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The course of cytokine and chemokine gene expression in clinically suspect arthralgia patients during progression to inflammatory arthritis

Heutz, J.W.; Rogier, C.; Niemantsverdriet, E.; Eeden, S.J.F. van den; Jong, P.H.P. de; Lubberts, E.; ... ; Mil, A.H.M.V.

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

S van Beest¹, M Kloppenburg^{1,2}, FR Rosendaal², LA van de Stadt¹

¹Department of Rheumatology, Leiden University Medical Center, Leiden, the Netherlands

²Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, the Netherlands

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.

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,

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

E-mail: l.a.van_de_stadt@lumc.nl

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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 open-ended 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 sex-specific Dutch population-based norm scores (20) were used to derive norm-based scores (mean \pm 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) [scaphotrapezotrapezoid (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

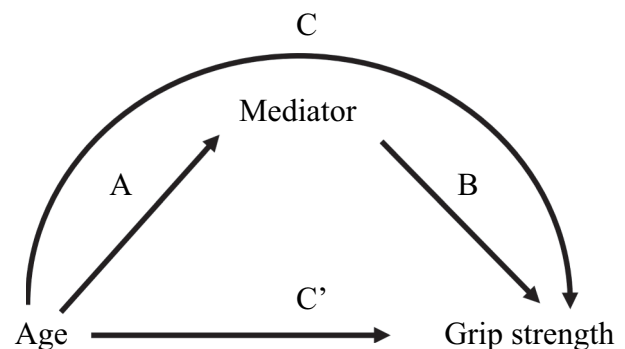


Figure 1. Assumptions of the Baron and Kenny framework (23). (i) Age is associated with grip strength (total effect C). (ii) Age is associated with the mediator (osteoarthritis) (indirect effect part A). (iii) The mediator (osteoarthritis) is associated with grip strength (indirect effect part B). (iv) 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 ²)		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		
Radiography		
Summated OARSI osteophyte scores (0–29)	Dominant hand	5 (2–8)
Summated OARSI JSN scores (0–29)	Non-dominant hand	4 (1–9)
CMC1 subluxation		32 (15.9)*
Hand strength (kg)		
Pinch grip strength, total		3.58 ± 1.48†
Pinch grip strength, women		3.36 ± 1.28
Pinch grip strength, men		4.91 ± 1.92
Cylinder grip strength, total		23.8 ± 10.3§
Cylinder grip strength, women		21.7 ± 7.9
Cylinder grip strength, men		36.3 ± 13.8
Hand strength self-rated as (very) good		85 (22.2)
Satisfied with hand strength		142 (37.1)
		120 (31.3)
		169 (44.1)

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

*n = 201; †n = 532; ‡n = 531; §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 [β (kg), dominant: -0.253 , 95% CI -0.356 ; -0.150 , non-dominant: -0.282 , 95% CI -0.381 ; -0.183]. BMI had little impact on hand strength: for pinch grip [β (kg), dominant: 0.022 , 95% CI -0.007 ; 0.050 , non-dominant: 0.026 , 95% CI -0.001 ; 0.053] and cylinder grip [β (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 [β (kg), dominant: -0.090 , 95% CI -0.120 ; -0.060 , non-dominant: -0.073 , 95% CI -0.102 ; -0.044] and cylinder grip [β (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 β -coefficients remained clinically relevant.

At the 2 year follow-up visit, the median change (Δ) 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 Δ pinch grip was 1.37 kg and 1.27 kg for the dominant and non-dominant hand, respectively, and the standard deviation of Δ cylinder grip was 8.71 kg and 7.52 kg, respectively. Δ Grip strength was positively associated with Δ 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 cross-sectional 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 cross-sectionally 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 $5 \times 37 \text{ g} = 185 \text{ g}$ 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.

†Adjusted for age, sex, and body mass index (BMI); §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)
Δ 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 hand†	-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 hand†	-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.

‡Adjusted for sex and body mass index (BMI); §adjusted for sex, BMI, and age. *n = 526; †n = 525; ‡n = 201; **n = 201.

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

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)

β , grip strength (kg) per year of age; CI, confidence interval; JSN, joint space narrowing; CMC1, first carpometacarpal joint; 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.

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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.

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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>

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Supplementary material

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