The effect of an exercise program in patients with thumb base osteoarthritis: a prospective cohort study with propensity score matching

Masterthesis

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“ONDERGETEKENDE

Robbert Maarten Wouters,

bevestigt hierbij dat de onderhavige verhandeling mag worden geraadpleegd en vrij mag worden gefotokopieerd. Bij het citeren moet steeds de titel en de auteur van de verhandeling worden vermeld.”

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SAMENVATTING

Doelstelling: Dit onderzoek vergelijkt het effect van een combinatie van oefen- en spalktherapie met spalktherapie alleen op pijn en activiteiten in het dagelijks leven (ADL) bij patiënten met arthrose (OA) van de duimbasis (CMC-1). Daarnaast worden predictoren van uitkomsten op pijn en ADL onderzocht om zorg voor individuele patiënten met CMC-1 OA te optimaliseren.

Methode: Een prospectieve cohortstudie is uitgevoerd in elf behandelcentra voor handchirurgie en handtherapie in Nederland. Een combinatie van oefentherapie en spalktherapie is vergeleken met spalktherapie alleen door propensity score matching (PSM) toe te passen. Primaire uitkomsten in deze studie waren pijn en ADL na drie maanden, hetgeen gemeten is met een Visual Analogue Scale (VAS) en Michigan Hand outcomes Questionnaire (MHQ). Linear mixed model analyse is gebruikt om de groepen onderling te vergelijken en multipele regressie analyse is gebruikt op baseline karakteristieken van de totale spalk- en oefentherapiegroep om predictoren van uitkomsten te identificeren.

Resultaten: In totaal werden 107 participanten geïncludeerd, waarvan er 44 gematched zijn met behulp van PSM. Een grotere afname in VAS pijn bij fysieke belasting werd gevonden in de oefentherapie groep (35 punten) in vergelijking met de spalktherapie groep (19.5 punten, $p=0.012$). Uitkomsten op de MHQ-score lieten geen klinisch relevante verschillen zien. Behandeling van de dominante zijde, hogere flexie van het eerste metacarphophalangeale gewricht, hogere leeftijd en type werk met zware fysieke belasting voorspelden uitkomsten op pijn en ADL in de totale oefentherapiegroep ($N=85$).

Conclusie: Er werden betere resultaten gevonden in de oefentherapiegroep dan in de spalktherapiegroep, hetgeen positieve effecten van oefentherapie indiceert. Daarnaast zijn er verscheidene predictoren voor uitkomsten na oefentherapie geïdentificeerd. Toekomstig onderzoek dient oefentherapie en predictoren van uitkomsten in een grotere steekproef en meer gestandaardiseerde setting te onderzoeken.

Klinische relevantie: Het toepassen van oefentherapie in de klinische praktijk blijkt van meerwaarde te zijn voor individuele patiënten met CMC-1 OA.

Nederlands Trial Register Trial ID: NTR5627.

ABSTRACT

Aim: This study compares the effect of a combination of an exercise program and splinting with splinting alone on pain and activities in daily life (ADL) in patients osteoarthritis (OA) of the thumb base joint (CMC-1). Furthermore, this study investigates predictors for outcomes on pain and ADL in order to optimize healthcare for individual patients with CMC-1 OA.

Methods: A prospective cohort study was conducted in eleven outpatient clinics for hand surgery and hand therapy in the Netherlands. A combination of an exercise program and splinting was compared with splinting alone using propensity score matching (PSM). Primary outcomes included pain and ADL at three months, measured with a Visual Analogue Scale (VAS) and the Michigan Hand outcomes Questionnaire (MHQ). Linear mixed model analysis was used to study between-group differences and multiple regression analysis on baseline characteristics for the total exercise program group was used in order to identify predictors for outcome.

Results: In total, 107 participants were included, of which 44 were matched using PSM. A larger decrease in VAS pain during physical load was found in the exercise program group (35 points) compared to the splint group (19.5 points, p=0.012). Outcomes on the MHQ score showed no clinically relevant differences. Treatment of the dominant side, higher flexion of the first metacarpophalangeal joint, higher age and type of work with heavy physical labor predicted outcomes on pain or ADL for the total exercise program group (N=85).

Conclusion: Superior results were found for the exercise program group when compared to the splint group, indicating positive effects of an exercise program. Furthermore, several predictors for outcomes on splinting combined with an exercise program were identified. Future research should study exercise programs and predictors of outcome in a larger sample and a more standardized setting.

Clinical Relevance: Applying exercise programs in clinical practice appears to be beneficial for individual patients with CMC-1 OA.

Dutch Trial Register Trial ID: NTR5627.

Keywords (MeSH): Thumb, Osteoarthritis, exercise therapy, propensity score

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] CMC-1 OA is classified using the Eaton classification, which runs from stage I (no degeneration) to IV (extensive degeneration of both the CMC-1 and scaphotrapeziotrapezoid joint (STT)).[4] There is a modest to strong association between radiologically diagnosed CMC-1 OA and older age, thumb pain, limitations in ADL and other clinical features of CMC-1 OA such as thenar muscle wasting, presence of nodes or thumb deformity.[2,5] The number of patients with CMC-1 OA is expected to increase because of the ageing population.[6]

CMC-1 OA arises due to multiple factors, such as age, gender, biological factors, genetic associations and several factors related to characteristics of the joint.[1,7-11] The CMC-1 is a saddle joint, which allows wide range of motion (ROM), but offers little stability.[7,9,10,12] The dorsal ligament complex, inter metacarpal ligament and volar beak ligament become lax as one ages, resulting in more instability.[9] Instability of the CMC-1 leads to high peak load at the joint surface, which is up to twelve times the force applied at the distal end of the thumb.[7,13-15] The high peak load at the joint surface results in synovitis and cartilage degeneration, ultimately resulting in OA.[7,13-15] As a result of degeneration and instability, an adduction contracture with loss of the first web space may occur.[15] Patients with CMC-1 OA often experience pain, have reduced pinch- and/or grip strength and report limitations in activities of daily life (ADL).[16]

The Dutch Society for Hand Surgery (NVvH) recommends to treat patients with CMC-1 OA conservatively before surgery should be considered.[17] When conservative treatment fails to reduce pain and limitations in ADL, CMC-1 arthroplasty may be considered.[17-19] However, the high costs of surgery are unfavorable since the costs for patients with OA increased with 55.6% in the Netherlands between 2007 and 2011 and the CMC-1 OA prevalence increases.[6,20] Furthermore, CMC-1 surgery is accompanied by long recovery, resulting in prolonged patient discomfort and further increase of costs due to more hand therapy sessions and inability to work.[18,19]

Although there is no consensus on the best conservative treatment, interventions such as exercise programs and splinting are applied in clinical practice.[15,21-26] Because the CMC-1 becomes less stable during flexion and adduction,[7,9-11] most exercise programs intend to improve active stability and positioning of the CMC-1 into extension and abduction, since the joint is more stable in these positions.[7,9,23,25,26] The intrinsic thenar muscles (except the adductor pollicis), extensor pollicis brevis and the first dorsal interosseus prevent subluxation and support the CMC-1 in abduction and extension.[7] Therefore, these muscles are often trained in order to maintain the first web space, improve thumb positioning, pinch strength and active stability of the CMC-1.[7,15,24-26] Splinting often complements exercise programs, in order to reduce subluxation and inflammation.[7,24]

In spite of promising results of exercise programs and splinting on pain and ADL, it remains difficult to define an evidence based conservative treatment strategy since few studies regarding exercise programs are conducted, and those available are of low methodological quality.[21,22,24] Furthermore, it is unclear which patients benefit from exercise programs.[25] It is, for example, unclear if strengthening exercises should be applied in patients with Eaton stage >III.[4,25] More research regarding the effect of exercise programs and splinting is needed because of the indications for effectiveness, low costs and fast recovery.[21,22,24,26] This prospective cohort study aims to compare the effect of a combination of an exercise program and splinting with splinting alone on pain and ADL in patients with CMC-1 OA. The risk of indication bias is minimized by using propensity score matching (PSM), which allows researchers to correct for observed covariates when randomization is not feasible or ethical.[27,28] Furthermore, this study investigates predictors for outcomes of a combination of an exercise program and splinting on pain and ADL in order to optimize healthcare for individual patients with CMC-1 OA.

MATERIALS & METHODS

Study design

This is a prospective cohort study with PSM using a nonprobability consecutive sample, reported following the STROBE statement.[29] Prospective data collection was part of usual care. Participants with CMC-1 OA were matched using PSM in order to compare a combination of an exercise program and splinting with splinting alone. PSM 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.[27,28] PSM 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.[28]

Setting

This study was performed in eleven outpatient clinics for hand surgery and hand therapy in The Netherlands. Data collection took place between October 2015 and June 2016. The Medical Research Ethical Committee of the Erasmus MC Rotterdam approved the fulfillment of this study. Written informed consent was not obtained, since data collection was part of usual care. A certified hand surgeon diagnosed patients with CMC-1 OA using the NVvH guideline,[17] which includes physical examination and radiographic evaluation to determine Eaton stage[4] using standardized methods. After diagnosis, patients with CMC-1 OA were referred for hand therapy and treatment was initiated. Due to the observational study design, treatment was not completely standardized as in randomized controlled trials. However, the hand therapists carried out the treatment following the guideline developed by Handtherapie Nederland B.V.[30] Furthermore, the hand therapists completed a survey at baseline, six weeks and three months, providing information about the content of treatment to ensure guideline usage.[30] The guideline includes splinting and an exercise program, but the exercise program is not applied for every patient (i.e. due to costs of hand therapy or traveling distance).

Follow-up with the hand surgeon took place after three months.

Participants

In order to be eligible to participate in this study, participants needed to meet the following criteria: 1) adult; 2) CMC-1 OA diagnosed by a certified hand surgeon using the NVvH guideline[17]; 3) Eaton I-IV.[4] Subjects were excluded if they met the following criteria: 1) secondary CMC-1 OA (i.e. due to Bennett's fracture); 2) comorbidity that interferes with treatment or outcome (i.e. Quervain's tenosynovitis); 3) patient history includes surgery that interferes with treatment or outcome; or 4) steroid injection <6 weeks in hand or wrist.

Treatment

Participants in the exercise program group received an exercise program which included hand therapy sessions and a splint in order to reduce synovitis and instability of the CMC-1.[24,31] The splint immobilized the CMC-1 in extension and abduction and the first metacarpophalangeal joint (MCP-1) in flexion. The aim of the exercise program was to improve active stability of the CMC-1 during pinch in extension and abduction, as instability and degeneration occurs in flexion and adduction.[7,9-11,15,25] In the first phase of treatment (week 0-6), the intrinsic thenar muscles (except the adductor pollicis), extensor pollicis brevis and the first dorsal interosseus were trained.[7,15,25] In the second phase (week 6 – 3 months), splint usage is reduced and strengthening exercises for the thenar muscles (accept the adductor pollicis) were applied.[15,25] More details on the exercise program can be found in Appendix 1. Participants in the splint group were provided with the same splint, but no hand therapy sessions were conducted.

Variables

The primary outcomes of this study were pain and ADL. Pain at rest and during physical load was measured at baseline, six weeks and three months using a Visual Analogue Scale (VAS, range: 0-100, higher scores indicate more pain). The VAS is a simple, reliable and valid instrument to measure pain intensity in patients with rheumatic diseases.[32] The minimal detectable change (MDC) of the VAS is eleven points in patients with rheumatoid arthritis.[32] ADL was measured at baseline and three months using the Michigan Hand Outcomes Questionnaire – Dutch Version (MHQ), which measures hand function (defined as ADL in this study).[33] The MHQ has six subscales: overall hand function, ADL, pain, work performance, aesthetics and satisfaction (range: 0–100, higher scores indicate better performance except for the subscale pain).[33] The MHQ total score was a primary outcome and subscales were secondary outcomes. The MHQ has a high internal consistency, high internal validity, acceptable reliability and is particularly applicable for patients with hand OA.[33] The minimal clinical important difference (MCID) for the MHQ is 10.8 (10.9 – 21.3 for the subscales) in patients with hand disorders.[34]

The secondary outcomes of this study are pinch & grip strength, return to work and patient satisfaction. Pinch & grip strength was measured at baseline and three months using the Biometric E-Link© following Mathiowetz et al., which is reliable and valid.[35-37] Despite that

pinch & grip strength concern physical forces, outcomes on pinch & grip strength are often expressed in kilograms or pounds instead of Newton.[36,38] The MCID for grip strength is 0.84 kg in patients with CMC-1 OA.[39] No usable MCID was found for pinch strength in the literature, since the Biometric© pinchmeter differs from standard pinchmeters.[37] Pinch strength measures included key, three-jaw (also known as palmar) and tip-to-tip pinch (also known as tip-pinch).[35]
Outcomes on return to work and patient satisfaction were collected at three months using self-designed questionnaires, containing five and two items respectively. The return to work questionnaire focuses on the employability of the patient (N/A for unemployed participants) and the patient satisfaction questionnaire asks the patient's opinion about the results of treatment.

Additional characteristics were obtained at baseline in order to predict primary outcomes for exercise program group, including: MCP-1 hyperextension, MCP-1 flexion, inter metacarpal distance (IMD), presence of STT OA (Eaton >III), age, gender, type of work (unemployed, light, moderate or heavy physical labor), therapy frequency, duration of symptoms and dominant side treated. MCP-1 ROM (flexion/hyperextension) was measured using the recommendations of the American Society of Hand Therapists.[40] IMD during abduction of the CMC-1 was measured using a caliper, because its reliability is superior compared to goniometric measurements.[41,42] IMD measurements were used to compare the affected with the unaffected side, since IMD differs between subjects due to differences in hand size.[42] Stage of CMC-1 OA was determined in a standardized method by a certified hand surgeon using the Eaton classification.[4,17] Age, female gender, type of work, therapy frequency, duration of symptoms and dominant side treated was determined using the Pulse database and surveys completed by the hand therapists.

Data sources/measurement

Data was registered in the shared database of the Erasmus MC, Handtherapie Nederland B.V. and Xpert Clinic, called Pulse. Pulse includes standardized forms for data registration in this study.

Bias

Usually, comparing groups in observational studies is difficult due to the presence of covariates.[43] PSM accounts for this if all relevant covariates are included in the model estimating the propensity score, which allows group comparisons without introducing indication bias.[43] Furthermore, measurement bias is prevented since the hand therapists performed and registered all measurements using standardized forms and were trained to conduct measurements using standardized methods.[35,40]

Study size

A priori power analysis was performed using a conventional effect size of .25,[44] resulting in a total sample of 88 for a Power of .95 (α=0.05). However, due to the nature of PSM, a part of the sample will be excluded from the analysis. No recommendations regarding power analysis in PSM were found in the literature. A study regarding Dupuytren's disease by Zhou et al.[45] used PSM as well, in which 60% of the total sample was included in the final analysis. Therefore, it was estimated that at least 60% of the total sample would be included in the final analysis, resulting in an estimated sample of 146 prior to PSM.

Quantitative variables

Outcomes on VAS, MHQ and pinch & grip strength contained resulted in continuous variables in the analyses. The return to work and patient satisfaction questionnaires contained ordinal, dichotomous and continuous outcomes.

The presence of hyperextension at the MCP-1 was dichotomized and MCP-1 flexion was used as a continuous variable. Measurements regarding IMD were dichotomized, in which 3.3 mm difference between the unaffected and affected side was defined as limited IMD, since 3.3 mm is the MDC for IMD measurements.[42] In bilateral involvement, the hand with the worst baseline MHQ score was considered as the affected hand.

Statistical methods

Between-group differences in demographic characteristics were analyzed using independent samples t-tests and Chi square tests. If the assumption that 20% of the cells have an expected count of <5 was not met, Fisher's exact test was used.

The propensity scores were estimated using logistic regression, in which treatment status is regressed on baseline characteristics.[27,28,46] The following baseline characteristics were used to determine the propensity score: 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), age, gender, type of work, duration of symptoms and dominant side treated. The propensity scores were then 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.[28,46]

The primary and secondary outcomes (except return to work and patient satisfaction) were analyzed using univariate Linear Mixed Model regression (LMM) analysis after PSM. Residual plots were used to evaluate normality, linearity and homoscedastic assumptions. Return to work and patient satisfaction were analyzed on independent questionnaire items. Continuous outcomes were tested using independent samples t-tests if data were normally distributed. Outcomes on questions with ordinal, dichotomous or not normally distributed continuous outcomes were tested using Mann-Whitney tests.

Multiple regression analysis was used on all the unmatched participants in the exercise program group in order to predict outcomes on the primary outcomes. The following characteristics were used in multiple regression analysis: MCP-1 hyperextension, MCP-1 flexion, limited IMD, presence of STT OA (Eaton >III), age, gender, type of work, duration of symptoms and dominant side treated. Categorical or dichotomous variables were recoded into dummy variables. The data were checked for multicollinearity using correlation coefficients and the variance inflation factor (VIF). A VIF >10 was considered an indication for multicollinearity.[47]

Missing data were present in the Pulse database in 25-52% of the datasets for patients with CMC-1 OA between 2012 and 2014. Hence, missing data were expected in this study. To determine if missing data were missing completely at random (MCAR), Little's test was used.[48-50] When data were MCAR, multiple imputation (MI) on predictors was used to obtain missing data. No MI was used on outcome variables, since treatment effect is the unknown independent factor and imputations may influence outcomes.[48,51,52]

RESULTS

Initially, 115 participants were included in this study (Figure 1). One participant (0.9%) was excluded due to comorbidity (Bennett's fracture in history) and seven participants (6.1%) were excluded because of corticosteroid injection(s) due to comorbidity. Hence, 107 participants were finally included. The splint group contained 22 participants and the exercise program group contained 85 participants. On baseline characteristics needed for PSM, missing values were found for VAS pain at rest and during physical load (3.7%), MHQ total score (59.8%), MCP-1 hyperextension (22.4%), MCP-1 flexion (22.4%) and limited IMD (26.2%). Analysis of the missing values showed a non-significant Little's test (p=0.134), which confirmed the hypothesis that the missing values were MCAR. Hence, MI was used to obtain these values. After PSM, both groups contained 22 participants. No significant differences on baseline characteristics were found between the groups before and after PSM (Table 1).

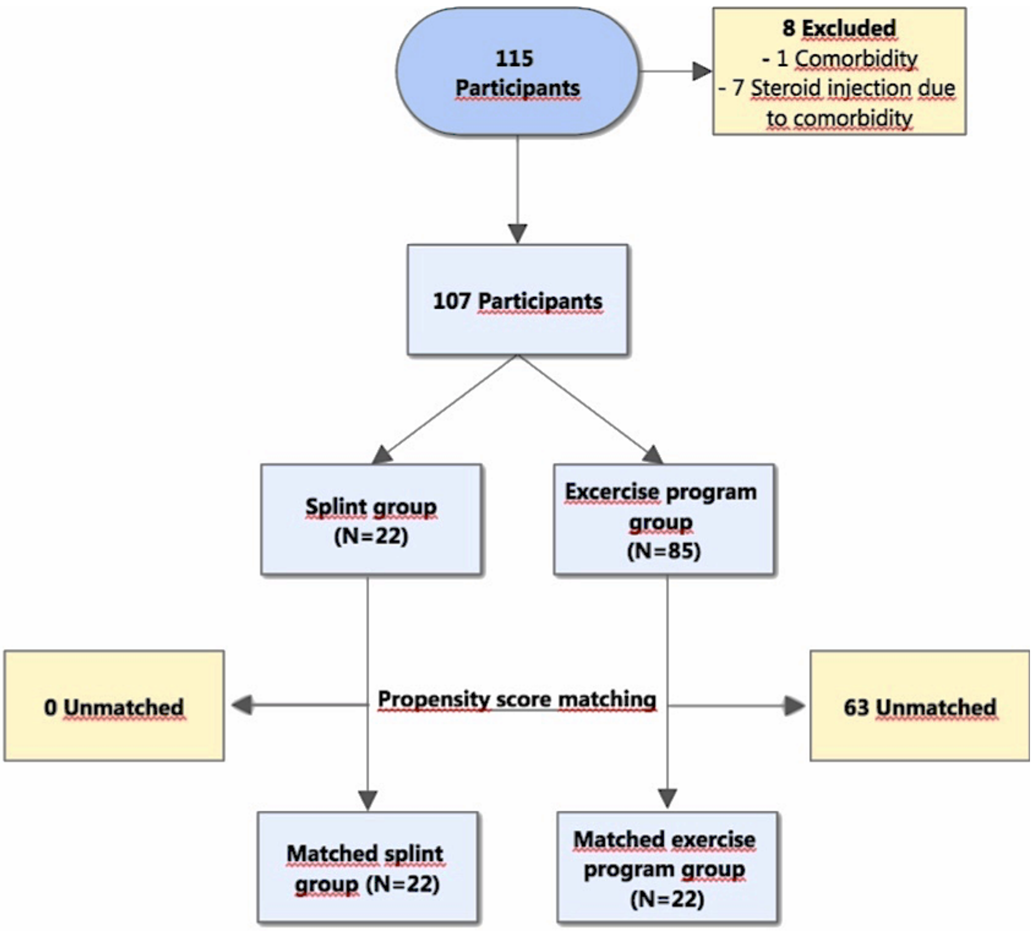

Figure 1: Flow chart of this study

Table 1: Demographic characteristics of the unmatched and matched participants. Characteristics between the groups were compared before and after matching 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.

			All Participants			Matched Participants		
			Splint group	*Exercise program group*	*p-value*	*Splint group*	*Exercise program group*	*p-value*
Participants, N		107	22	85		22	22	
Demographics								
Age in years, mean (SD)		61.2 (8.7)	60.0 (9.8)	61.5 (8.4)	0.481	60.0 (9.8)	60.1 (9.1)	0.968
Females, N (%)		77 (72.0%)	15 (68.2%)	62 (72.9%)	0.658	15 (68.2%)	15 (68.2%)	1.000
Dominant side treated, N (%)		52 (48.6%)	13 (59.1%)	39 (45.9%)	0.341	13 (59.1%)	13 (59.1%)	1.000
Type of work, N (%)	*Unemployed*	50 (46.7%)	12 (54.5%)	38 (44.7%)	0.802	12 (54.5%)	11 (50.0%)	0.875
	Light physical labor	21 (19.6%)	3 (13.6%)	18 (21.2%)	0.802	3 (13.6%)	5 (22.7%)	0.875
	Moderate physical labor	22 (20.6%)	5 (22.7%)	17 (20.0)	0.802	5 (22.7%)	5 (22.7%)	0.875
	Heavy physical labor	14 (13.1%)	2 (9.1%)	12 (14.1%)	0.802	2 (9.1%)	1 (4.5%)	0.875
Duration of symptoms in months, mean (SD)		27.5 (32.8)	24.6 (19.2)	28.3 (35.6)	0.637	24.6 (19.2)	34.4 (41.1)	0.316
Eaton Stage OA, N (%)	*I-III*	90 (84.1%)	18 (81.8%)	72 (84.7%)	0.748	18 (81.8%)	20 (90.9%)	0.644
	IV	17 (15.9%)	4 (18.2%)	13 (15.3%)	0.748	4 (18.2%)	2 (9.1%)	0.644
MCP-1 Hyperextension, N (%)		77 (72%)	14 (63.6%)	63 (74.1%)	0.577	15 (68.2%)	16 (72.7%)	0.517
MCP-1 flexion in degrees, mean (SD)		51.2 (12.3)	49.3 (11.3)	51.7 (12.6)	0.479	49.5 (11.6)	48.6 (15.5)	0.872
IMD limited, N (%)		36 (33.6%)	6 (27.3%)	30 (35.3%)	0.409	5 (22.7%)	6 (27.3 %)	1.000

Primary & secondary outcomes

Table 2 provides an overview of the outcomes of the matched participants. The mean number of therapy sessions was 7.2 (SD 2.2) in the exercise program group. There were missing data in 38.6% for the VAS scores and 59.1% for the MHQ scores at three months. Missing value analysis showed a non-significant Little's test (p=0.410), hence it was assumed that missing values were MCAR.

VAS pain at rest showed a larger decrease in the exercise program group (15.6 points) compared to the splint group (5.7 points, p=0.173). Furthermore, a larger decrease in VAS pain during physical load was found in the exercise program group (35 points) compared to the splint group (19.5 points, p=0.012, Figure 2). Significant between-group differences were found on the MHQ total score (p=0.028) and the MHQ subscale aesthetics (p=0.019). No significant differences were found on other MHQ subscales or pinch & grip strength.
Outcomes on return to work were available for 27 (61.4%) of the matched participants, of which 23 were unemployed at baseline. Hence, statistical testing between the groups was considered nonsensical en was not performed.
Sixteen (36.4%) of the matched participants (five in the splint group, eleven in the exercise program group) completed the patient satisfaction questionnaire. No between-group differences were found in experienced treatment result (p=0.320) or the wish to undergo the treatment again (p=0.320).

Table 2: Outcomes of matched participants. The p-values displayed indicate significance of treatment effect in linear mixed model analysis. VAS = Visual Analogue Scale, MHQ = Michigan Hand Outcomes Questionnaire – Dutch Version, ADL = activities in daily life.

	Splint group			**Exercise program group**			**p-value**
	Baseline	*6 weeks*	*3 months*	*Baseline*	*6 weeks*	*3 months*	
VAS pain rest, mean (SD)	32.8 (21.8)	28.6 (26.6)	27.1 (22.0)	29.4 (24.7)	16.1 (20.9)	13.8 (18.6)	0.173
VAS pain physical load, mean (SD)	69.9 (15.4)	50.1 (23.7)	50.4 (21.2)	64.6 (19.5)	43.1 (22.6)	29.4 (24.3)	0.012
MHQ, mean (SD) Total	50.1 (14.6)	-	65.0 (23.8)	55.7 (21.1)	-	71.5 (15.5)	0.028
Subscales:							
- Overall hand function	51.0 (15.2)	-	61.0 (18.5)	57.5 (12.7)	-	64.6 (10.1)	0.197
- ADL	62.0 (23.6)	-	81.0 (17.8)	68.5 (17.3)	-	75.4 (22.9)	0.841
- Work performance	62.0 (39.6)	-	57.0 (44.7)	61.0 (28.8)	-	73.1 (29.6)	0.650
- Pain	55.0 (26.9)	-	51.0 (36.5)	60.0 (23.6)	-	39.6 (17.6)	0.659
- Aesthetics	072.5 (14.4)	-	67.3 (39.4)	86.9 (14.0)	-	92.3 (12.1)	0.019
- Satisfaction	50.6 (23.6)	-	57.5 (30.7)	49.6 (21.6)	-	62.2 (19.5)	0.707
Grip strength, mean (SD)	23.6 (8.7)	-	19.2	21.9 (11.4)	-	24.3 (10.0)	0.785
Key pinch, mean (SD)	4.7 (2.5)	-	4.1	5.2 (2.0)	-	5.1 (1.4)	0.603
Three jaw pinch, mean (SD)	4.1 (1.8)	-	4.0	3.9 (1.5)	-	4.3 (2.8)	0.976
Tip to tip pinch, mean (SD)	2.8 (1.4)	-	3.7	3.0 (1.4)	-	3.1 (1.8)	0.636
Experienced treatment result, %							0.320
- Excellent			0 %			9.1%	
- Good			20%			36.4%	
- Fair			20%			18.2%	
- Moderate			40%			27.3%	
- Poor			20%			9.1%	
Participants that would undergo treatment again, %			40 %			72.7%	0.320

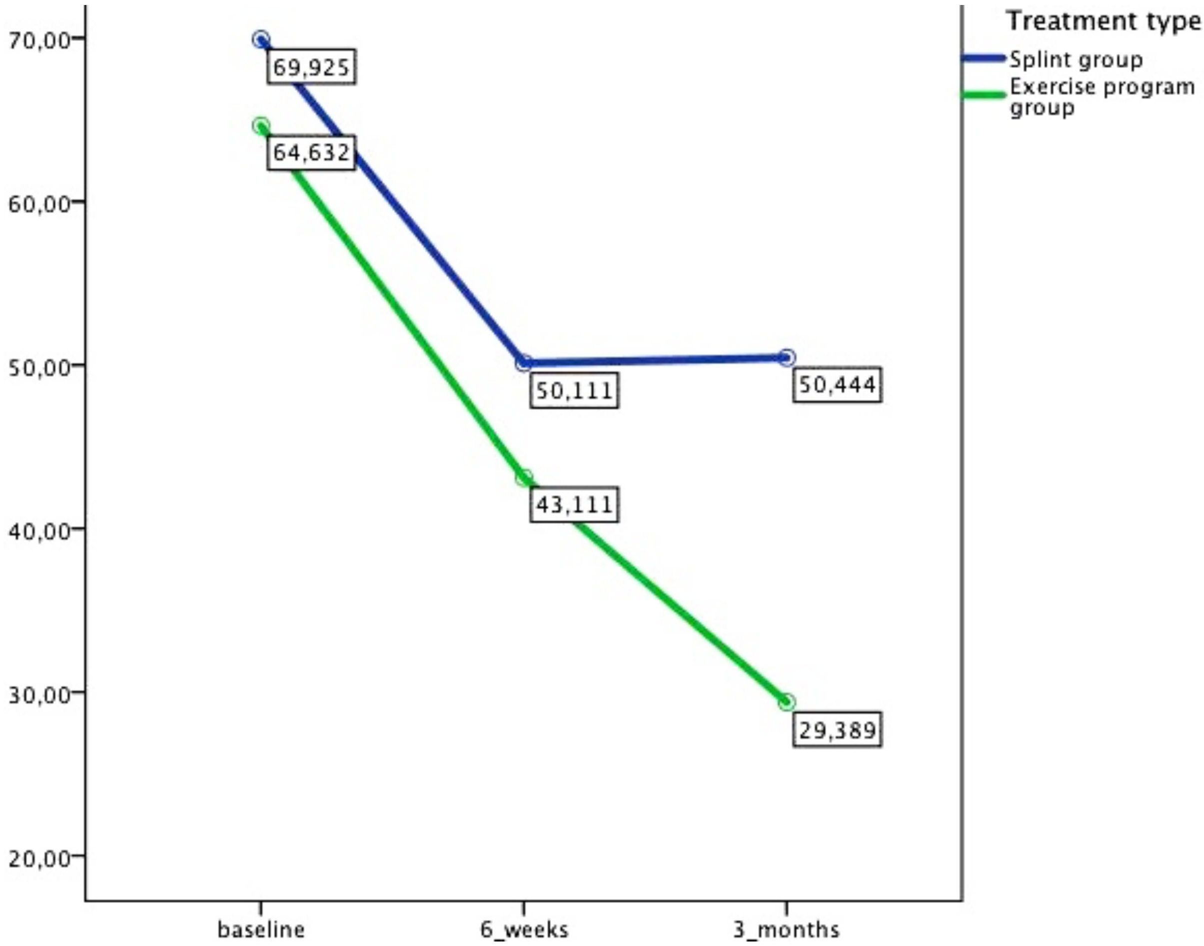

Figure 2: Development for Visual Analogue Scale pain during physical load over time for the splint group (blue line) and the exercise program group (green line)

Prediction of outcome

Backward multiple regression identified several predictors for the primary outcomes in the total exercise program group (n=85, Table 3). No indications for multicollinearity were found. Multivariate analyses suggested a relationship between treatment of the dominant side and lower VAS pain at rest score (adjusted R-square=0.035). Furthermore, higher MCP-1 flexion and higher age was related with a lower VAS pain during physical load score (adjusted R-square=0.052). In addition, type of work with heavy physical labor was related with a lower MHQ total score (adjusted R-square=0.057).

Table 3: Predictors for outcomes in the exercise program group on Visual Analogue Scale (VAS) pain during physical load and at rest and the Michigan Hand Outcomes Questionnaire – Dutch Version (MHQ) total score.

Predictor	Exp (B)	Adjusted R square	p-value
VAS pain rest		0.035	
- Dominant side treated	-7.884		0.065
VAS pain physical load		0.052	
- Age	-0.591		0.064
- ROM MCP-1 flexion	-0.434		0.051
MHQ total score		0.057	
- Type of work: heavy physical labor	-13.690		0.081

DISCUSSION

The aim of this prospective cohort study was to investigate the effect of a combination of an exercise program and splinting compared to splinting alone on pain and ADL in patients with CMC-1 OA. Furthermore, this study aimed to investigate predictors for outcomes of a combination of an exercise program and splinting on pain and ADL in order to optimize healthcare for individual patients with CMC-1 OA. This study showed superior results on pain during physical load for the exercise program group when compared to the splint group (Table 2). Significant differences were found on outcomes on MHQ total and the subscale aesthetics No significant differences were found for other MHQ subscales, VAS pain at rest, pinch & grip strength and patient satisfaction. Several predictors for outcome were identified, including treatment of the dominant side, higher MCP-1 flexion, higher age and type of work with heavy physical labor (Table 3).

The findings with regard to treatment effect are not completely in line with the literature. The studies of O'Brien et al.[26] and Wajon et al.[23] found positive results on pain and ADL for exercise programs in patients with CMC-1 OA as well. In contrast, three systematic reviews found insufficient evidence for the use exercise programs for patients with CMC-1 OA.[21,22,24] However, these different findings may be due to large differences in exercise programs, since the studies by O'Brien et al.[26] and Wajon et al.[23] conducted similar exercise programs and used similar splints as in this study, while the studies included in the systematic reviews mainly applied manual mobilizations of the CMC-1.[21,22,24] Furthermore, methodological flaws were present in the studies included in the systematic reviews.[21,22,24]

This study found a significant between-group difference for the MHQ total score (p=0.028, Table 2). However, there was only a between-group difference of 0.8 points at three months. The significant outcome on LMM analysis may be since the groups were not similar at baseline (difference = 5.6 points), which indicates that this difference is not clinically relevant.

This study found relationships between treatment of the dominant side and VAS pain at rest, between higher MCP-1 flexion, higher age and VAS pain during physical load and between type of work with heavy physical labor and outcomes on and MHQ total score. STT OA was no predictor for outcome in this study, indicating that the exercise program was feasible for patients with Eaton stages I-IV CMC-1 OA. The findings with regard to MCP-1 flexion suggest that the exercise program may have had a positive influence on biomechanics during pinch force, since prevention of MCP-1 hyperextension and applying MCP-1 flexion during pinch force prevents subluxation en further degeneration of the CMC-1.[7,9-11,25]
It is unclear why type of work with heavy physical labor was related with a lower MHQ total score. A possible explanation may be that it is more difficult for patients with heavy physical labor to adapt in ADL. However, no literature regarding this predictor was found. Furthermore, it is unclear why treatment of the dominant side and higher age is related with lower outcomes on pain. The adjusted R squares that were found in multiple regression implicate that the identified predictors only explain 3.5-5.7% of the variance in outcome (Table 3). In addition, bias may be present due to the observational character of this study. Therefore, these predictors should be interpreted with caution and further research on predictors for outcomes of exercise programs for patients with CMC-1 OA is needed in a more standardized setting.

It is a strength that, to our knowledge, this is the first prospective study that compared an exercise program combined with splinting to splinting alone in patients with CMC-1 OA. Furthermore, another strength is that this is the first study on patients with CMC-1 that identifies predictors for outcomes of conservative treatment.

A limitation of this study is that indication bias may have occurred in treatment allocation. Despite the use of PSM, unidentified covariates may be present that influence treatment allocation or outcome. Further exploration of the treatment effect of exercise programs is needed, for example in randomized controlled trials.
Another limitation of this study is that the estimated total sample was not reached due to time constrains. Furthermore, there were large differences in group size before PSM. Despite several significant findings, less statistical power is achieved due to the small sample size and a larger treatment effect then identified in this study may be present. For example, VAS pain at rest or MHQ work performance showed superior but non-significant results in the exercise program group (Table 2). Hence, it is recommended that future research on this topic is employed in a larger study sample and that future studies using PSM account for differences in group size prior to data collection.
In addition, a limitation of this study is the presence of missing values. The use of MI on baseline measures may have introduced bias, although missing values were MCAR. Despite that LMM analysis allows missing values,[51] substantial statistical power is lost and bias may be present. Therefore, it is recommended that future research on this topic focuses on the prevention of missing data during data collection.

CONCLUSION

In conclusion, this study found positive effects of an exercise program on pain during physical load in patients with CMC-1 OA. Furthermore, treatment of the dominant side, higher MCP-1 flexion, higher age and type of work with heavy physical labor predict outcomes for splinting combined with an exercise program. Future research should study exercise programs and predictors of outcome in a larger sample and more standardized setting.

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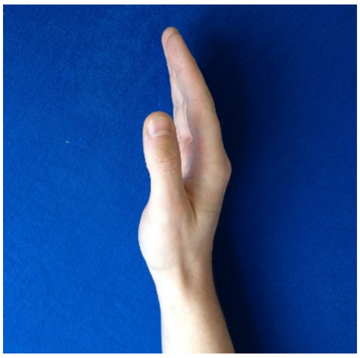
APPENDIX 1

First phase of treatment (week 0-6)

Examples of the exercises, performed 4-6 times a day, 10-15 repetitions.[25,30]

1 – Abductor pollicis brevis, opponens pollicis

A



B

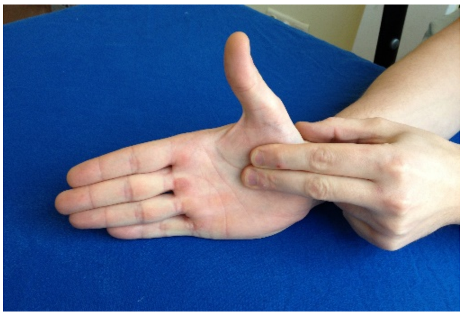
2 – Extensor pollicis brevis

A

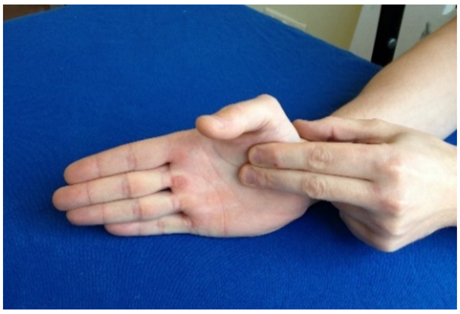
B

3 – Flexor pollicis brevis

A



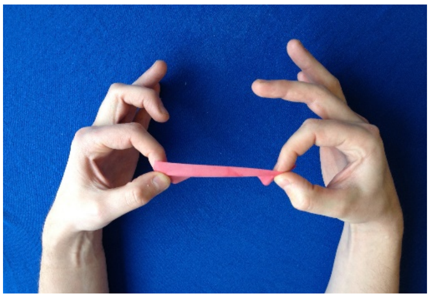
B



Second phase of treatment (week 6 – 3 months)

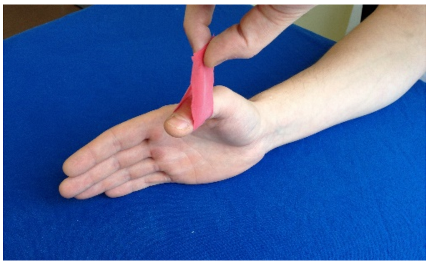
Examples of the exercises, performed 2-3 times a day, build up until 50-100 repititions.[25,30]

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



5 – Applying manual resistance at the radial part of proximal phalanx in closed and correct key pinch

6 – Pulling a rubber band in open chain



7 – Applying manual resistance at the radial aspect of the proximal phalanx in open chain