcomes. These results indicate that shorter immobilization is safe and can be recommended, since discomfort of longer immobilization may be prevented and patients may be able to recover sooner which may lead to reduced loss of productivity. Future studies need to investigate effectiveness of early active and more progressive hand therapy following CMC-1 arthroplasty.

INTRODUCTION

Osteoarthritis (OA) of the thumb base joint (CMC-1) is a common disorder in the elderly, with a radiologically diagnosed prevalence of 33-40% amongst females aged ≥50 years.[1-3] CMC-1 osteoarthritis can occur in both thumbs, and patients often experience pain, reduced pinch- or grip strength and limitations in activities of daily life (ADL).[1,4] There is an overall weakened hand strength due to muscular atrophy, incorrect thumb position, and by avoiding painful movements or activities.[4] Limitations in activity of daily living usually comprises of pinch movements with the thumb, such as turning a key, opening a jar or gripping a pen.[1,4] When non-operative treatment modalities (i.e. orthosis, hand therapy, steroid injections, analgesics or patient education) fail to provide sufficient pain relieve or functional improvement, CMC-1 arthroplasty may be indicated.[5]

Several studies emphasize the importance of postoperative rehabilitation for patients who underwent CMC-1 arthroplasty to reduce postoperative pain and improve function, limitations in ADL, satisfaction, range of motion (ROM) and grip & pinch strength.[6-8] Recently, we published a systematic review on postoperative rehabilitation following CMC-1 arthroplasty, which indicated, based on very limited evidence, that early active rehabilitation (including shorter immobilization and early initiation of exercises/hand therapy) is increasingly used in literature without worse outcomes or more complications.[7] Theoretically, early active recovery would be beneficial by preventing longer patient discomfort and reducing postoperative complications due to longer immobilization. In addition, a shorter immobilization period allows the patient to return to daily activities more quickly during rehabilitation.

Various time frames on postoperative immobilization after CMC-1 arthroplasty have been reported in literature, with cast immobilization varying from zero to five weeks, while the total immobilization period even varies between two to twelve weeks postoperatively.[7] However, no evidence is available whether a long period of immobilization is necessary and if shorter immobilization will lead to similar results. Therefore, more insight in the effectiveness of shorter immobilization following CMC-1 arthroplasty is needed to ensure that it is safe, does not lead to more complications and has at least similar outcome in terms of pain and hand function.

The aim of this prospective cohort study is to investigate if shorter immobilization is non-inferior to longer immobilization after CMC-1 arthroplasty (Weilby procedure) in terms of hand function and pain intensity postoperatively. Shorter immobilization comprises a 3-5 days plaster cast followed by a thermoplastic thumb spica orthosis immobilization until 4 weeks, while longer immobilization comprises 10-14 days plaster cast followed by a thermoplastic thumb spica orthosis immobilization until 6 weeks.

METHODS

Study design

This is a prospective cohort study with propensity score matching (PSM), reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[9] We compared short versus longer immobilization by comparing patients that were treated in two different time periods, in which different postoperative regimes were used and matched the participants using propensity score matching.

This study was performed in sixteen outpatient clinics of a specialized treatment center for hand surgery and hand therapy in The Netherlands and data collection was part of usual care. The Medical Research Ethical Committee of the Erasmus MC Rotterdam approved this study and written informed consent was obtained from all participants. Certified hand surgeons diagnosed patients with CMC-1 OA by physical examination and radiographic evaluation to determine Eaton stage.[10] Following the treatment protocol, all the participants received three months of non-operative treatment first, regardless of the disease severity or duration of symptoms.[5] The decision to proceed to surgery was made when patients had insufficient pain relieve or insufficient functional improvement.

Participants

Participants were eligible for inclusion when they were: 1) adult and diagnosed with stage I-IV[10] CMC-1 OA by a certified hand surgeon and 2) underwent a Weilby-sling procedure. Exclusion criteria included: 1) secondary CMC-1 OA (i.e. due Bennett's fracture); 2) occurrence of a co-intervention (i.e. carpal tunnel release); 3) patient history of surgery interfering with treatment or outcome (i.e. due to Bennett's fracture); or 4) steroid injections given within 6 weeks in hand or wrist prior to surgery due to 1) it was not part of the treatment protocol and 2) to keep the studied population as homogenous as possible.

Surgical treatment

The surgical treatment consisted of a Weilby procedure: after a Wagner incision over the radial side of the CMC-1 joint and preservation of the radial superficial nerve, the trapezium was fully removed. Subsequently, either a Flexor Carpi Radialis (FCR) or Abductor Pollicis Longus (APL) tendon graft was intertwined in a figure-of-eight-reconstruction between the remaining half of the its own insertion and the APL/FCR insertion. The remaining tendon split was stored in the trapezial cavity.[11,12]

Postoperative treatment

Due to the observational design of this study, the postoperative treatment was not completely standardized such as in most randomized controlled trials. However, the hand therapists of all treatment locations carried out the same, protocolized postoperative regime following strict guidelines developed by Handtherapie Nederland, which is based on the Dutch national guideline and recent literature.[7,13] Naturally, all hand therapists were informed when the new postoperative regime was introduced and compliance was randomly checked internally by auditing patient charts. To further ensure that all therapists had adjusted to the new protocol and did not (partly) used the previous protocol, we created a half year inclusion gap for this study. More specifically, all patients treated between January 2012 and April 2015 were included in the longer immobilization group and all patients treated between October 2015 and April 2017 were included in the shorter immobilization group.

The patients in the longer immobilization group were primarily immobilized in a plaster cast for 10-14 days. After this period, the hand therapist removed the cast and a thermoplastic thumb spica orthosis including wrist immobilization (Figure 1) was applied until 6 weeks postoperatively. Patients were instructed to wear the thermoplastic thumb spica orthosis 24 hours/day, except during exercises. Afterwards, a butterfly orthosis (Figure 1) was applied 24 hours/day until 8 weeks (except during exercises), which was phased out until 3 months postoperatively.

The patients in the shorter immobilization group were primarily immobilized in a plaster cast for 3-5 days. The hand therapist removed the cast and a thermoplastic thumb spica orthosis including wrist immobilization was applied until 4 weeks postoperatively. Patients were instructed to wear the thermoplastic thumb spica orthosis 24 hours/day, except during exercises. Afterwards, a butterfly orthosis was applied until 8 weeks 24 hours/day, except during exercises, which

was phased out until 10 weeks postoperatively. Figure 1 provides a graphic overview of the immobilization periods for both groups.

The rationale for selecting these orthotic devices was to provide enough protection and stability for these specific postoperative phases, while allowing range of motion exercises when safe and preventing excessive joint stiffness. All orthotic devices were fabricated by experienced and trained hand therapists to assure consistency and quality of application.

In both groups, the hand therapy exercises directly postoperatively (acute phase) included tendon-gliding exercises of the fingers and the thumb interphalangeal joint. After 10-14 days, sutures were removed. Hand therapy and home exercises in the unloaded phase (2-6 weeks) focused on active wrist flexion/extension, CMC-1 palmar and radial abduction and metacarpophalangeal (MCP-1) flexion (with support to the first metacarpal), along with scar management. In this phase, no flexion/adduction and thumb opposition were allowed. The functional phase included the initiation of static pinch exercises by 6 weeks, after which increased grip & pinch exercises were performed, usually until three months postoperatively.

Variables

Primary outcomes

The primary outcomes in this study were hand function, measured with the Michigan Hand outcomes Questionnaire (MHQ) and pain, measured with a Visual Analogue Scale (VAS) at baseline, six weeks, three months and twelve months. The rationale behind measuring pain and function is that the decision to proceed to surgery is usually based on persistent pain and limited hand function, and outcomes on these domains are highly relevant for this particular group of patients.

The MHQ (range: 0–100, higher scores indicate better performance except for the subscale pain) is a validated questionnaire with a high internal consistency, high internal validity, acceptable reliability and is particularly applicable for patients with hand OA. The minimal clinical important difference (MCID) for the MHQ is 8-13 (3-23 for the subscales).[14-16] The MHQ subscales were secondary outcomes.

For pain, we measured VAS pain at rest (range: 0-100, higher scores indicate more pain) and VAS pain during physical load. The VAS is a reliable and valid instrument to measure pain intensity in patients with rheumatic diseases and has a minimal detectable change (MDC) of eleven points.[17] For this article, we decided to report VAS pain and MHQ at three months as primary outcome, since we assumed that three months after surgery is the first relevant moment to experience improvement in pain and function due to the surgery and the different immobilization periods.[5,6] However, outcome in VAS pain at six weeks and twelve months are also reported, as well as outcome in MHQ at twelve months, to study both early recovery as well as long-term recovery.

Secondary outcomes

Secondary outcomes were complications, ROM, grip & pinch strength, return to work and an additional satisfaction with treatment questionnaire. Complications of surgery were scored by authors JT & RW by reviewing patient charts. The following events were scored as a complication: tendovaginitis stenosans of the thumb, Quervain tenosynovitis, FCR tendinitis, FCR rupture, carpal tunnel syndrome, complex regional pain syndrome (CRPS), presence of neuroma, infection, clinically and radiologically diagnosed metacarpal abutment with the scaphoid, radial superficial nerve injury or revision surgery.

ROM measurements were performed at baseline and three months using the recommendations of the American Society of Hand Therapists.[18] Grip & key pinch strength was measured at baseline and three months using the Biometric E-Link© following Mathiowetz et al.[19-21] Return to work and patient satisfaction was assessed at three months using self-designed questionnaires on the patient's ability to work and the experienced treatment effect respectively.

Study size

In non-inferiority studies, a priori power analysis is different from the more commonly used superiority studies. It has been described that defining the non-inferiority margin should be based on clinical judgment and statistical reasoning.[22] We used a conventional small to medium effect size of .35, defined by Cohen et al.[23] as a non-inferiority margin, resulting in a total sample of 204 participants for a power of .80 (α=0.05).

Due to the nature of propensity score matching, a number of participants will not be matched to other participants and will therefore be excluded from the analysis.

In a study by Zhou et al. on Dupuytren's disease[24], propensity score matching was also used and 60% of the total sample was included in the final analysis. To account for this, we decided to enlarge the total sample to >400 participants.

Statistical methods

Usually, comparing groups in observational studies is difficult due to the presence of covariates.[25] propensity score matching involves the use of a propensity score, which is the probability for an individual to be assigned to a particular treatment given a vector of observed covariates.[26,27] propensity score matching allows researchers to compare matched individuals without introducing bias, the only difference being whether the individual is treated with the intervention of interest or not, assuming that all relevant covariates are included in the model estimating the propensity score. [25,27]

The propensity scores were estimated using logistic regression, in which treatment status is regressed on baseline characteristics. [26-28] The following baseline characteristics were used as covariates for estimating the propensity score: age, gender, type of work, duration of symptoms, dominant side treated, the MHQ subscales, VAS pain at rest, VAS pain during physical load, grip strength, key pinch strength, CMC-1 palmar abduction angle, CMC-1 radial abduction angle, MCP-1 flexion angle and MCP-1 extension angle. The propensity scores were subsequently used to match participants on a one-to-one basis using a nearest-neighbor algorithm with a matching tolerance width of 0.2 SD of the logit of the propensity score.[26-28]

Since the matched samples were dependent, the between-group differences in demographic characteristics were analyzed using Standard Error of Mean Difference (SEMD). A SEMD of greater than 10 percent was suggested as substantial imbalance in a certain variable between groups.[29] Propensity score matching was performed using the MatchIt package. Between group differences were tested with Whitney tests.

We performed Chi-square tests to study both differences in total number of complications as well as individual complications between both groups.

Group	WEEK													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Short immobilization	**3-5 days**													
Prolonged immobilization	**10-14 days**													

Legend

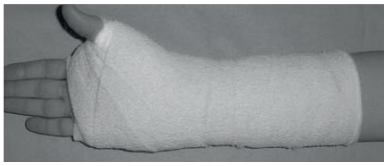
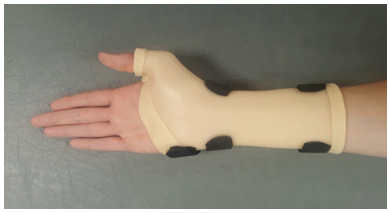
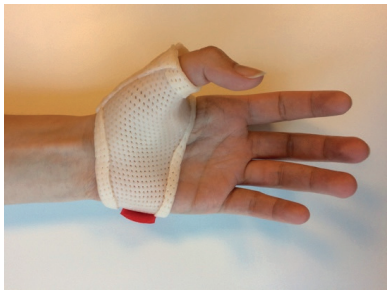
Phase	Short Immobilization	Prolonged Immobilization
Plaster cast immobilization: 	3-5 days	10-14 days
Thumb spica splint incl. wrist immobilization: 	Until 4 weeks	Until 6 weeks
Thumb butterfly splint: 	Until 8 weeks	Until 8 weeks
Orthosis phased out	Until 10 weeks	Until 3 months
Orthosis completely discontinued	>10 weeks	> 3 months

Figure 1. Timeline and legend for postoperative immobilization period and methods.

As described earlier, a conventional small to medium effect size of .35 was used as a non-inferiority margin. Following Hahn[22], equality was considered if the 95% CIs lie within both the negative and positive non-inferiority margin, whereas non-inferiority was considered if one bound of the 95% CI lies outside the non-inferiority margin but an effect size of zero lies within the other bound.[22] All analyses were performed in R, version 3.4.1.

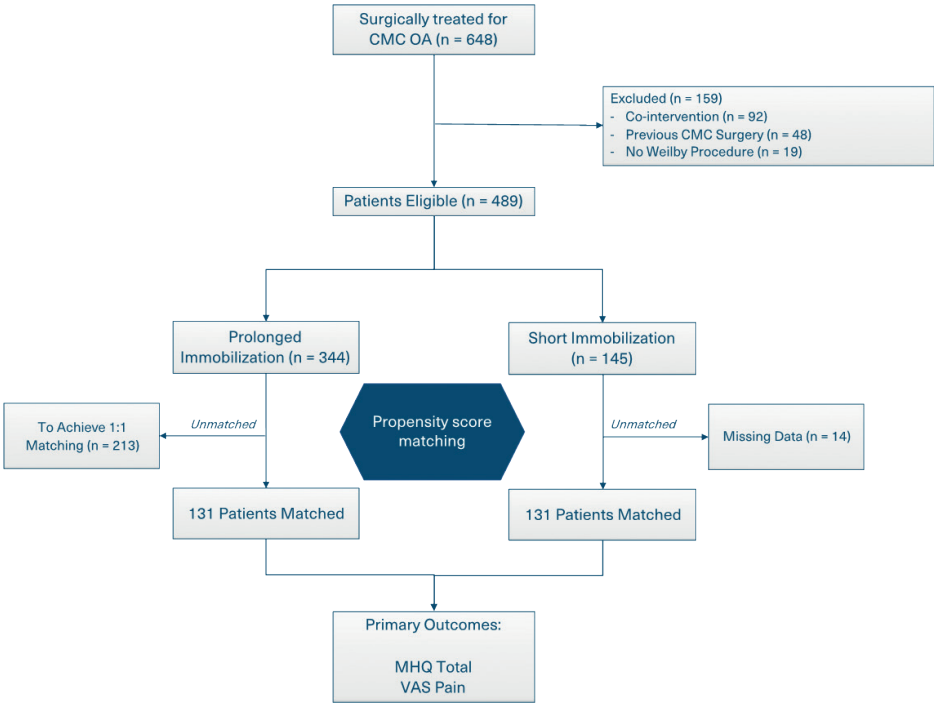


Figure 2. Flowchart of the study.

RESULTS

Patient characteristics

Between 2011 and 2017, a total of 648 patients underwent a Weilby procedure in one of our clinics. After applying the eligibility criteria, 489 patients were included in the initial cohort. After surgery, 70% underwent longer immobilization and 30% shorter immobilization, reflecting the shorter inclusion period for the shorter immobilization. After propensity score matching, each group contained 131 patients (Figure 2).

Table 1 shows the baseline characteristics of the patients before and after propensity score matching. Before propensity score matching, the shorter immobilization group had on average a slightly shorter duration of symptoms, higher pain during physical load, larger MCP-1 extension and less range of motion during MCP-1 flexion at baseline. After propensity score matching, the standardized error mean difference between the groups were within the margin of ten percent for all variables except some small imbalance in age, RAB angle and moderate workload (Table 1).

Table 1. Baseline characteristics before and after propensity score matching.

	All patients		**Matched patients**		
Continuous variables	*Prolonged immobilization group (N= 344)*	*Short immobilization group (N= 145)*	*Prolonged immobilization group (N= 131)*	*Short immobilization group (N= 131)*	*Standard error of mean difference (%)*
Age	60 ± 8	60 ± 9	61 ± 8	60 ± 8	12.5
Duration complaints (months)	44 ± 51	38 ± 41	39 ± 49	39 ± 42	0
MHQ function	49 ± 15	51 ± 19	51 ± 16	52 ± 19	5.7
MHQ ADL	52 ± 22	55 ± 21	55 ± 22	55 ± 22	0
MHQ work	49 ± 24	49 ± 26	49 ± 25	49 ± 26	0
MHQ pain	35 ± 14	35 ± 14	35 ± 14	35 ± 14	0
MHQ esthetics	80 ± 19	79 ± 21	79 ± 20	80 ± 21	4.9
MHQ satisfaction	31 ± 18	32 ± 20	33 ± 20	32 ± 20	5.0
VAS pain during rest	49 ± 22	51 ± 23	52 ± 22	50 ± 18	9.5
VAS pain during physical load	73 ±19	75 ± 17	74 ± 17	75 ± 17	9.9
PAB angle	46 ± 10	46 ± 11	46 ± 9	46 ± 11	0
RAB angle	47 ± 28	52 ± 46	47 ± 10	53 ± 47	18
MCP extension	-14 ± 15	-16 ± 12	-16 ± 15	-16 ± 12	0
MCP flexion	67 ±13	64 ± 14	64 ± 13	64 ± 14	0
Categorical variables					
Gender, female (%)	80	75	70	74	8.9
Treated side dominant side (%)	48	48	45	48	6.0
Workload					
Not working (%)	46	51	52	50	4.0
Light work (%)	21	16	18	17	2.6
Moderate work (%)	23	23	18	23	12.4
Heavy work (%)	10	10	12	10	6.4

Abbreviations: MHQ: Michigan hand questionnaire, VAS: Visual Analogue Scale, SEMD: Standard error of mean difference, MCP: Metacarpophalangeal, PAB: Palmar abduction, RAB: Radial abduction

Outcomes for MHQ total and MHQ subscales are displayed in Figure 3. Both the MHQ total (effect size 0.01, 95% C.I. -0.23 - 0.25) as well as the MHQ subscales at three months did not show any significant differences between both groups. Outcome in MHQ total and subscales at twelve months was similar to the three months outcome, with no significant differences between both groups (Supplementary Figure 1).

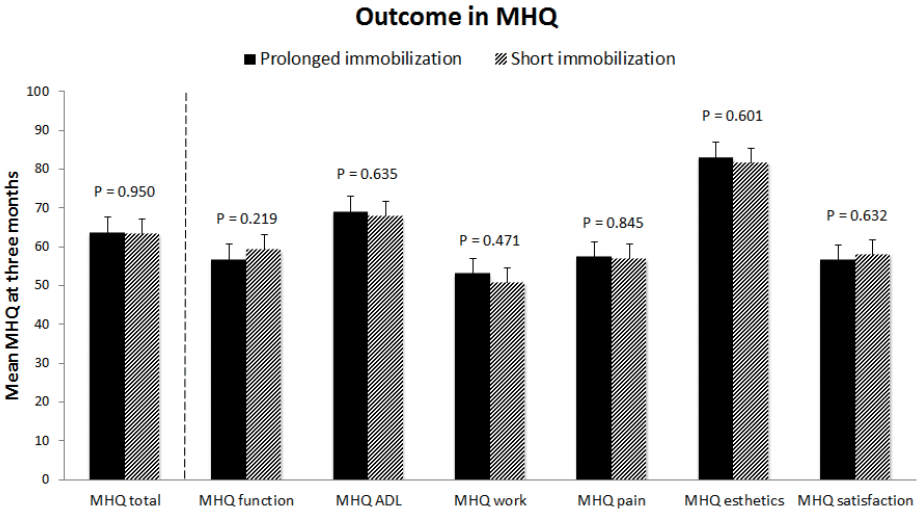


Figure 3. Outcome in Michigan Hand Outcomes Questionnaire at 3 months for the longer and shorter immobilization group. Error bars indicate standard errors. Abbreviation: ADL, activities of daily living.

In addition, both groups showed highly similar improvements in pain during physical load and pain during rest compared to preoperative measures (Figure 4). Moreover, outcome in pain during physical load and pain during rest showed no significant differences between both groups at three months; effect size 0.11, 95% C.I. -0.12 - 0.35 for VAS pain during physical load at three months and effect size 0.03, 95% C.I. -0.21 - 0.27 for VAS pain during rest at three months (Figure 4). The magnitude of the effect sizes for the MHQ and VAS and their confidence intervals (lying within non-inferiority margin of 0.35) indicate equality for the MHQ and VAS pain during rest and non-inferiority for VAS during physical load. In addition, outcome in pain during physical load and pain during rest compared at six weeks and twelve months was similar to the three months outcome, with no significant differences between both groups (Figure 4).

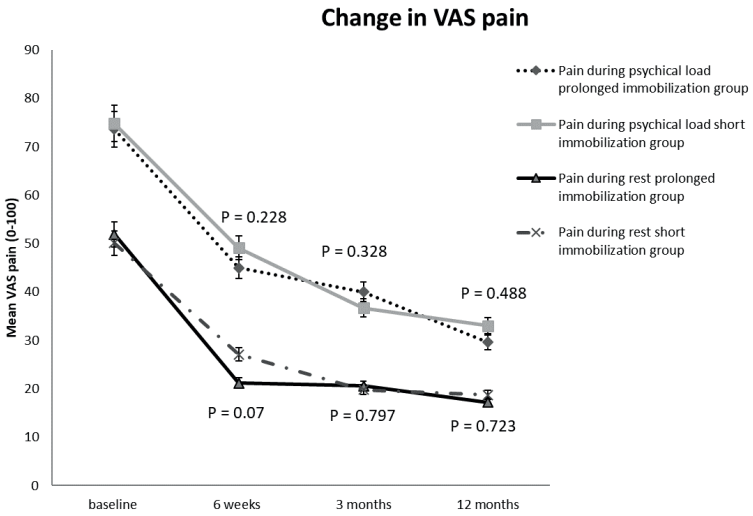


Figure 4. Change in visual analog scale pain at baseline, 6 weeks, 3 months, and 12 months postoperatively for the longer and shorter immobilization group. P-values correspond to the comparisons between groups at follow-up.

Figure 5 shows the satisfaction with treatment of the patients at three months, where both groups expressed similar satisfaction with treatment (p=0.274). In addition, 80% of the patients in the shorter immobilization group would choose the same operation again, versus 82% of the longer immobilization group (p=0.706).

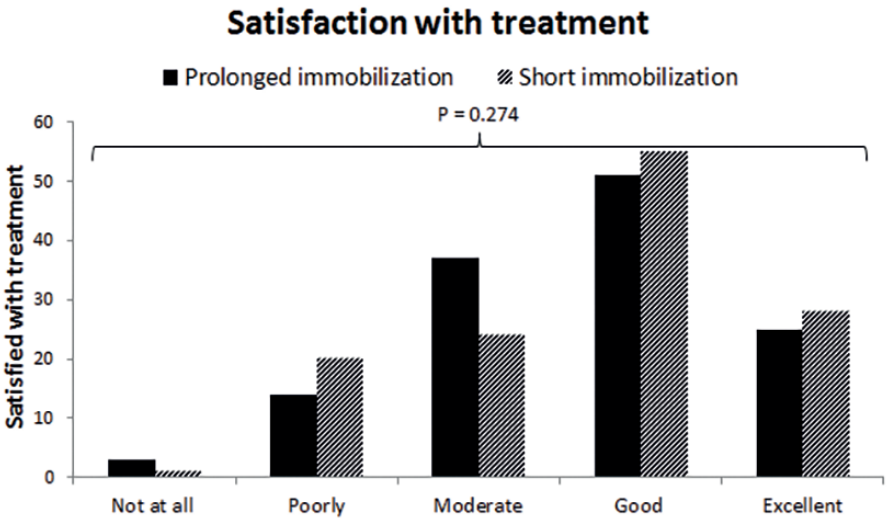


Figure 5. Outcome in overall treatment satisfaction at 3 months in the longer and shorter immobilization group.

Table 2 displays the number of complications in the longer and the shorter immobilization group. No significant differences in complication rate were present in the longer immobilization group compared to the shorter immobilization group (p= 0.102). At baseline, 50-52% of the patients were unemployed or retired. Of the people that were employed, no significant differences in return to work after three months were found between the groups (Table 3).

Table 2. Complications in the prolonged and short immobilization group.

Complications	Prolonged immobilization group (N= 131)	Short immobilization group (N= 131)	p-value
Total No. complications	27	23	0.102
Tendovaginitis Stenosans	4	9	
Carpal tunnel syndrome	3	1	
Tendinitis	9	3	
Neuroma	0	0	
Quervain	8	4	
FCR rupture	0	2	
CRPS	3	1	
Infection	0	1	
Sensory changes	0	1	
MC abutment	0	1	

Furthermore, range of motion and grip & pinch strength (Table 3) were not significantly different between groups, except for radial abduction with 3 degrees in favor of the longer immobilization group (p=0.040). However, this difference lies within the generally accepted measurement error in goniometry measurements, which is more than 5 degrees.[30]

Table 3. Outcome in work and objective measures. Since more than 50% was not currently working, only data of patients that were working was collected. This resulted in a lower number of patients.

Outcome at 3 months	Prolonged immobilization group (N= 46)	Short immobilization group (N= 38)	p-value
Currently working			1.0
- Yes (%)	96	79	
- No, due to thumb complaints (%)	0	0	
- No, due to other reasons (%)	4	21	
Performing original working activities (%)	61	53	0.655
Current number of hours working / week	26 ± 12	23 ± 10	0.191
Key pinch (kg)	3.3 ± 1.4	3.3 ± 1.5	0.824
JAMAR (two-position) (kg)	17.4 ± 1.2	17.6 ± 1.3	0.839
PAB (º)	45 ± 8	44 ± 8	0.267
RAB (º)	47 ± 9	44 ± 14	0.040
MCP extension (º)	-10 ± 12	-8 ± 19	0.430
MCP flexion (º)	60 ± 13	61 ± 18	0.749

DISCUSSION

The aim of this study was to investigate if shorter immobilization is non-inferior compared to longer immobilization after CMC-1 arthroplasty for outcomes on hand function and pain intensity postoperatively. We found that shorter immobilization was equal to longer immobilization in our primary outcomes in terms of MHQ function and VAS pain at six weeks, three months and twelve months. In addition, no significant differences between groups were found in our secondary outcomes in terms of complications, return to work, range of motion, satisfaction with treatment, grip and pinch strength.

The results of our study are in line with several other studies. For example, Horlock et al.[1] compared early with late mobilization in patients after simple trapeziectomy and found no significant differences between both groups in terms of pain, hand function, satisfaction, range of motion and pinch strength. However, patients in the early group experienced significantly more convenience with the post-operative treatment. In addition, Prosser et al.[2] compared rigid with semi-rigid immobilization following trapeziectomy with or without ligament reconstruction and tendon interposition and also found no difference in pain, hand function and pinch strength. Furthermore, when comparing our results with a study by Davis et al.[3] that used a 6-week period of plaster cast immobilization,

again, very similar outcomes are found. For example, 15 out of 62 patients had pain during use at three months, while we found in our study that the mean pain during physical load was 37 on a 0-100 scale. In addition, mean key pinch was 3.1 kg at three months in the study of Davis et al., while our mean key pinch was 3.3 kg at three months. Moreover, both study of Davis et al. and our study showed very low infection rates (<1%).

As mentioned above, our study found equal outcomes on pain and function. These findings suggest that shorter cast immobilization may lead to the same functional outcomes and an even more convenient treatment experience for individual patients. We postulate that shorter cast immobilization will lead to faster recovery of the patient with similar outcomes, which in turn will lead to reduced loss of productivity in working life. A study of Marks et al.[4] showed that the average sick leave in patients treated with a LRTI was 10 weeks, with an average cost due to loss of productivity of €7500. We hypothesize that by applying shorter immobilization, patients will be able to start recovering more quickly while returning earlier to work and daily activities. Hence further cost effectiveness studies on this subject are needed to confirm this hypothesis.

Our study showed that shorter immobilization is safe and will not lead to more complications or worse outcome for patients following Weilby procedure for CMC-1 OA. Conventionally, patients were immobilized for a substantial amount of time after surgery, without sufficient evidence showing that this long period of immobilization was necessary.[5] This study suggests that shorter immobilization may be beneficial by preventing longer patient discomfort. In this study, we only investigated the effect of shorter immobilization, but not of early active and more progressive hand therapy, including early initiation of ROM and strengthening exercises. Future research should investigate the feasibility and possible beneficial effects of early active hand therapy in addition to shorter immobilization. Early active hand therapy may be preferable, since less postoperative stiffness and muscle atrophy will occur. Therefore, longer patient discomfort may be prevented and again, patients will recover more quickly while returning earlier to work and daily activities. Hence, future studies are needed in order to determine the effectiveness of early active and more progressive hand therapy. In addition, we did not assess the effect of different types of orthosis on outcome. Possibly, a different type of orthosis may influence outcome more than different duration of immobilization. Future research should further investigate this.

Study Limitations

Our study has a number of strengths and limitations. The main strength of this study is the large sample size of 262 patients that were included after propensity score matching. To our knowledge, this is the largest study comparing different time frames of immobilization. While the observational character of this study may be a limitation, it is also a strength due to the pragmatic nature; since our data is collected in daily practice it represents the outcomes of actual daily clinical care. Another limitation of this study is that patients were included in two different time periods, resulting in therapists knowing which treatment patients were receiving. However, therapists treating the patients were not aware of the present research question at the time of treatment. Furthermore, we used propensity score matching to correct for potential bias, the only risk being that selection bias still might have occurred if not all relevant covariates were measured at baseline. Furthermore, a limitation of this study is that deviations of the postoperative treatment protocol may have occurred. However, the therapists were extensively trained in using the treatment guidelines and several checks were randomly performed to monitor adherence. Another limitation of this study is that we investigated shorter cast immobilization and earlier transition to an orthosis without wrist immobilization, but only small differences were present in total immobilization period. For example, we did not study potential differences in outcome following 6 weeks or 10 weeks of total immobilization. Therefore, the effect of different time frames in total immobilization periods remains partially unclear and future studies should address this.

Furthermore, a limitation of this study is that we only report outcomes following Weilby procedure. Hence, it is unclear if this postoperative treatment is feasible as well for other surgical procedures on CMC-1 OA, thus future studies should investigate different types of postoperative immobilization for different surgical procedures.

CONCLUSIONS

In conclusion, the present study shows that shorter immobilization provides equal outcomes compared to longer immobilization after Weilby procedure for CMC-1 OA. Hence, we conclude that shorter immobilization is safe and can be recommended due to its potential benefits compared to longer immobilization. More high-quality studies on early active rehabilitation are needed in order to

understand which factors improve patient comfort and return to functional activities.

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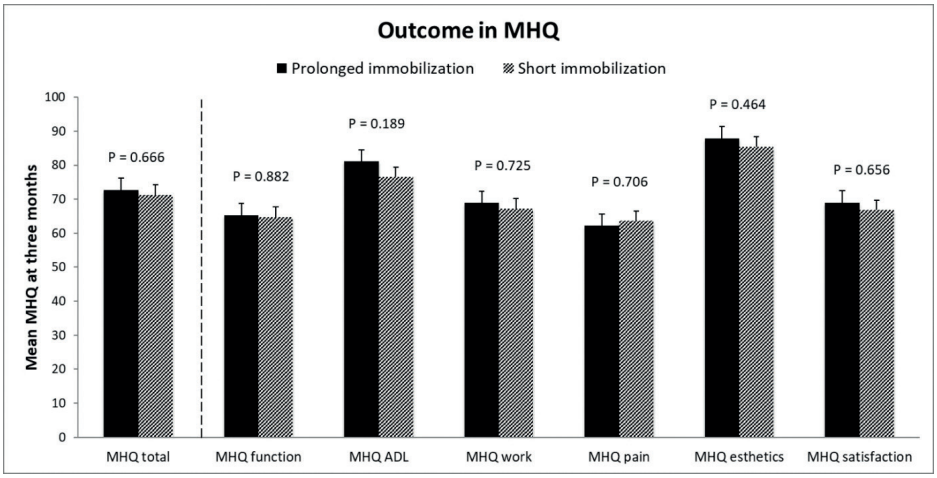

Supplementary Figure 3: Outcome in MHQ total and subscales at twelve months.

GENERAL DISCUSSION

GENERAL DISCUSSION

In this thesis, multiple aspects of the non-operative and postoperative treatment of thumb base (CMC-1) osteoarthritis (OA) were addressed along with outcome measurement in hand and wrist conditions. This general discussion is structured in three parts, following the general structure of this thesis: 1) non-operative treatment and conversion to surgery, 2) postoperative treatment, and 3) outcome measurement in hand and wrist conditions. The main findings of the aforementioned parts and their limitations, implications, and future perspectives are discussed in this chapter.

Part 1 - Non-operative treatment and conversion to surgery

The aims of Part 1 were:

- To describe the outcomes following non-surgical treatment for CMC-1 OA and CMC-1 instability;
- To investigate the added value of exercise therapy in addition to an orthosis in patients with CMC-1 OA;
- To investigate predictors for the outcomes of non-surgical treatment of CMC-1 OA; and
- To compare patients scheduled for CMC-1 resection arthroplasty with their non-surgical counterparts, in terms of sociodemographics, clinical, and psychological factors.

In Part 1, we found beneficial effects of exercise therapy and an orthosis on pain, hand function and several other outcome domains. For CMC-1 OA, only 15% of the patients were surgically treated after a mean follow-up of 2.2 years, and for CMC-1 instability, only 14% were surgically treated after 2.9 years. In patients with CMC-1 OA, exercise therapy in addition to an orthosis was much more effective than an orthosis alone for outcomes on pain and hand function. Further, in Part 1, we found that baseline pain, hand function, satisfaction with the hand, metacarpophalangeal flexion, presence of scaphotrapeziotrapezoid OA, and heavy physical labor predict outcome following non-surgical treatment. In addition, when comparing patients scheduled for CMC-1 resection arthroplasty with their non-surgical counterparts, we found that patients scheduled

to undergo surgery for CMC-1 OA have more symptoms, worse psychological profile and higher treatment expectations than those scheduled for non-surgical treatment. Moreover, we found that having a longer symptom duration, a second-opinion visit, lower satisfaction with the hand, higher treatment expectations, shorter perceived timeline, worse personal control and worse emotional response increased the probability of being scheduled for surgery.

Limitations of Part 1

Several limitations should be acknowledged concerning the studies in Part 1. First, the studies in Part 1 are based on observational data. Hence, the adherence to treatment guidelines might have been suboptimal in some cases, thereby underestimating or overestimating the actual treatment effects. However, the therapists carrying out the treatment were trained to use our treatment guidelines. An additional limitation is that using data collected in daily practice also comes with missing data. This may have biased our results. However, throughout our studies we have performed extensive missing data analyses and consistently found that our data can be qualified as missing completely at random, for which we used appropriate statistical techniques.[1-5] Additionally, in spite of the potential disadvantages of our observational study designs, a major advantage is the ecological validity, since our data are collected in actual daily practice. Hence, our results may be more representative for daily practice compared to standardized randomized controlled trials using strict inclusion criteria. Furthermore, in most studies in this thesis involving patient recruitment, we were able to include relatively high numbers of patients making our studies unique in present literature.

A limitation of Chapter 3 might be that if unidentified covariates were present, indication bias may have occurred in treatment allocation despite the use of propensity score matching (PSM). For example, factors such as treatment costs or traveling distance may have influenced patient preferences. However, again, an advantage of PSM in observational setting is that it allows comparing treatments while maintaining high ecological validity. Furthermore, PSM studies may be more feasible and less burdensome and expensive to perform in daily clinical practice compared to more conventional randomized controlled trials.

An additional limitation of Part 1 is that we only investigated the outcomes of one (Chapter 2, 4 and 5) or two (Chapter 3) different non-operative treatments. Hence, based on the work in this thesis, we now have more evidence for the application of exercise therapy in addition to an orthosis, but we did not compare it with other

non-operative treatments such as injections or placebo treatment. Hence, future studies should compare the outcomes of different non-operative treatments.

Implications and future perspectives of Part 1

Whereas systematic reviews[6-9] and the Dutch treatment guideline[10] advise non-surgical treatment prior to surgical treatment for patients with CMC-1 OA, strong evidence supporting this recommendation was previously lacking. Based on the findings in Part 1, we now have more evidence supporting this recommendation and we therefore strongly recommend non-surgical treatment. Our studies indicate that exercise therapy should be a key element of non-surgical treatment, since we found a relatively large treatment effect compared to using only an orthosis. Furthermore, *no rules of thumb* apply to individuals with CMC-1 OA and baseline factors such as pain, hand function, satisfaction with the hand, metacarpophalangeal flexion, presence of scaphotrapeziotrapezoid OA, heavy physical labor, longer symptom duration, a second-opinion visit, treatment expectations and several aspects of illness perception should be considered in clinical decision making and patient education. Future studies may determine how these factors can be used in clinical practice, for example by implementing them in prediction models.

Since PSM studies may be more feasible and less burdensome and expensive to perform in daily clinical practice compared to more conventional randomized controlled trials, future research should investigate if, and under which conditions PSM studies yield similar outcomes as randomized controlled trials. As we have recently obtained a ZonMW grant, we will perform a multicenter randomized controlled trial on the (cost-) effectiveness of exercise therapy in addition to an orthosis in patients with CMC-1 OA in the near future. In addition to the primary research aims, our new study will present the opportunity to investigate if a randomized controlled trial on exercise therapy in patients with CMC-1 OA leads to similar outcomes as the PSM study in this thesis. In addition, future research might explore if a new level of evidence paradigm is needed, and when randomized controlled trials are necessary considering new statistical techniques and the rise of big data sources.

As Part 1 identified multiple factors that influence treatment choices and treatment outcomes, future research should further study these determinants and aim to develop personalized prediction models. Personalized models that predict the clinical course of patients with CMC-1 OA might help clinicians and

patients in making treatment choices, thereby improving outcome. In addition to personalized prediction models, personalized treatment should also be a topic for future research. In many of the studies in Part 1, we found large variability in outcome, indicating that not every patient fits the mean and that no general *rules of thumb* apply for treating patients with CMC-1 OA. This means, for example, that while this thesis presents more evidence for the application of exercise therapy in patients with CMC-1 OA, future research should investigate the optimal exercise therapy content, number of treatment sessions, and other aspects of exercise therapy to tailor the treatment to individual patients with CMC-1 OA.

Part 2 - Postoperative treatment

The aims of Part 2 were:

- To perform a systematic review on the postoperative rehabilitation following CMC-1 resection arthroplasty;
- To compare the outcomes of shorter and longer immobilization following CMC-1 resection arthroplasty;
- To investigate predictors for acute postoperative pain following CMC-1 resection arthroplasty.

In Part 2, we performed a systematic review to guide clinicians on the content of postoperative rehabilitation for CMC-1 arthroplasty. In this review, we provide an overview of the postoperative rehabilitation protocols used for CMC-1 arthroplasty in literature. We found that early active recovery is used more often in the literature and does not lead to worse outcomes or more complications. However, the review also clearly identified the almost complete lack of high-quality comparative studies on postoperative rehabilitation after CMC-1 arthroplasty. Therefore, we compared shorter immobilization (3-5 days plaster cast followed by a thumb spica orthosis including wrist until 4 weeks postoperatively) with more prolonged immobilization (10-14 days plaster cast followed by a thumb spica orthosis including wrist until 6 weeks postoperatively) following Weilby[11] procedure. In this study, we found that shorter immobilization is equal to more prolonged immobilization for outcomes on pain, hand function, and our secondary outcomes. This finding indicates that shorter immobilization is safe and can be recommended since discomfort of more prolonged immobilization may be prevented. In addition, patients may be able to recover sooner, which

may lead to reduced loss of productivity. In another cohort study, we found that psychological factors, female sex, and opioid usage enhance the prediction of acute postoperative pain beyond type of surgery, sociodemographic and clinical characteristics. Female sex and opioid usage were the strongest predictors, even after controlling for psychological factors. In addition, mean acute postoperative pain scores were lower than mean preoperative pain scores, although it should be taking into account that we found large variability in pain scores.

Limitations of Part 2

Similar to Part 1, Part 2 consists of several observational studies. Hence, the aforementioned limitations and advantages of Part 1 should be considered as well in Part 2. Furthermore, in Part 2, a limitation of our systematic review in Chapter 7 is that we found only a few high-quality studies addressing our research questions on postoperative rehabilitation. Therefore, despite the consistency across the included studies, no definite conclusions on the effectiveness of the specific content of postoperative rehabilitation can be drawn. Another limitation in Part 2, Chapter 8, is that only relatively small differences were present in the immobilization scheme between both groups. Therefore, the difference in outcomes following either shorter or longer immobilization after CMC-1 resection arthroplasty remains partially unclear. A limitation in Part 2, Chapter 9, is that although medication usage was standardized and monitored, deviations on the actual reported opioid usage may have occurred. While opioid usage might also have been influenced by psychological factors[12], this may have contributed to random error or bias, explaining why we found a small explained variance.

Implications and future perspectives of Part 2

In patients surgically treated for CMC-1 OA we recommend short postoperative immobilization based on our systematic review and cohort study. However, more high-quality studies comparing different postoperative rehabilitation protocols (i.e., including early initiation of range of motion or strengthening exercises or larger differences in postoperative immobilization) are needed to understand which factors improve patient comfort and accelerate return to work or other functional activities. Additionally, we strongly recommend that future studies on CMC-1 arthroplasty provide adequate descriptions of their postoperative regime.

With regard to acute postoperative pain, we conclude that *no rules of thumb* apply and that factors such as female sex, opioid usage, preoperative higher satisfaction with the patient's hand, self-reported consequences, and coherence

should be recognized by healthcare providers. These factors might help to better cope with acute postoperative pain and prevent chronic pain[13,14], e.g., by adjusting postoperative medication or improving patient education prior to surgery. Future studies should investigate the influence of psychological characteristics on long-term outcomes following surgery for CMC-1 OA. Additionally, future studies should investigate sex-based approaches and optimal patient education strategies for coping with acute postoperative pain.

Part 3 - Outcome measurement in hand and wrist conditions

The aims of Part 3 were:

- To present the development, design and implementation of the hand and wrist study cohort;

- To describe the process of international standardization of outcome measurement in hand and wrist care, by developing the ICHOM standard set for hand and wrist conditions.

In Part 3, we described how we successfully implemented the design of a routine outcome measurement system in hand and wrist care, with a total of 52.000 individual patients included in our database. Furthermore, we described how our data is collected and used for improving clinical care and performing scientific research. In addition, we described the development of the ICHOM standard set for hand and wrist conditions, for which consensus was reached on creating five measurement tracks: a thumb, finger, wrist, nerve, and severe hand and/or forearm trauma track. Within these tracks, distinction is made between 'regular' and 'extended' tracks. The following outcome domains were considered essential for both the regular and extended thumb track: pain, grip & pinch strength, patient reported hand function and activities of daily living, health-related quality of life, return to work, satisfaction with treatment result, complications, and revision. In addition, range of motion was considered essential for the extended thumb track.

Limitations of Part 3

The compliance of both patients and clinicians remains a big challenge in our routine outcome measurement system.[15] We took several measures to optimize compliance, for example by minimizing the burden of measurements, improving the use of data during interactions between patients and clinicians and

increasing awareness of the value of having outcome data available. Although the value of outcome information is broadly acknowledged, more research is needed to understand how outcome data can be effectively used to improve the quality of care.

When considering our study cohort described in Chapter 10, it should be acknowledged that it represents a very specific group of patients with hand and wrist conditions seeking treatment in the setting of a specialized clinic for hand surgery and therapy. Hence, our study cohort does not always allow generalization to other populations. Additionally, our database does not allow studies on patients with severe hand traumas or severe comorbidity, since those may be treated more often in other healthcare settings such as (academic) hospitals. Another limitation of our study cohort might be that if patients seek treatment elsewhere, they might get out of our sight with insufficient follow-up available.

A limitation of Chapter 11 can be that our consensus initiative reflects an opinion of a selected group of experts. However, we performed multiple systematic reviews to support our choices with evidence and a transparent and structured Delphi-process[16-18] was used. Additionally, the open review period and patient surveys will be used to evaluate support for our approach.

Implications and future perspectives of Part 3

Although implementing a system for routine outcome measurement in daily care comes with several challenges, it would be of great value if more healthcare providers in hand and wrist care would routinely measure outcomes. This would allow comparisons across organizations, treatments and countries, which in turn will facilitate value-based healthcare for patients with hand and wrist conditions globally. In addition to our example of implementing a routine outcome measurement system, we hope that the development of the ICHOM hand and wrist standard set will lead to a common ground for more widespread comparisons of outcomes. However, the feasibility, completeness, and the burden of this newly developed standard set should be evaluated in the future, both from a patient and clinician perspective. Nevertheless, global standardization of outcome measurement using a specific set of outcome measures is needed, e.g., by using the ICHOM standard set for hand and wrist conditions. While measuring outcomes is a first step in providing value-based healthcare, next steps might be to use the collected data to improve the value of care, establish outcome transparency, and develop value-based payment models.

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CHAPTER 13

SUMMARY

SUMMARY

In this thesis, treatment and measurement for thumb base (CMC-1) osteoarthritis (OA) are described. In the following sections, the main findings are summarized, structured by the general parts of this thesis: 1) non-operative treatment and conversion to surgery, 2) postoperative treatment, and 3) outcome measurement in hand and wrist conditions.

Part 1 - Non-operative treatment and conversion to surgery

Treatment guidelines for CMC-1 OA advise starting non-operative treatment before considering surgical interventions, although strong evidence for this was previously lacking. Therefore, in **Chapter 2**, we studied the outcomes of non-operative treatment for CMC-1 OA in daily clinical practice and investigated how many patients converted to surgery. In a sample of 809 patients with CMC-1 OA, we found beneficial effects of non-operative treatment up to 12 months. Moreover, after a mean follow-up of 2.2 years, only 15% of these patients were surgically treated.

To explore the effectiveness of non-operative treatment in more detail, we investigated the added value of exercise therapy in addition to an orthosis in **Chapter 3**. In this prospective observational study, we used propensity score matching and compared a combination treatment of exercise therapy and an orthosis with an orthosis alone (n=84 matched participants) and found that the combination treatment was more effective in reducing pain and improving aspects of hand function than an orthosis alone. In addition, we found that baseline pain, hand function, metacarpophalangeal flexion, presence of scaphotrapeziotrapezoid OA, and heavy physical labor predicted outcome for the group receiving both exercise therapy and an orthosis (n = 131).

Since no studies on non-operative treatment for patients with symptomatic CMC-1 instability are described in literature, and to investigate if our findings in Chapter 2 and 3 apply to patients with symptomatic CMC-1 instability as well, we studied the outcomes of non-operative treatment for CMC-1 instability in **Chapter 4**. In Chapter 4, we analyzed a cohort of patients (n = 431) receiving non-operative treatment, including exercise therapy and an orthosis, and found clinically relevant improvements in pain and hand function. Furthermore, after a median follow-up of 2.8 years, only 14% of all patients were surgically treated.

In **Chapter 5**, we performed a more in-depth analysis of predictors for outcome of non-operative treatment for CMC-1 OA. In this multi-center cohort study (n = 809), the multivariable regression models explained 34% of the variance in outcome for pain and 42% for hand function. In these models, we found that baseline pain, hand function, and satisfaction with the hand were predictors for the outcome at three months or eventually converting to surgery. Furthermore, 73% and 83% of the patients with no clinically relevant improvement in respectively pain and function after 6 weeks, demonstrated no clinically relevant improvement after 3 months.

To investigate conversion to surgery in patients with CMC-1 OA in more detail, we compared patients scheduled for CMC-1 resection arthroplasty with their non-surgical counterparts in **Chapter 6**. In our sample, we found that patients scheduled to undergo surgery (n = 208) have more symptoms, worse psychological profile and higher treatment expectations than patients scheduled for non-surgical treatment (n = 376). Furthermore, in the hierarchical logistic regression analysis we found that having a longer symptom duration, a second-opinion visit, lower satisfaction with the hand, higher treatment expectations, shorter perceived timeline, worse personal control, and worse emotional response increased the probability of being scheduled for surgery.

Part 2 - Postoperative treatment

Despite that the Dutch guideline and systematic reviews emphasize the importance of postoperative rehabilitation following CMC-1 arthroplasty, there is no consensus on the most effective implementation of postoperative rehabilitation. Therefore, we performed a systematic review on postoperative rehabilitation following CMC-1 arthroplasty in **Chapter 7**. Twenty-seven studies were included in this systematic review, consisting of 1015 participants in whom 1118 surgical procedures were performed. We found considerable variation in postoperative immobilization schemes and exercise or therapy regimens. Furthermore, we found that early active recovery (including short immobilization, early initiation of range of motion, and strength exercises) is used more often in the literature and does not lead to worse outcomes or more complications, but comparative studies were lacking. Furthermore, three postoperative exercises/therapy phases were identified: 1) the acute phase, 2) the unloaded phase, and 3) the functional phase.

Since our systematic review identified an almost complete lack of high-quality comparative studies on postoperative rehabilitation following CMC-1 arthroplasty, we compared two different postoperative immobilization schemes in **Chapter 8**. We used propensity score matching in a sample of 262 patients to investigate if shorter immobilization (including 3-5 days plaster cast followed by a thumb spica orthosis including wrist until 4 weeks postoperatively) is non-inferior to longer immobilization (including 10-14 days plaster cast followed by a thumb spica orthosis including wrist until 6 weeks postoperatively). Following the general principles of non-inferiority analyses, we found equality for hand function and pain at rest and non-inferiority for pain during physical load when comparing shorter immobilization with longer immobilization. In addition, no differences were found in complication rate or other secondary outcomes, indicating that shorter immobilization is safe and can be recommended.

In contrast to long-term outcomes for postoperative pain following CMC-1 arthroplasty, little is known about acute postoperative pain following CMC-1 arthroplasty. In **Chapter 9,** we found that psychological factors, female sex, and opioid usage enhanced the prediction of acute postoperative pain beyond surgery type, sociodemographic and clinical characteristics in a sample of 215 patients treated surgically for CMC-1 OA. Female sex and opioid usage were the strongest predictors, even after controlling for psychological factors. In addition, mean acute postoperative pain scores were lower than preoperative pain levels.

Part 3 - Outcome measurement in hand and wrist conditions

In **Chapter 10** we described the development, design and implementation of the Hand and Wrist Study Cohort at our treatment centers for hand and wrist care (currently 22) in the Netherlands, starting in 2011. Using this routine outcome measurement system, the total number of yearly assigned measurement tracks increased up to over 16.500 in 2018, adding up to 85.000 tracks in 52.000 patients in total. Implementing this system was feasible using a highly automated data collection infrastructure, tightly linked to the patient journey and the workflow of healthcare professionals. We hope that our example of a routine outcome measurement system encourages other healthcare providers in hand and wrist care globally to measure and compare outcomes.

With an emphasis on thumb conditions, **Chapter 11** describes the design and principles for developing the standard set for hand and wrist conditions by the International Consortium for Health Outcome Measurement (ICHOM).

An international working group of experts in hand and wrist care representing eleven countries was assembled to review literature and practices for assessing outcomes of treatment for hand and wrist conditions. Consensus was reached on five measurement tracks: the thumb, finger, wrist, nerve and severe trauma track, with a distinction between 'regular' and 'extended' tracks. The following outcome domains were considered 'essential' for the thumb track: pain, grip & pinch strength, patient reported hand function and activities in daily living, health-related quality of life, return to work, satisfaction with treatment result, complications, revision and range of motion (the last only in the extended track).

Chapter 12 discusses the main findings of Parts 1-3, their limitations, implications and future perspectives.

CHAPTER 14

NEDERLANDSE SAMENVATTING

NEDERLANDSE SAMENVATTING

In dit proefschrift worden de behandeling en uitkomstmetingen voor duimbasis (CMC-1) artrose (OA) beschreven. In de volgende paragrafen worden de belangrijkste bevindingen samengevat, gestructureerd conform de algemene delen van dit proefschrift: 1) niet-operatieve behandeling en conversie naar chirurgie; 2) postoperatieve behandeling; en 3) uitkomstmetingen in hand- en polsaandoeningen.

Deel 1 - Niet-operatieve behandeling en conversie naar chirurgie

Behandelrichtlijnen voor CMC-1 OA adviseren om met niet-operatieve behandeling te starten alvorens chirurgische ingrepen te overwegen, hoewel daarvoor eerder geen sterk bewijs was. Daarom hebben we in **hoofdstuk 2** de uitkomsten van niet-operatieve behandeling van CMC-1 OA in de dagelijkse klinische praktijk bestudeerd en onderzocht hoeveel patiënten zijn overgegaan naar operatieve behandeling. In een steekproef van 809 patiënten met CMC-1 OA vonden we gunstige effecten van niet-operatieve behandeling tot 12 maanden na aanvang van de behandeling. Bovendien werd na een gemiddelde follow-up van 2,2 jaar slechts 15% van deze patiënten chirurgisch behandeld.

Om de effectiviteit van niet-operatieve behandeling in meer detail te onderzoeken, hebben we de toegevoegde waarde van oefentherapie naast het gebruik van een duimspalk onderzocht in **hoofdstuk 3**. In deze prospectieve observationele studie hebben we propensity score matching gebruikt en een combinatiebehandeling van oefentherapie en een duimspalk vergeleken met een behandeling bestaande uit alleen een duimspalk (n = 84 deelnemers). Uit deze studie bleek dat de combinatiebehandeling effectiever was in het verminderen van pijn en het verbeteren van aspecten van handfunctie dan alleen een duimspalk. Bovendien bleek dat factoren zoals baseline pijn, handfunctie, metacarpophalangeale flexie, aanwezigheid van scaphotrapeziotrapezoïde artrose en zware fysieke arbeid de uitkomst voorspelde voor de groep die zowel oefentherapie als een duimspalk kreeg (n = 131).

Omdat er geen studies bestaan in de literatuur over niet-operatieve behandeling voor patiënten met symptomatische CMC-1-instabiliteit en om te onderzoeken of onze bevindingen uit hoofdstuk 2 en 3 ook van toepassing zijn op patiënten met symptomatische CMC-1-instabiliteit, hebben we de uitkomsten van niet-operatieve behandeling voor CMC-1 instabiliteit onderzocht in **hoofdstuk 4**. In dit

hoofdstuk analyseerden we een cohort van patiënten (n = 431) die niet-operatieve behandeling ontvingen, bestaande uit oefentherapie en een duimspalk. We constateerden klinisch relevante verbeteringen op de uitkomstmaten pijn en handfunctie. Bovendien werd na een mediane follow-up van 2,8 jaar slechts 14% van alle patiënten chirurgisch behandeld.

In **hoofdstuk 5** hebben we een meer diepgaande analyse van voorspellers voor de uitkomst van niet-operatieve behandeling van CMC-1 OA uitgevoerd. In dit multicenter cohortonderzoek (n = 809), verklaarden de multivariabele regressiemodellen 34% van de variantie in uitkomst voor pijn en 42% in de uitkomst voor handfunctie. In deze modellen vonden we dat baseline pijn, handfunctie en tevredenheid met de hand voorspellers waren voor de uitkomst na drie maanden of conversie naar chirurgie. Wanneer er na de eerste 6 weken geen klinisch relevante verbetering was opgetreden in respectievelijk pijn en handfunctie, bleek dit in 73% en 83% van de patiënten na 3 maanden ook niet het geval.

Om de conversie naar chirurgie bij patiënten met CMC-1 OA in meer detail te onderzoeken, vergeleken we patiënten die waren gepland voor CMC-1 resectie-arthroplastiek met hun niet-chirurgische tegenhangers in **hoofdstuk 6**. In dit onderzoek vonden we dat patiënten die gepland waren om een operatie te ondergaan (n = 208) meer symptomen, een slechter psychologisch profiel en hogere verwachtingen van de behandeling hadden dan patiënten gepland voor niet-chirurgische behandeling (n = 376). Verder vonden we in de hiërarchische logistische regressieanalyse dat een langere duur van klachten, een second opinion bezoek, lagere tevredenheid met de hand, hogere verwachtingen van de behandeling, kortere verwachting van de ziekteduur, slechtere persoonlijke controle en slechtere emotionele respons de kans vergroten om gepland te worden voor operatieve behandeling.

Deel 2 - Postoperatieve behandeling

Ondanks dat de Nederlandse richtlijn en systematische reviews het belang van postoperatieve revalidatie na CMC-1-artroplastiek benadrukken, bestaat er geen consensus over de meest effectieve invulling van postoperatieve revalidatie. Daarom hebben we in **hoofdstuk 7** een systematisch literatuuronderzoek uitgevoerd omtrent postoperatieve revalidatie na CMC-1-arthroplastiek. In dit systematische literatuuronderzoek werden 27 studies opgenomen, waarin totaal 1015 personen deelnamen en 1118 chirurgische procedures werden uitgevoerd. We vonden aanzienlijke variatie in postoperatieve immobilisatieduur en oefen- of

therapieschema's. Verder hebben we geconstateerd dat vroeg actieve revalidatie (bestaande uit korte immobilisatie en vroege initiatie van mobiliteits- en krachtoefeningen) steeds vaker wordt toegepast in de literatuur en niet tot slechtere uitkomsten of meer complicaties leidt, echter ontbraken vergelijkende studies. Tevens werden drie postoperatieve therapiefasen geïdentificeerd: 1) de acute fase, 2) de onbelaste fase en 3) de functionele fase.

Omdat onze systematische literatuurstudie aantoonde dat er een vrijwel geen vergelijkende studies van hoge kwaliteit zijn uitgevoerd omtrent postoperatieve revalidatie na CMC-1-arthroplastiek, vergeleken we twee verschillende postoperatieve immobilisatieschema's in **hoofdstuk 8**. We gebruikten propensity score matching in een steekproef van 262 patiënten om te onderzoeken of kortere immobilisatie (bestaande uit 3-5 dagen gipsverband gevolgd door een verlengde duimspalk inclusief de pols tot 4 weken na de operatie) minder goede resultaten geeft in vergelijking met langere immobilisatie (bestaande uit 10-14 dagen gipsverband gevolgd door een verlengde duimspalk inclusief de pols tot 6 weken na de operatie). In deze non-inferioriteitsstudie vonden we dat de twee verschillende postoperatieve immobilisatieprotocollen gelijke resultaten gaven voor uitkomsten op handfunctie en pijn in rust en non-inferieure resultaten voor pijn tijdens belasting. Bovendien werden geen verschillen gevonden in complicaties of andere secundaire uitkomstmaten, hetgeen aangeeft dat kortere immobilisatie veilig is en kan worden aanbevolen.

In tegenstelling tot de langetermijnresultaten voor postoperatieve pijn na CMC-1-artroplastiek is er weinig bekend over acute postoperatieve pijn na CMC-1-artroplastiek. In **hoofdstuk** 9 vonden we in een steekproef van 215 patiënten die chirurgisch werden behandeld voor CMC-1 OA dat psychologische factoren, vrouwelijk geslacht en opioïdengebruik de voorspelling van acute postoperatieve pijn verbetert, boven type chirurgie, sociodemografische of klinische kenmerken. Vrouwelijk geslacht en gebruik van opioïden waren de grootste voorspellers, zelfs na controleren voor psychologische factoren. Bovendien waren de gemiddelde acute postoperatieve pijnscores lager dan preoperatieve pijnscores.

Deel 3 - uitkomstmetingen in hand- en polsaandoeningen

In **hoofdstuk 10** hebben we de ontwikkeling, het design en de implementatie van het "Hand and Wrist Study Cohort" in onze behandelcentra voor hand- en polszorg (momenteel 22) in Nederland beschreven, hetgeen plaatsvindt sinds 2011. Met behulp van dit routinematige uitkomstmeetsysteem werden in 2018

een totaal van 16.500 meettrajecten toegewezen. Over alle jaren heen zijn er inmiddels meer dan 85.000 trajecten toegewezen aan 52.000 patiënten. De implementatie van dit systeem was mogelijk vanwege een zeer geautomatiseerde infrastructuur voor dataverzameling, nauw verbonden met de zogenaamde “patient journey” en de workflow van zorgprofessionals. We hopen dat het voorbeeld van ons systeem andere zorgaanbieders wereldwijd aanmoedigt om ook uitkomsten te meten en deze met elkaar te vergelijken.

Met de nadruk op duimaandoeningen wordt in **hoofdstuk 11** het design en de principes voor het ontwikkelen van een standaard set voor hand- en polsaandoeningen beschreven, welke wordt ontwikkeld door het International Consortium for Health Outcome Measurement (ICHOM). Een internationale werkgroep van experts in hand- en polszorg uit elf landen werd samengesteld, om literatuur en methodes te beoordelen voor het meten van uitkomsten van de behandeling voor hand- en polsaandoeningen. Consensus werd bereikt omtrent vijf meettrajecten: het duim-, vinger-, pols-, zenuw- en ernstige traumatraject, met een onderscheid tussen ‘reguliere’ en ‘uitgebreide’ trajecten. De volgende uitkomstdomeinen werden als ‘essentieel’ beschouwd voor het duimtraject: pijn, knijp- & pinchkracht, patiënt-gerapporteerde handfunctie en activiteiten in het dagelijks leven, gezondheid gerelateerde kwaliteit van leven, werkhervatting, tevredenheid met het resultaat van de behandeling, complicaties, revisie en bewegingsuitslag (laatstgenoemde alleen in het uitgebreide traject).

Hoofdstuk 12 bespreekt de belangrijkste bevindingen van deel 1-3, de beperkingen, implicaties en perspectieven voor toekomstig onderzoek.

APPENDICES

ABOUT THE AUTHOR
PHD PORTFOLIO
AUTHORS AND AFFILIATIONS
LIST OF PUBLICATIONS
ACKNOWLEDGEMENTS

ABOUT THE AUTHOR

Robbert Wouters was born on December 19th, 1988 in Nieuwegein, The Netherlands. After graduating from the Cals College, Nieuwegein, he studied Physical Therapy at Hogeschool Utrecht. His interest in hand and wrist conditions arose during the minor Hand Rehabilitation, organized at the Utrecht Hand Center (Handencentrum Utrecht, Handtherapie Nederland). Subsequently, he did an internship at the Hand Therapy Department of Erasmus MC, University Medical Center Rotterdam, and graduated as a Physical Therapist in 2010. Following his graduation, he started working as a Hand Therapist at Handtherapie Nederland / Xpert Clinic and became a Certified Hand Therapist (CHT-NL). After working as a Physical Therapist for a few years, his interest in research increased and he obtained a Master's degree in Clinical Health Sciences, direction Physiotherapy Science in 2016 at Utrecht University. He did an internship at the Department of Rehabilitation Medicine and Plastic, Reconstructive and Hand Surgery during this master's under the supervision of Dr. Ruud Selles. After he graduated as a Clinical Health Scientist, he continued to do research on Hand Surgery and Rehabilitation and started his PhD trajectory, supervised by Em. Prof. Dr. Henk Stam, Dr. Ruud Selles and Dr. Harm Slijper. He was appointed as a Research Fellow at the International Consortium for Health Outcome Measurement (IHCOM) in 2018, aiming to develop the ICHOM Standard Set for Hand and Wrist conditions in close collaboration with Em. Prof. Dr. Steven Hovius, who is the project chair. During his PhD period, he did research internships at the Program in Placebo Studies & Integrated Brain Health Clinical and Research Program of Harvard Medical School (Dr. Ana-Maria Vranceanu), and at the Faculty of Health Sciences and Department of Plastic and Reconstructive Surgery, Epidemiology & Physical Therapy of McMaster University and Western University (Prof. Dr. Joy MacDermid). In 2019, he obtained a ZonMW Doelmatigheid Grant of €451.000 as main applicant in close collaboration with Dr. Ruud Selles, which facilitates him to continue to do research as a Postdoctoral Researcher.

PHD PORTFOLIO

Summary of PhD training and teaching

Name PhD student: Robbert Wouters Erasmus MC Department: Rehabilitation & Plastic Surgery Research School: NIHES	PhD period: Sept 2016 – Jul 2019 Promotor: Em. Prof. Dr. Henk J. Stam Copromotors: Dr. Ruud W. Selles, Dr. Harm P. Slijper

1. PhD training

	Year	Workload (ECTS)
General courses		
- Biomedical English Writing and Communication	2018	3
- Research Integrity	2018	0.3
- Statistics: Basic Course on R	2019	1.8
- BROK ('Basiscursus Regelgeving Klinisch Onderzoek'	2018	1.5
Specific courses (e.g. Research school, Medical Training)		
- Summer School Research Methods in Hand Rehabilitation and Hand Surgery	2018	2.1
Seminars and workshops		
- Research meetings Hand Wrist Study Group, Erasmus MC	2016-2019	3.6
- Scientific meeting of the Royal Dutch Physical Therapy Society (KNGF)	2017	0.3
- Scientific meeting of the Royal Dutch Physical Therapy Society (KNGF)	2018	0.3
- Scientific meeting of the Royal Dutch Physical Therapy Society (KNGF)	2019	0.3
Presentations – oral		
EUROHAND 2017 (FESSH/EFSHT combined congress), Budapest, Hungary:		
- Exercise therapy in addition to an orthosis reduces pain more than an orthosis alone in patients with thumb base osteoarthritis: a propensity score matching study	2017	0.7
- Conservative treatment in thumb base osteoarthritis: what we have learned of our data	2017	0.7
National Physical Therapy Congress (DVDF) of the Royal Dutch Physical Therapy Society (KNGF), Barneveld, The Netherlands:		
- Routine outcome measurement as a part of usual care: application in scientific research on thumb base osteoarthritis	2017	0.7
MacHand Grand Rounds, McMaster University, Hamilton, Canada:		
- Defining an International Standard Set of Outcome Measures for Patients with Hand & Wrist conditions: Consensus of the International Consortium for Health Outcomes Measurement (ICHOM) Hand & Wrist Working Group – an update (invited speaker)	2018	0.7
Congress of Dutch Society for Surgery of the Hand & Dutch Hand Therapy Association, Arnhem, The Netherlands:		

Summary of PhD training and teaching

	Year	Workload (ECTS)
- Defining an International Standard Set of Outcome Measures for Patients with Hand & Wrist conditions: Consensus of the International Consortium for Health Outcomes Measurement (ICHOM) Hand & Wrist Working Group – an update	2018	0.7
Hand Unit Meeting in Nuffield Orthopaedic Centre, Oxford University, UK:		
- Defining an International Standard Set of Outcome Measures for Patients with Hand & Wrist conditions: Consensus of the International Consortium for Health Outcomes Measurement (ICHOM) Hand & Wrist Working Group – an update (invited speaker)	2019	0.7
IFSSH/IFSHT combined congress 2019, Berlin, Germany:		
- Beneficial Effects of Non-surgical Treatment for Symptomatic Thumb Carpometacarpal Instability in Clinical Practice: A Cohort Study	2019	0.7
- International Standardization of Outcome Measurement for Patients with Hand & Wrist conditions: Consensus by the International Consortium for Health Outcome Measurement (ICHOM) Hand & Wrist Working Group (keynote invited speaker)	2019	0.9
Presentations – poster		
National Physical Therapy Congress (DVDF) of the Royal Dutch Physical Therapy Society (KNGF), Maarssen, The Netherlands:		
- Exercise therapy in addition to an orthosis reduces pain more than an orthosis alone in patients with thumb base osteoarthritis: a propensity score matching study	2016	0.4
Annual meeting of American Society for Surgery of the Hand (ASSH), Boston, USA:		
- Short immobilization is non-inferior to prolonged immobilization after surgery for thumb base osteoarthritis: a propensity score matching study	2018	0.4
National Physical Therapy Congress (DVDF) of the Royal Dutch Physical Therapy Society (KNGF), Den Bosch, The Netherlands:		
- Short immobilization is non-inferior to prolonged immobilization after surgery for thumb base osteoarthritis: a propensity score matching study	2018	0.4
(Inter)national conferences		
- Dutch Hand Therapy Society (NVHT) symposium: Fractures, Breukelen, The Netherlands	2016	0.4
- Dutch Hand Therapy Society (NVHT) symposium: Nerves, Bussum, The Netherlands	2018	0.4
- Federation of European Societies for Surgery of the Hand (FESSH) annual meeting, Copenhagen, Denmark	2018	1.1
- School of physical therapy research symposium, Western University, London (Ontario), Canada	2018	0.4
- Big data symposium, Maastricht University Medical Center	2019	0.3
- International Consortium for Health Outcome Measurement (ICHOM) conference, Rotterdam, The Netherlands	2019	0.7
- Buckinghamshire Hand Symposium, Postgraduate Centre, Stoke Mandeville Hospital/Oxford University, UK	2019	0.3

Summary of PhD training and teaching

	Year	Workload (ECTS)
2. Teaching		
Lecturing		
- All-round Opleiding Handtherapie (AOHT); education in Hand Therapy (CMC-1 OA, Joint prostheses, Rheumatoid Arthritis), Utrecht, The Netherlands	2016-2019	4.4
- Rehabilitation of the hand and wrist in daily practice – Thumb base osteoarthritis: background and clinical practice, KU Leuven, Leuven, Belgium (invited speaker)	2017	1.1
- Hand Therapy Education, the thumb unraveled, Hilversum, The Netherlands	2017	0.6
- Minor teacher medical training, Erasmus MC, anatomy of the hand and forearm and injuries of the upper extremity	2017-2018	0.6
- Hand Therapy Education, Masterclass Thumb: Thumbs Up, Utrecht, The Netherlands	2019	0.9
Supervising students		
- Minor students systematic review, Erasmus MC	2018	0.4
- Master's student, NIHES, Erasmus MC: The longitudinal course of radiographic thumb base osteoarthritis signs in a Dutch population-based study cohort: the Rotterdam study	2018-2019	1.4
Other		
- Research internship, Program in Placebo Studies & Integrated Brain Health Clinical and Research Program, Massachusetts General Hospital & Harvard Medical School, Boston, USA	2018	4.3
- Research internship, Faculty of Health Sciences, McMaster University & Dept. of Plastic and Reconstructive Surgery, Epidemiology & Physical Therapy, Western University, Hamilton/ London Ontario, Canada	2018	4.3
Grants		
- Stichting Geert Geertsen: €25.000 (main applicant)	2017	
- ZonMW Doelmatigheid: 451.000 (main applicant)	2019	
Total		41.8 ECTS

AUTHORS AND AFFILIATIONS

Jonathan Tsehaie

- Dept. of Rehabilitation Medicine, Erasmus MC, Rotterdam, the Netherlands.
- Dept. of Plastic and Reconstructive, and Hand surgery, Erasmus MC, Rotterdam, the Netherlands.
- Hand and Wrist Center, Xpert Clinic, the Netherlands.

Kim R. Spekreijse

- Dept. of Rehabilitation Medicine, Erasmus MC, Rotterdam, the Netherlands.
- Dept. of Plastic and Reconstructive, and Hand surgery, Erasmus MC, Rotterdam, the Netherlands.
- Hand and Wrist Center, Xpert Clinic, the Netherlands.

Harm P. Slijper

- Dept. of Rehabilitation Medicine, Erasmus MC, Rotterdam, the Netherlands.
- Dept. of Plastic and Reconstructive, and Hand surgery, Erasmus MC, Rotterdam, the Netherlands.
- Hand and Wrist Center, Xpert Clinic, the Netherlands.

Reinier Feitz

- Hand and Wrist Center, Xpert Clinic, the Netherlands.

Steven E.R. Hovius

- Dept. of Plastic Surgery, Radboud UMC, Nijmegen, the Netherlands.
- Former head of Dept. of Plastic and Reconstructive, and Hand surgery, Erasmus MC, Rotterdam, the Netherlands.
- Hand and Wrist Center, Xpert Clinic, the Netherlands.

Ruud W. Selles

- Dept. of Rehabilitation Medicine, Erasmus MC, Rotterdam, the Netherlands.
- Dept. of Plastic and Reconstructive, and Hand surgery, Erasmus MC, Rotterdam, the Netherlands.

Lisa Esteban Lopez

- Center for Hand Therapy, Handtherapie Nederland, The Netherlands.

Ana-Maria Vranceanu

- Integrated Brain Health Clinical and Research Program, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA.

Guus M. Vermeulen

- Hand and Wrist Center, Xpert Clinic, the Netherlands.

Mark J.W. van der Oest

- Dept. of Rehabilitation Medicine, Erasmus MC, Rotterdam, the Netherlands.
- Dept. of Plastic and Reconstructive, and Hand surgery, Erasmus MC, Rotterdam, the Netherlands.
- Hand and Wrist Center, Xpert Clinic, the Netherlands.

Burcu Dilek

- Department of Physical Therapy and Rehabilitation, Medipol University, Istanbul, Turkey.

J. Sebastiaan Souer

- Hand and Wrist Center, Xpert Clinic, the Netherlands.

Joy C. MacDermid

- School of Physical Therapy, Western University, London, ON, Canada.
- School of Rehabilitation Science, McMaster University, Hamilton, ON, Canada.
- The Hand and Upper Limb Centre, St Joseph's Health Centre, London, ON, Canada.

Ralph Poelstra

- Dept. of Rehabilitation Medicine, Erasmus MC, Rotterdam, the Netherlands.
- Dept. of Plastic and Reconstructive, and Hand surgery, Erasmus MC, Rotterdam, the Netherlands.
- Hand and Wrist Center, Xpert Clinic, the Netherlands.

Thybout M. Moojen

- Hand and Wrist Center, Xpert Clinic, the Netherlands.

Yara E. van Kooij

- Dept. of Rehabilitation Medicine, Erasmus MC, Rotterdam, the Netherlands.
- Dept. of Plastic and Reconstructive, and Hand surgery, Erasmus MC, Rotterdam, the Netherlands.
- Center for Hand Therapy, Handtherapie Nederland, The Netherlands.

Pierre Y. Pennehouat

- Center for Hand Therapy, Handtherapie Nederland, The Netherlands.

Rob van Huis

- Hand and Wrist Center, Xpert Clinic, the Netherlands.

Adedayo O. Jobi-Odeneye

- International Consortium for Health Outcomes Measurement, London, United Kingdom.

Alethse de la Torre

- International Consortium for Health Outcomes Measurement, London, United Kingdom.

Alexander Y. Shin

- Dept. of Orthopaedic Surgery, Division of Hand and Microvascular Surgery, Mayo Clinic, Rochester MN, USA.

David Warwick

- Dept. of Hand Surgery, University Hospital Southampton, Southampton, United Kingdom.

Christine B. Novak

- Dept. of Plastic & Reconstructive Surgery; Dept. of Surgery, University of Toronto and Hospital for Sick Children, Toronto ON, Canada.

Goo Hyun Baek

- Department of Orthopaedic Surgery, Seoul National University Hospital and Seoul National University College of Medicine, Seoul, Korea.

Gregory I. Bain

- Department of Orthopaedics, Flinders University; Flinders Medical Center, Bedford Park, SA, Australia.

Christina Jerosch-Herold

- School of Health Sciences, University of East Anglia, Norwich, United Kingdom.

Kevin C. Chung

- Dept. of Plastic Surgery, The University of Michigan Medical School, Ann Arbor MI, USA.

Lars B. Dahlin

- Dept. of Translational Medicine - Hand Surgery, Lund University; Dept. of Hand Surgery, Skåne University Hospital, Malmö, Sweden.

Martin Iglesias

- Dept. of Plastic Surgery, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico.

Çigdem Öksüz

- Dept. of Occupational Therapy, Faculty of Health Sciences, Hacettepe University, Ankara, Turkey.

S. Raja Sabapathy

- Dept. of Plastic, Hand and Microsurgery and Burns, Ganga Hospital, Coimbatore, India.

Lucelle van de Ven-Stevens

- Dutch Association of Occupational Therapy, Dutch Society for Hand Surgery, Dutch Society for Hand Therapy, The Netherlands.

Ryan Trickett

- Dept. of Trauma and Orthopaedics, Cardiff and Vale University Health Board, Cardiff, United Kingdom.

Gürsel Leblebicioğlu

- Dept. of Orthopaedic Surgery and Traumatology, Division of Hand Surgery, Hacettepe University, Ankara, Turkey.

Maurizio Calcagni

- Dept. of Plastic Surgery and Hand Surgery, University Hospital Zurich, Switzerland.

LIST OF PUBLICATIONS

Publications in this thesis

Tsehaie J, Spekreijse KR, **Wouters RM**, Slijper HP, Feitz R, Hovius SE, Selles RW. Outcome of a Hand Orthosis and Hand Therapy for Carpometacarpal Osteoarthritis in Daily Practice: A Prospective Cohort Study. *The Journal of hand surgery.* 2018;43(11):1000-1009. e1001.

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*both authors contributed equally to this article

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Wouters RM, Jobi-Odeneye AO, de la Torre A, Shin AY, MacDermid JC, Warwick D, Novak CB, Baek GH, Bain GI, Jerosch-Herold C, Chung KC, Dahlin LB, Iglesias M, Öksüz C, Sabapathy SR, van de Ven-Stevens LA, Trickett R, Leblebicioğlu G, Calcagni M, Selles RW, Hovius SER. Standardization of Outcome Measurement in Hand & Wrist conditions: The Design and Principles of the International Consortium for Health Outcomes Measurement (ICHOM) Hand & Wrist Standard Set. *Submitted.* 2019.

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Esteban Lopez L, Schoneveld K, **Wouters RM**, Kiers H. Wat is het beloop bij patiënten met CMC1-instabiliteit tijdens een conservatief behandeltraject gemeten met de MHOQ en VAS? *Ned Tijdschr HT.* 2016;Nov 2016.

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Oest MJW, Hoogendam L, **Wouters RM**, Vermeulen GM, Slijper HP, Selles RW, Vranceanu AM, Porsius JT, Study Group H-W. More positive treatment outcome expectations and better illness understanding are associated with better outcomes: a cohort study on non-operative treatment of first carpometacarpal osteoarthritis. *Submitted.* 2019.

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Ik waardeer je voortdurende aandrang om de invloed van ‘mindset’ op fysiek ongemak te begrijpen en ben hier dankzij jou ook meer en meer gefascineerd door geraakt. Het was geweldig om je in Boston op te zoeken en laten we snel weer eens proosten met een goede IPA!

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Prof. Dr. Joy MacDermid, dear Joy, thank you for the opportunity to collaborate on several projects. To me, you are an example as a researcher and I have learned a lot from working together and visiting you at McMaster/Western. Hopefully, we can continue this in the future.

Dr. Ana-Maria Vranceanu, dear Ana-Maria, I would like to thank you for hosting me at Harvard/MGH in Boston and critically appraising our papers. Your efforts have improved every manuscript and it is inspiring to observe your urge to create more awareness for the influence of a patient's mindset.

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