

## Subluxation of the first carpometacarpal joint and age are important factors in reduced hand strength in patients with hand osteoarthritis

Beest, S. van; Kloppenburg, M.; Rosendaal, F.R.; Stadt, L.A. van de

#### Citation

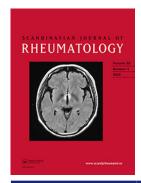
Beest, S. van, Kloppenburg, M., Rosendaal, F. R., & Stadt, L. A. van de. (2023). Subluxation of the first carpometacarpal joint and age are important factors in reduced hand strength in patients with hand osteoarthritis. *Scandinavian Journal Of Rheumatology*. doi:10.1080/03009742.2023.2215016

Version: Publisher's Version

License: Creative Commons CC BY-NC-ND 4.0 license

Downloaded from: <a href="https://hdl.handle.net/1887/3630373">https://hdl.handle.net/1887/3630373</a>

**Note:** To cite this publication please use the final published version (if applicable).



#### Scandinavian Journal of Rheumatology



ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/irhe20

# Subluxation of the first carpometacarpal joint and age are important factors in reduced hand strength in patients with hand osteoarthritis

S van Beest, M Kloppenburg, FR Rosendaal & LA van de Stadt

**To cite this article:** S van Beest, M Kloppenburg, FR Rosendaal & LA van de Stadt (2023): Subluxation of the first carpometacarpal joint and age are important factors in reduced hand strength in patients with hand osteoarthritis, Scandinavian Journal of Rheumatology, DOI: 10.1080/03009742.2023.2215016

To link to this article: <a href="https://doi.org/10.1080/03009742.2023.2215016">https://doi.org/10.1080/03009742.2023.2215016</a>

© 2023 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.	+ View supplementary material ☑
Published online: 21 Jun 2023.	Submit your article to this journal 🗹
Article views: 93	View related articles ☑
View Crossmark data ☑	

## Subluxation of the first carpometacarpal joint and age are important factors in reduced hand strength in patients with hand osteoarthritis

S van Beest<sup>1</sup>, M Kloppenburg<sup>1,2</sup>, FR Rosendaal<sup>2</sup>, LA van de Stadt<sup>1</sup>

**Objective:** To investigate the determinants of hand strength in patients with hand osteoarthritis (OA).

**Method:** Pinch and cylinder grip strength were measured in 527 patients with hand OA diagnosed by their treating rheumatologist from the Hand OSTeoArthritis in Secondary care (HOSTAS) study. Radiographs of hands (22 joints) were scored 0–3 (scaphotrapeziotrapezoid and first interphalangeal joints 0–1) on osteophytes and joint space narrowing following the Osteoarthritis Research Society International atlas. The first carpometacarpal joint (CMC1) was scored 0–1 for subluxation. Pain was assessed with the Australian/Canadian Hand Osteoarthritis Index pain subscale, and health-related quality of life with the Short Form-36. Regression analysis served to investigate associations of hand strength with patient, disease, and radiographic features.

**Results:** Hand strength was negatively associated with female sex, age, and pain. Reduced hand strength was associated with reduced quality of life, although less after adjusting for pain. Radiographic features of hand OA were associated with reduced grip strength when solely adjusted for sex and body mass index, but only CMC1 subluxation in the dominant hand remained significantly associated with pinch grip adjusted additionally for age (-0.511 kg, 95% confidence interval -0.975; -0.046). Mediation analysis showed low and not significant percentages of mediation of hand OA in the association between age and grip strength.

**Conclusions:** Subluxation of CMC1 is associated with reduced grip strength, whereas associations with other radiographic features seem to be confounded by age. In the relationship between age and hand strength, radiographic hand OA severity is not an important mediator.

Hand osteoarthritis (OA) is one of the most prevalent OA phenotypes, with a considerable disease burden. It is associated with pain, stiffness, functional impairment, and a reduction in quality of life (QoL) (1–4). Functional impairment is thought to be caused in part by reduced strength in the hands, which is considered an important symptom by patients with hand OA, as shown in studies of patient perspective (5). Hand strength is also considered a core domain to be assessed in clinical studies of hand OA by the international organization Outcome Measures in Rheumatology (OMERACT) (6). Cylinder grip and pinch grip strengths are the recommended measurements to assess hand strength. However, the literature shows variable results regarding whether cylinder grip strength and pinch grip strength are associated with hand OA.

LA van de Stadt, Department of Rheumatology, Leiden University Medical Center, C1-R, PO Box 9600, 2300 RC Leiden, the Netherlands.

E-mail: 1.a.van\_de\_stadt@lumc.nl

Received 28 January 2023; Accepted 15 May 2023

Most studies comparing patients with hand OA and healthy controls have reported lowered hand strength in patients with hand OA [cylinder (1, 7, 8) or cylinder and pinch grip strength (9, 10)]. However, other studies did not find an association of grip strength with hand OA (11, 12). Studies have reported different associations for men and women (although this concerned incident radiographic hand OA) (13) or different associations for different forms of hand OA; OA affecting the first ray, including thumb base OA, was more likely to be associated with reduced grip strength than OA of the other digits (14). Some reports have suggested that the association between grip strength and hand OA is mediated by pain (14, 15), and one study found an association between radiographic severity as well as hand pain and reduced grip strength in patients with hand OA, but mediation of pain between radiographic severity and grip strength was not addressed (7).

Furthermore, hand strength is highly associated with age, and reduced cylinder grip strength is considered a measure of frailty (16). Hand OA could be a mediator in the association between age and reduced hand strength,

<sup>&</sup>lt;sup>1</sup>Department of Rheumatology, Leiden University Medical Center, Leiden, the Netherlands

<sup>&</sup>lt;sup>2</sup>Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, the Netherlands

partly explaining this association. The purpose of this study was to investigate hand strength and its impact in patients with symptomatic hand OA, the determinants of hand strength in these patients, and, in particular, the role of hand OA in the association between age and hand strength.

#### Method

#### Study population

We used baseline and 2 year follow-up data from the ongoing Hand OSTeoArthritis in Secondary care (HOSTAS) study, in which consecutive patients diagnosed with primary hand OA by their treating rheumatologist were included between 2009 and 2015. The study is described elsewhere in more detail (17). Exclusion criteria were any other pathological condition explaining the hand symptoms and secondary OA. Written informed consent was obtained from all participants. The study was approved by the Leiden University Medical Center medical ethics committee. The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Declaration of Helsinki of 1975, as revised in 2000.

#### Assessments

Demographic and clinical characteristics were collected by standardized questionnaires, including hand dominance and the Australian/Canadian Hand Osteoarthritis Index (AUSCAN). Race was self-reported in an openended question as well as a fixed set of categories. In cases where hand dominance was unclear or unknown, right-hand dominance was presumed. For health-related quality of life (HRQoL), the Medical Outcomes Study Short Form-36 (SF-36) (18, 19) separate subscale and summary component scores were calculated: physical health (PCS) and mental health (MCS), and standardized scores on a scale of 0 to 100. Age- and sexspecific Dutch population-based norm scores (20) were used to derive norm-based scores (mean ± sd 50 ± 10). Higher SF-36 scores represent better HRQoL. Trained research nurses performed the physical examination, including assessment of bony enlargements and soft swelling of the hand joints. Assessment of the maximal isometric pinch grip and cylinder grip strength of both hands, using a fixed protocol with a Seahan pinch grip gauche and Seahan hand dynamometer, respectively, was carried out following a standardized protocol: patients were seated, with the elbow flexed at 90 degrees and unsupported. Measurements were performed twice with 30s rest in between. Each patient's height and weight were measured.

#### Radiography

Thumb base, and distal interphalangeal (DIP) and peripheral interphalangeal (PIP) joints of both hands (n = 22)were scored 0-3 for osteophytes and joint space narrowing (JSN) [scaphotrapeziotrapezoid (STT) and first interphalangeal joints were scored 0-1) following the Osteoarthritis Research Society International (OARSI) atlas (21). Radiographic hand OA severity was assessed as the sum scores of the osteophytes or JSN of all joints together (0– 58). First carpometacarpal joint (CMC1) subluxation was scored 0-1 according to the OARSI atlas (21). Radiographs were scored blinded for demographic and clinical data. Intraobserver reliability was assessed; the intraclass correlation coefficient was > 0.9 for different scores by a single reader and the prevalence-adjusted bias-adjusted kappa was > 0.80 for CMC subluxation consensus scores by two readers, as described in previous publications on the HOSTAS cohort (17, 22).

#### Statistical analysis

Associations between patient and disease characteristics (independent) and grip strength (dependent) were analysed with linear regression analysis. Regression was performed crude and adjusted for age, sex, body mass index (BMI), and hand pain. To investigate whether hand OA mediates the association between age and grip strength, sequential regression analyses were performed according to the Baron and Kenny framework (Figure 1) (23). In this framework, pathway C represents the total effect of the exposure (age) on the outcome (grip strength). This effect can be divided into the direct effect (pathway C') and the indirect effect via the potential mediator (through pathways A and B). Mediation was suspected when the four

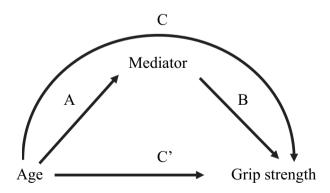


Figure 1. Assumptions of the Baron and Kenny framework (23).(i) Age is associated with grip strength (total effect C). (ii) Age is associated with the mediator (osteoarthritis) (indirect effect part A). (iii) The mediator (osteoarthritis) is associated with grip strength (indirect effect part B). (iv) The association between age and grip strength is attenuated after adding the mediator to the model (direct effect C'), owing to the indirect effect through pathway AB. In summary, direct effect plus indirect effect equals total effect (C' + AB = C).

assumptions of the Baron and Kenny framework were satisfied: (i) age was associated with grip strength; (ii) age was associated with the potential mediator (radiographic hand OA features); (iii) the potential mediator was associated with hand strength; and (iv) the association between age and hand strength was attenuated after adding the potential mediator (radiographic hand OA features) to the model.

The first three assumptions were judged based merely on effect size, not on statistical significance. If these four conditions were met, we used PROCESS version 3.5 for SPSS (available at processmacro.org/download.html) to estimate the indirect effect size with bootstrapped 95% confidence intervals (CIs). Because indirect effect sizes were small, we used 5000 bootstrap samples for estimating more reliable 95% CI limits. To aid with the interpretation, we transformed the absolute effect sizes into percentages of indirect effect relative to the total effect. All mediation analyses were adjusted for sex and BMI. Data were analysed with SPSS for Windows, version 26.0 (IBM Corp., Armonk, NY, USA).

#### Results

#### Study population

Baseline characteristics of 535 patients in the HOSTAS cohort with hand strength data are described in Table 1. The majority of patients were white (94%) and most were middle-aged women who were overweight. Furthermore, 90% fulfilled the American College of Rheumatology (ACR) hand OA classification criteria and most were right-handed. Average pinch grip strength was 3.6 kg and cylinder grip strength 24 kg. The large majority reported that their hand strength was not good and that they were not satisfied with their hand strength.

#### Determinants of hand strength

There were large individual differences regarding hand strength. Age and sex were strong determinants for both pinch and cylinder grip. Men pinched on average 1.78

Table 1. Baseline characteristics of 535 patients with hand osteoarthritis (OA) in the HOSTAS cohort with available grip strength data.

Age (years)		61.0 ± 8.6
Women		460 (86.0)
BMI (kg/m <sup>2</sup> )		26.2 (23.7–29.5)
Self-reported handedness		
Right		416 (77.8)
Left		67 (12.5)
Cross-dominance/unknown		52 (9.7)
Hand OA symptom duration (years)		5.2 (1.9–12.2)
Fulfilling ACR classification criteria		482 (90.1)
General and disease-specific burden		
Self-reported health-related quality of life		
PCS		45.2 (39.1–50.8)
MCS		53.9 (48.4–57.4)
AUSCAN pain (0–20)		10 (6–12)
AUSCAN stiffness (0–4)		2 (1–2)
AUSCAN function (0–36)		16 (9–22)
AUSCAN total score (0–60)		27 (17–36)
Hand-specific disease characteristics	Dominant hand	Non-dominant hand
Radiography		
Summated OARSI osteophyte scores (0–29)	5 (2–9)	5 (2–8)
Summated OARSI JSN scores (0-29)	4 (1–8)	4 (1–9)
CMC1 subluxation	32 (15.9)*	23 (11.4)*
Hand strength (kg)		
Pinch grip strength, total	$3.64 \pm 1.56 \dagger$	$3.58 \pm 1.48 \ddagger$
Pinch grip strength, women	3.39 ± 1.37	$3.36 \pm 1.28$
Pinch grip strength, men	5.17 ± 1.77	4.91 ± 1.92
Cylinder grip strength, total	24.5 ± 10.7§	23.8 ± 10.3§
Cylinder grip strength, women	$22.5 \pm 8.7$	21.7 ± 7.9
Cylinder grip strength, men	$36.7 \pm 13.4$	$36.3 \pm 13.8$
Hand strength self-rated as (very) good	85 (22.2)	142 (37.1)
Satisfied with hand strength	120 (31.3)	169 (44.1)

Data are shown as mean  $\pm$  sd, n (%), or median (interquartile range).

<sup>\*</sup>n = 201;  $\dagger n$  = 532;  $\dagger n$  = 531;  $\delta n$  = 533; ||n| = 383.

ACR, American College of Rheumatology; AUSCAN, Australian/Canadian Hand Osteoarthritis Index; BMI, body mass index; CMC1, first carpometacarpal joint; ; HOSTAS, Hand OSTeoArthritis in Secondary care; JSN, joint space narrowing; MCS, mental component summary scale; OARSI, Osteoarthritis Research Society International; PCS, physical component summary scale.

(1.43; 2.14) and 1.56 (1.22; 1.89) kg indicate mean (95% CI) more with their dominant and non-dominant hand, respectively, compared with women. Cylinder grip was also higher in men than women, with a mean difference of 14.2 (11.8; 16.5) kg and 14.6 (12.4; 16.8) kg indicate mean (95% CI) for the dominant and non-dominant hand, respectively. Years of age were negatively associated with pinch grip [β (kg), dominant: -0.028, 95% CI -0.043; -0.012, non-dominant: -0.028, 95% CI-0.043; -0.013] and cylinder grip [ $\beta$  (kg), dominant: -0.253, 95% CI -0.356; -0.150, non-dominant: -0.282, 95% CI -0.381; -0.1831. BMI had little impact on hand strength: for pinch grip [\beta (kg), dominant: 0.022, 95\% CI -0.007; 0.050, non-dominant: 0.026, 95% CI -0.001; 0.053] and cylinder grip [ $\beta$  (kg), dominant: 0.114, 95% CI -0.078; 0.306, non-dominant: 0.139, 95% CI -0.046; 0.324]. Patients with more hand pain had lower hand strength, as shown by the association of the AUSCAN pain score with pinch grip  $[\beta]$  (kg), dominant: -0.090, 95% CI -0.120; -0.060, non-dominant; -0.073, 95% CI -0.102; -0.044] and cylinder grip [ $\beta$  (kg), dominant: -0.760, 95% CI -0.963; -0.557, non-dominant: -0.600, 95% CI -0.798; -0.403]. In summary, hand strength in patients with hand OA was associated with age, sex, and hand pain.

#### Impact of decrease in hand strength

At baseline, the median PCS score of the norm-based self-reported HRQoL (SF-36) was lower than the reference population median of 50.0 (Table 1). Hand strength (independent variable) was significantly associated with the PCS score (outcome), with effect sizes exceeding the minimally clinically important difference (i.e. 2 points) per standard deviation grip strength (Table 2). Cylinder grip of the dominant and the non-dominant hand were similarly associated with the PCS score, whereas pinch grip of the dominant hand was more strongly associated with the PCS score than the non-dominant hand. Additional adjustment for

AUSCAN hand pain score reduced the effect sizes; however, the  $\beta$ -coefficients remained clinically relevant.

At the 2 year follow-up visit, the median change ( $\Delta$ ) in pinch grip and cylinder grip was zero; however, at the individual level increases and decreases were present (Supplementary figure S1). The standard deviation of  $\Delta$  pinch grip was 1.37 kg and 1.27 kg for the dominant and non-dominant hand, respectively, and the standard deviation of  $\Delta$  cylinder grip was 8.71 kg and 7.52 kg, respectively. Δ Grip strength was positively associated with  $\Delta$  PCS score, when adjusted for age, sex, and BMI; however, after additionally factoring in the change in AUSCAN pain scores the association decreased (Table 3). Similarly to the crosssectional associations (Table 2), associations pertaining to cylinder grip were symmetrical, whereas associations pertaining to pinch grip were stronger for the dominant hand. So, hand strength was crosssectionally associated with HRQoL, regardless of hand pain. Hand strength varied over 2 years in patients with hand OA and changes were associated with changes in HRQoL.

### Cross-sectional associations of structural signs of hand OA and hand strength

We tested the associations of several radiographic OA features (independent variable) with two measures of grip strength (outcome): results pertaining to pinch grip are tabulated in Table 4(A) and those referring to cylinder grip in Table 4(B). Regression coefficients represent kilogram grip strength per scoring point for osteophyte and JSN scores, whereas CMC1 subluxation is dichotomous with absent subluxation as reference category. To aid the interpretation of these results, coefficients can also be viewed in grams, e.g. a patient with a JSN sum-score of 5 on the dominant hand would have  $5 \times 37$  g = 185 g less cylinder grip in that hand compared to a hand without any JSN (see Table 4B, right column).

Table 2. Cross-sectional associations between standardized grip strength (independent variable) and norm-based self-reported quality of life (Short Form-36) physical component scale score (PCS score; dependent variable) in 504 patients with hand osteoarthritis at baseline.

	Crude		Adjusted‡		Adjusted§	
	β	95% CI	β	95% CI	β	95% CI
Pinch grip						
Dominant hand*	2.15	(1.46; 2.84)	2.32	(1.56; 3.08)	1.49	(0.80; 2.18)
Non-dominant hand†	1.52	(0.81; 2.23)	1.51	(0.73; 2.28)	0.81	(0.11; 1.50)
Cylinder grip		, , ,				
Dominant hand	2.49	(1.80; 3.17)	2.86	(2.07; 3.66)	1.74	(1.00; 2.49)
Non-dominant hand	2.10	(1.41; 2.78)	2.44	(1.60; 3.27)	1.46	(0.69; 2.22)

β, PCS score point per sd grip strength; CI, confidence interval.

<sup>‡</sup>Adjusted for age, sex, and body mass index (BMI);  $\alpha$  adjusted for age, sex, BMI, and Australian/Canadian Hand Osteoarthritis Index (AUSCAN) pain score. \*n = 503; †n = 502.

Table 3. Longitudinal associations between standardized change in grip strength (independent variable) and change in norm-based self-reported quality of life (Short Form-36) physical component scale score (PCS score; dependent variable) in 391 patients with hand osteoarthritis at 2 year follow-up.

	Crude		Adjusted‡		Adjusted§	
	β	95% CI	β	95% CI	β	95% CI
Δ Pinch grip						
Dominant hand*	0.61	(-0.05; 1.27)	0.67	(0.01; 1.32)	0.47	(-0.18; 1.11)
Non-dominant hand†	0.22	(-0.46; 0.90)	0.30	(-0.39; 0.99)	0.12	(-0.56; 0.79)
$\Delta$ Cylinder grip						
Dominant hand	0.82	(0.07; 1.57)	0.86	(0.11; 1.61)	0.59	(-0.15; 1.34)
Non-dominant hand	0.95	(0.18; 1.72)	1.03	(0.26; 1.80)	0.70	(-0.07; 1.47)

β, change in PCS score per sd change in grip strength; CI, confidence interval.

‡Adjusted for age, sex, and body mass index (BMI); §adjusted for age, sex, BMI, and change in Australian/Canadian Hand Osteoarthritis Index (AUSCAN) pain score. \*n = 390; †n = 389.

Table 4. Cross-sectional associations between radiographic osteoarthritis (OA) features (independent variables) and (A) pinch grip strength and (B) cylinder grip strength (dependent variable) in 527 patients with hand OA at baseline.

	Crude		Adjusted‡		Adjusted§	
	β	95% CI	β	95% CI	β	95% CI
(A) Pinch grip strength						
Osteophyte sum-score						
Dominant hand*	-0.021	(-0.048; 0.005)	-0.027	(-0.051; -0.003)	0.003	(-0.023; 0.030)
Non-dominant handt	-0.019	(-0.044; 0.006)	-0.026	(-0.049; -0.002)	0.003	(-0.023; 0.029)
JSN sum-score						
Dominant hand*	-0.019	(-0.045; 0.007)	-0.036	(-0.060; -0.012)	-0.013	(-0.038; 0.013)
Non-dominant handt	-0.023	(-0.046; 0.001)	-0.035	(-0.057; -0.014)	-0.016	(-0.039; 0.006)
CMC1 subluxation						
Dominant hand‡	-0.673	(-1.228; -0.118)	-0.631	(-1.101; -0.161)	-0.511	(-0.975; -0.046)
Non-dominant hand‡	-0.323	(-0.635; -0.011)	-0.282	(-0.554; -0.010)	-0.214	(-0.484; 0.057)
(B) Cylinder grip strength						
Osteophyte sum-score						
Dominant hand	-0.223	(-0.401; -0.044)	-0.260	(-0.420; -0.101)	-0.001	(-0.173; 0.170)
Non-dominant hand	-0.253	(-0.425; -0.081)	-0.309	(-0.459; -0.160)	-0.037	(-0.196; 0.122)
JSN sum-score						
Dominant hand	-0.125	(-0.300; 0.050)	-0.253	(-0.409; -0.097)	-0.037	(-0.200; 0.126)
Non-dominant hand	-0.209	(-0.367; -0.052)	-0.317	(-0.454; -0.180)	-0.128	(-0.267; 0.011)
CMC1 subluxation						
Dominant hand**	-1.837	(-5.953; 2.278)	-1.167	(-4.556; 2.222)	0.137	(-3.097; 3.370)
Non-dominant hand**	-1.807	(-4.094; 0.479)	-0.983	(-2.791; 0.825)	-0.070	(-1.751; 1.611)

β, grip strength (kg) per score-point; CI, confidence interval; CMC1, first carpometacarpal joint.

Given the possible scoring range (i.e. 0–29), total osteophyte and total JSN sum-score per hand have moderately sized associations with both measures of grip strength in sex- and BMI-adjusted analyses. However, when including age in the equation (i.e. last column in Table 4), the associations largely disappear, but for CMC1 subluxation and pinch grip in the dominant hand only (Table 4A).

Mediating role of OA in the association between age and hand strength

Since analyses adjusted for age abolished all but one of the associations between radiographic OA features and hand

strength, we next performed mediation analyses on the association between age (independent variable) and grip strength (outcome), with the radiographic hand OA features added as potential mediators (Figure 1). In all 12 studied models, age was associated with outcome and mediator – in compliance with the first and second assumptions of the Baron and Kenny framework (23) – however, only nine models additionally met the third and fourth assumptions. None of the models showed a substantial indirect effect or relevant percentage mediation (Table 5).

#### **Discussion**

In this study on patients with hand OA, hand strength was negatively associated with female sex, age, and

<sup>‡</sup>Adjusted for sex and body mass index (BMI); \$adjusted for sex, BMI, and age. \*n = 526; †n = 525; ‡n = 201; \*\*n = 201.

Table 5. Cross-sectional associations between age and grip strength in 527 patients with hand osteoarthritis (OA) at baseline, with analyses of mediation through radiographic hand OA parameters, adjusted for sex and body mass index.

Mediators	Osteophytes		JSN		CMC1 subluxation‡	
	β (%)	95% CI	β (%)	95% CI	β (%)	95% CI
Pinch grip dominant*						_
Total effect (β) C	-0.039	(-0.053; -0.025)	-0.039	(-0.053; -0.025)	-0.037	(-0.058; -0.017)
Direct effect (β) C'	-0.040	(-0.056; -0.024)	-0.036	(-0.052; -0.021)	-0.034	(-0.054; -0.013)
Indirect effect (β) AB	na		-0.003	(-0.009; 0.003)	-0.004	(-0.008; 0.0001)
Indirect/total effect (%)	na		7.7	(-8.4; 23.2)	9.4	(-0.3; 22.2)
Pinch grip non-dominant†						
Total effect (β) C	-0.037	(-0.051; -0.024)	-0.037	(-0.051; -0.024)	-0.033	(-0.054; -0.013)
Direct effect (β) C'	-0.038	(-0.053; -0.023)	-0.034	(-0.048; -0.019)	-0.030	(-0.051; -0.010)
Indirect effect (β) AB	na		-0.004	(-0.009; 0.001)	-0.003	(-0.007; 0.002)
Indirect/total effect (%)	na		10.2	(-3.2; 24.4)	8.5	(-3.2; 26.5)
Cylinder grip dominant						
Total effect (β) C	-0.342	(-0.432; -0.251)	-0.342	(-0.432; -0.251)	-0.366	(-0.507; -0.226)
Direct effect (β) C'	-0.341	(-0.443; -0.240)	-0.333	(-0.432; -0.235)	-0.367	(-0.510; -0.225)
Indirect effect (β) AB	-0.000	(-0.058; 0.063)	-0.009	(-0.052; 0.042)	na	
Indirect/total effect (%)	0.1	(-18.5; 16.9)	2.5	(-12.3; 15.3)	na	
Cylinder grip non-dominant						
Total effect (β) C	-0.369	(-0.453; -0.285)	-0.369	(-0.453; -0.285)	-0.407	(-0.533; -0.281)
Direct effect (β) C'	-0.360	(-0.453; -0.266)	-0.340	(-0.429; -0.250)	-0.406	(-0.534; -0.278)
Indirect effect (β) AB	-0.010	(-0.055; 0.039)	-0.029	(-0.066; 0.008)	-0.001	(-0.017; 0.042)
Indirect/total effect (%)	2.6	(-10.6; 15.0)	8.0	(-2.1; 18.0)	0.2	(-10.2; 4.3)

 $\beta$ , grip strength (kg) per year of age; CI, confidence interval; JSN, joint space narrowing; CMC1, first carpometacarpal join; na, not applicable; AB, C, and C' refer to the graph in Figure 1. In three analyses, the association between age and grip strength did not attenuate after adding the mediator to the model; in all other cases, the assumptions of the Baron and Kenny framework (23) were met. Age was associated with all mediators (indirect effect part A), as shown in Supplementary table S2. The association between mediators and grip strength (indirect effect part B) is shown in Table 4. \*n = 526; †n = 525; ‡n = 201.

pain. Reduced cylinder grip strength was associated with a reduced physical QoL, as assessed by SF-36 PCS, in both hands equally, whereas reduced pinch grip strength in the dominant hand had a more pronounced effect on the physical QoL when compared with the non-dominant hand. Radiographic features of hand OA were associated with reduced cylinder grip strength and pinch grip in crude analysis as well as after adjusting for sex and BMI, but only CMC1 subluxation in the dominant hand remained significantly associated with pinch grip after additional adjustment for age. Mediation analysis showed only low percentages of mediation of hand OA in the association between age and hand strength.

These results indicate that in patients with hand OA, reduced hand strength may be caused by increased age and not radiographic severity, except for subluxation of the CMC1 joint, which was associated with reduced pinch grip strength after adjustment for age. In this case, a cause of reduced grip strength may be instability of the thumb joint, and therefore stabilizing therapy such as splinting, exercise, or surgery may be an option to increase grip strength, although we did not analyse the influence of instability in this study. Whether grip strength should be a target in clinical studies remains a question, although patients mention reduced grip strength as an important part of their complaints. Data supporting grip strength as a clinical target or as an

outcome measurement in clinical studies are scarce. In a study in which patients with hand OA were treated with prednisolone, hand strength was not increased, whereas pain (the primary endpoint) was reduced and several secondary endpoints were reached (24), indicating that hand strength may not be influenced even when the therapy is successful, at least over the course of a few weeks. In addition, decreased hand strength may affect QoL, but in our study change in hand strength was not associated with change in QoL when adjusted for pain, suggesting that although cross-sectionally there is an association between reduced hand strength and reduced QoL, changing the former will not result in change in the latter, which could be argued to be the goal of therapy. As an indirect measure of disease, hand strength may still be of value, but one must consider that factors other than disease or disease characteristics influence hand strength. For example, Haugen et al found that cylinder grip strength was associated with measures of reduced physical fitness (7). We found that including age in our model abolished most associations. In mediation analysis, different radiographic hand OA features did not mediate the relationship between age and grip strength, indicating that the increasing severity of hand OA with increasing age does not explain this relationship. In this study, we did not investigate the factor frailty, because variables to define frailty were lacking. Besides, most of the patients in our cohort were

relatively young and were referred to our clinic within a decade after experiencing the first symptoms of hand OA. In patients with long-standing disease, the association between radiography and hand strength could be different as a result of OA-related causes that may develop over time, such as muscle atrophy or compensatory mechanisms.

Future research could clarify the relationships between hand strength, hand OA, and frailty. Other factors that could influence grip strength, such as comorbidities, were not considered and would be best included in future studies, because a previous study (17) showed a relationship between the number and type of comorbidities and self-reported hand function assessed by AUSCAN, considering that six out of nine questions on function pertain to hand strength. We analysed cylinder grip strength as well as pinch grip strength, which we think is a valuable aspect of the present study. Furthermore, we addressed subluxation of CMC1, and performed mediation analyses and a longitudinal analysis of the association of hand strength and QoL in a well-defined hand OA cohort, making this a unique study.

#### Conclusion

Subluxation of the CMC1 joint is associated with reduced hand strength independently of age, but associations with other radiographic features seem to be confounded by age. In the relationship between age and hand strength, hand OA severity is not a mediator of importance.

#### **Acknowledgements**

The authors thank all individuals who participated in the HOSTAS study. The authors also thank research nurses B van Schie-Geyer, A Wongsodihardjo, and M Janson, and data managers J van Krol-Berkel and C Kromme in the Rheumatology Department of the LUMC, and technicians in the Radiology Department of the LUMC for support in data collection. The authors thank Dr HMJA Kroon for scoring CMC1 subluxation on radiographs.

#### **Author contributions**

Conception and design of the study: SvB and MK; acquisition of data: SvB, LAvdS, and MK; analysis: SvB, LAvdS, and MK; and interpretation of data: SvB, LAvdS, MK, and FR. All authors were involved in drafting the manuscript for intellectual content, and approved the final version.

#### **Disclosure statement**

MK reports research grants from the Dutch Arthritis Society and EULAR; consultancy fees from AbbVie, Pfizer, Kiniksa, Flexion, Galapagos, Jansen, CHDR, Novartis, and UCB; and royalty fees from Wolter Kluwer and Springer Verlag, all paid to her department. She is a board member of OARSI, a member of the EULAR Council,

and President of the Dutch Society for Rheumatology. All other authors report no conflicts of interest.

#### **Funding**

A grant from the Dutch Arthritis Society [LLP-24] for the HOSTAS cohort was paid to the institution.

#### **ORCID**

S van Beest http://orcid.org/0000-0002-2351-1976

M Kloppenburg http://orcid.org/0000-0002-9294-2307

FR Rosendaal http://orcid.org/0000-0003-2558-7496

LA van de Stadt http://orcid.org/0000-0002-3065-9549

#### References

- Zhang Y, Niu J, Kelly-Hayes M, Chaisson CE, Aliabadi P, Felson DT. Prevalence of symptomatic hand osteoarthritis and its impact on functional status among the elderly: the framingham study. Am J Epidemiol 2002;156:1021–7.
- Kloppenburg M, Kwok WY. Hand osteoarthritis—a heterogeneous disorder. Nat Rev Rheumatol 2011;8:22–31.
- 3. Kwok WY, Vliet Vlieland TPM, Rosendaal FR, Huizinga TWJ, Kloppenburg M. Limitations in daily activities are the major determinant of reduced health-related quality of life in patients with hand osteoarthritis. Ann Rheum Dis 2011;70:334–6.
- Loef M, Damman W, de Mutsert R, Rosendaal FR, Kloppenburg M. Health-related quality of life in patients with hand osteoarthritis from the general population and the outpatient clinic. J Rheumatol 2020;47:1409–15.
- Stamm T, van der Giesen F, Thorstensson C, Steen E, Birrell F, Bauernfeind B, et al. Patient perspective of hand osteoarthritis in relation to concepts covered by instruments measuring functioning: a qualitative European multicentre study. Ann Rheum Dis 2009;68:1453–60.
- Kloppenburg M, Bøyesen P, Smeets W, Haugen I, Liu R, Visser W, et al. Report from the OMERACT hand osteoarthritis special interest group: advances and future research priorities. J Rheumatol. 2014;41(4):810–8.
- Haugen IK, Aaserud J, Kvien TK. Get a grip on factors related to grip strength in persons with hand osteoarthritis: results from an observational cohort study. Arthritis Care Res 2021;73:794–800.
- Wen L, Shin MH, Kang JH, Yim YR, Kim JE, Lee JW, et al. Association between grip strength and hand and knee radiographic osteoarthritis in Korean adults: data from the Dong-gu study. PLOS ONE 2017;12:e0185343.
- Bagis S, Sahin G, Yapici Y, Cimen OB, Erdogan C. The effect of hand osteoarthritis on grip and pinch strength and hand function in postmenopausal women. Clin Rheumatol 2003;22:420

  –4.
- Villafañe JH, Valdes K, Bertozzi L, Negrini S. Minimal clinically important difference of grip and pinch strength in women with thumb carpometacarpal osteoarthritis when compared to healthy subjects. Rehabil Nurs 2017;42:139

  –45.
- 11. Tossini NB, Zacharias ALS, Abrantes LSS, da Silva Serrão PRM. Initial stages of hand osteoarthritis do not affect the extrinsic muscles of the hand: a cross-sectional study. Sci Rep 2021;11:5381.
- Güven N, Dinçer F, Çetin A, Güven SC. Hand strenght and dexterity in interphalangeal hand osteoarthritis and effects of osteophyte formations. Adv Rheumatol 2020;60:41.
- Chaisson CE, Zhang Y, Sharma L, Kannel W, Felson DT. Grip strength and the risk of developing radiographic hand osteoarthritis: results from the Framingham study. Arthritis Rheum 1999;42:33–8.

 Dominick KL, Jordan JM, Renner JB, Kraus VB. Relationship of radiographic and clinical variables to pinch and grip strength among individuals with osteoarthritis. Arthritis Rheum 2005;52:1424–30.

- 15. Jones G, Cooley HM, Bellamy N. A cross-sectional study of the association between Heberden's nodes, radiographic osteoarthritis of the hands, grip strength, disability and pain. Osteoarthritis Cartilage 2001;9:606–11.
- Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a Phenotype. J Gerontol 2001;56:M146–M57.
- 17. Damman W, Liu R, Kroon FPB, Reijnierse M, Huizinga TWJ, Rosendaal FR, et al. Do comorbidities play a role in hand osteoarthritis disease burden? Data from the hand osteoarthritis in secondary care cohort. J Rheumatol 2017;44:1659–66.
- Ware JE, Sherbourne CD, The MOS. 36-Item Short-Form Health Survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473–83.
- van der Zee K, Sanderman R. Measuring general health with the RAND-36, a manual. [Manual in Dutch], 2nd. Groningen: University of Groningen, Northern Center for Health Issues, 2012.

- Aaronson NK, Muller M, Cohen PDA, Essink-Bot ML, Fekkes M, Sanderman R, et al. Translation, validation, and norming of the Dutch language version of the SF-36 health survey in community and chronic disease populations. J Clin Epidemiol 1998;51:1055–68.
- Altman RD, Gold GE. Atlas of individual radiographic features in osteoarthritis, revised. Osteoarthritis Cartilage 2007;15 Suppl A: A1–A56.
- 22. van Beest S, Kroon FPB, Kroon HM, Damman W, Liu R, Bloem JL, et al. Assessment of osteoarthritic features in the thumb base with the newly developed OMERACT magnetic resonance imaging scoring system is a valid addition to standard radiography. Osteoarthritis Cartilage 2019;27:468–75.
- Baron RM, Kenny DA. The moderator–mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. J Pers Soc Psychol 1986;51:1173–82.
- 24. Kroon FPB, Kortekaas MC, Boonen A, Böhringer S, Reijnierse M, Rosendaal FR, et al. Results of a 6-week treatment with 10 mg prednisolone in patients with hand osteoarthritis (HOPE): a double-blind, randomised, placebo-controlled trial. Lancet 2019;394:1993–2001.

#### Supplementary material

Supplemental data for this article can be accessed online at https://doi.org/10.1080/03009742.2023.2215016