Hand osteoarthritis : natural course and determinants of outcome

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VALIDITY OF JOINT SPACE WIDTH MEASUREMENTS IN HAND OSTEOARTHRITIS

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ABSTRACT

Objective. To investigate the validity of joint space width (JSW) measurements in millimetres (mm) in hand osteoarthritis (OA) patients by comparison to controls, grading of joint space narrowing (JSN) and clinical features.

Methods. Hand radiographs of 235 hand OA patients (mean age 65 years, 83% women) and 471 controls were used. JSW was measured with semi-automated image analysis software in the distal interphalangeal, proximal interphalangeal and metacarpophalangeal joints (DIPJs, PIPJs and MCPJs). JSN (grade 0-3) was assessed using the Osteoarthritis Research Society International (OARSI) atlas. Associations between the two methods and clinical determinants (presence of pain, nodes and/or erosions, decreased mobility) were assessed using Generalised Estimating Equations with adjustment for age, sex, BMI and mean width of proximal phalanx.

Results. JSW was measured in 5631 joints with a mean JSW of 0.98 mm (SD 0.21), being the smallest for DIPJs (0.70 (SD 0.25)) and largest for MCPJs (1.40 (SD 0.25)). The JSN=0 group had a mean JSW of 1.28 mm (SD 0.34), the JSN=3 group 0.17 mm (SD 0.23). Controls had larger JSW than hand OA patients (p-value < 0.001). In hand OA, females had smaller JSW than men (β -0.08, (95%CI -0.15 to -0.01)) and lower JSW was associated with the presence of pain, nodes, erosions and decreased mobility (adjusted β (95%CI) -0.21 (-0.27 to -0.16), -0.37 (-0.40 to -0.34), -0.61 (-0.68 to -0.54) and -0.46 (-0.68 to -0.24) respectively). These associations were similar for JSN in grades.

Conclusion. In hand OA the quantitative JSW measurement is a valid method to measure joint space and shows a good relation with clinical features.

INTRODUCTION

Hand osteoarthritis (OA) is a prevalent musculoskeletal disease, which can lead to pain and functional limitations in daily life.[1,2] Classical structural features of hand OA, such as osteophytes and joint space narrowing (JSN) can be visualised on conventional radiographs[3], even if persons do not suffer from any complaints. These features are slowly progressive in time.[4,5] JSN in OA is considered to reflect damage and loss of articular cartilage.[6]

Several standardised visual grading methods are being used to score osteophytes and JSN together or separately in patients with hand OA.[3,7-9] However, these visual methods with graded scores have shortcomings. Visual grading methods are subjective and dependent on the scorer. Methods that measure these features in a more objective manner are preferable. Moreover, the visual grading methods are not able to discriminate small differences. A quantitative method would give opportunities to monitor small effects of these features. With visual grading methods it is not possible to score positive or negative changes of the joint space (e.g. widening, as present in early stages of osteoarthritis or in secondary OA, such as in acromegalic patients). For measurement of joint space widening or narrowing, a quantitative method to measure the joint space width (JSW) is desirable.

Van't Klooster et al. developed a semi-automated quantitative measurement method that is able to measure JSW in hand OA in a reproducible and accurate way.[10] This method has a high accuracy and repeatability in acrylic phantom joints and human-derived cadaver interphalangeal joints.[11] Until present, however, no data of studies are available which quantify JSW in a large population with hand OA patients and validate JSW against JSN in "in vivo" patients with hand OA.

The aim of this paper is to quantify the JSW in finger joints with a semi-automated quantitative method in hand OA patients and to validate it by comparing JSW with the JSW of normal controls and with the visual grading method of JSN. The association with clinical determinants on joint and patient level of JSW using the visual grading method of JSN as the standard method was also investigated.

PATIENTS AND METHODS

Study design and patient population

The Genetics ARthrosis and Progression (GARP)[12] study is a cohort study aimed at identifying determinants of OA susceptibility and progression. The study population comprises 192 Caucasian sibling pairs with symptomatic OA at multiple sites in the hand or in at least two of the following sites: hand, knee, hip or spine. Patients were recruited from rheumatologists, orthopaedic surgeons and general practitioners. Further details about the recruitment and selection have been published elsewhere.[12] The study was approved by the medical ethics committee.

Hand OA patients from this population that were evaluated after 6 years were eligible for the present study.[5] Hand OA was defined according to the American College of Rheumatology (ACR) criteria for clinical hand OA[13] or as the presence of structural abnormalities. Structural abnormalities were defined as the presence of bony swelling

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in at least two of the ten selected joints from the ACR criteria and a Kellgren-Lawrence score ≥2 in any interphalangeal or first carpometacarpal (CMC-1) joint.

Hand OA was scored for JSN using Osteoarthritis Research Society International (OARSI) atlas, and JSW was measured. Data from OA patients were compared with two control cohorts.

Control population for JSW measurements

A control group was selected from databases of the Leiden Early Arthritis Clinic (EAC, n=167) and a prospective study in patients with knee complaints (n=304). None of these controls had symptoms of the hands. The EAC study is a prospective study started in 1993 and includes patients with early arthritis with symptoms ≤2 years.[14] The aim is to detect inflammatory disorders early in the disease state and to treat these accordingly. In all patients, conventional radiographs of hands and feet were performed at baseline. For the purpose of the present study, a selection of patients without hand symptoms was made and hand radiographs of their inclusion visit were used.

The second control population was derived from an epidemiological study which includes patients with traumatic or non-traumatic sub-acute knee complaints (also known as the KART-study).[15] At a follow-up visit 10 years later, routine hand radiographs were performed in all patients. Since patients were not included in the study on the basis of hand joint pathology, we assumed that their hand joints are a valid sample of the general population for hand OA. Protocols of both studies were approved by the medical ethics committee. Written informed consent was given by all patients who participated in the studies.

Radiographic assessment

Digital hand radiographs (dorsal-volar) in both the GARP and KART study were obtained by a single radiographer using the same standard protocol with a fixed film focus distance (1.15 m) and tube voltage of 45 kVp, 250 mA and 3.2 mAs (type of film cassette Canon Detector CXDI-31, imaging geometry 2256 x 2878 mm, pixel spacing 100μm, gray scale resolution 12-bit). Of the EAC controls, 133 radiographs were analog and 39 were digital. For computerised analyses the analog radiographs were digitised first (VXR-12, VIDAR System Corporation, Herndon, VA). Radiographs of the EAC controls were made according to the standard usual care protocol, without a fixed film focus distance and 5.0 mAs.

Measurement of JSW

JSW was measured using a semi-automated method described extensively elsewhere.[10] In brief, JSW measurement was applied to the distal interphalangeal joints (DIPJs), proximal interphalangeal joints (PIPJs) and second to fifth metacarpophalangeal joints (MCPJs) of both hands. The joints of the thumb were omitted since they were not perpendicular to the image plane and could therefore not be assessed reliably. The image analysis software identifies all joints of interest and the corresponding joint margins and subsequently measures the JSW in millimetres (mm) within a measurement interval in each joint, which was determined by the width of the respective phalanx.

The automatic results of the image analysis from all study populations were reviewed by an expert (SHM) and corrected if needed. The intra-individual variation between repeat readings (n=24) was low, reflected by an intraclass correlation coefficient (ICC) of 0.99. The smallest detectable difference (SDD) is used to discriminate the JSW measurements above measurement error and was calculated as 1.96 x standard deviation (SD) of the difference between repeated JSW measurement divided by the square root of two.[16] The mean difference (SD) of repeated JSW measurements was 0.017 mm (0.04) and the SDD was 0.055. Regarding feasibility, the mean time to determine the JSW was 5 min and 7 s per patient (SD 2 min and 46 s).

Grading of JSN and other OA features

Using the visual grading method, JSN was graded 0-3 in the DIPJs, PIPJs and second to fifth MCPJs by consensus opinion of two experienced readers using the OARSI atlas in hand OA patients only.[3] MCPJs were not included in the original OARSI atlas, but for scoring these were regarded as PIPJs. In addition, osteophytes were graded 0-3 using the OARSI atlas. Erosions were scored by the Verbruggen-Veys scoring method and were defined as having eroded (E-phase) or remodeled irregular sclerotic subchondral plates (R-phase) in DIPJs or PIPJs.[9] Intrareader reproducibility of JSN based on 25 randomly selected pairs of radiographs was good with an ICC of 0.92.

Hand pain and functioning

Self-reported pain on joint level was assessed using a standard diagram including all hand joints on which the patient was asked to mark painful joints. Pain upon lateral joint pressure was graded 0-3 for each hand joint by a single observer (JB) during physical examination (0=no pain, 1=complaining of pain, 2=complaining of pain and wincing, 3=complaining of pain and withdrawal of the joint).

Self-reported hand pain and functional limitations on patient level were assessed with the pain (5 items) and function (9 items) subscales of the Australian/Canadian Osteoarthritis Hand Index (AUSCAN), on a five-point Likert scale (0=none to 4=extreme).[17] Higher scores indicate more pain and functional limitations.

Hand performance was assessed by measuring grip strength with a hydraulic hand dynamometer (Saehan corporation, Masan, South-Korea). Hand mobility was assessed with the Hand Mobility in Scleroderma test (HAMIS).[18] Using HAMIS, nine movements included in the range of motion of the hand were graded 0 (normal) to 3 (unable to do) for each hand and summed. The total score is the mean of two hands.

Statistical analysis

Data were analysed using SPSS, version 17.0 (SPSS Inc, Chicago, Illinois, USA). The JSW in relation with the JSN score was quantified and presented as mean scores with SDs.

To validate the JSW method we hypothesised that the JSW would be smaller in hand OA patients than controls and decrease with the presence of clinical determinants as age, female sex, nodes, erosive lesions and joint pain. Generalised Estimating Equations (GEE) models were performed to investigate the association of JSW with age and female sex, with adjustments for the presence of osteophytes. The

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GEE model is used to correct for effects within the same patient and family effects within sibling pairs in the patient population. In addition, the association of JSW with female sex was adjusted for the mean width of all phalanges of both hands. The width of the proximal phalanx was measured by detecting bone contours of the proximal phalanx with an edge detector and calculating the distance between the contours at the central part of the phalanx.[10] GEE models were also used to estimate β-coefficients for associations between JSW and JSN scores on joint level with clinical determinants with robust variance estimators to account for effects within the same patient, family effects within sibling pairs and mean width of the proximal phalanx. Adjustments were also made for age, sex and body mass index (BMI). For JSW, a positive or negative β-coefficient means an increase or decrease of the mean JSW (larger or smaller joint space), respectively. For the JSN score, a positive or negative β-coefficient represents an increase (smaller joint space) or decrease (wider joint space) of the mean JSN score, respectively.

To investigate the associations of JSW and JSN scores with clinical determinants on the patient level, the JSW and JSN score of both hands were summed up per patient. Associations between the summed JSW and summed JSN score with clinical determinants were estimated using a linear mixed model with adjustments for age, sex, BMI, family effects within sibling pairs and mean width of the proximal phalanx. The fixed effects were age, sex and BMI. A random intercept was used to adjust for family effects, meaning resemblance between siblings of one family, with an unspecified covariance matrix. An additional adjustment for osteophytes was made for the association between JSW and JSN score. The results are presented as unstandardised β-coefficients with 95% confidence interval (95%CI). Since the JSN score is not a continuous outcome measure, but a graded scoring method, the β-coefficients of the JSW and JSN score cannot be compared with each other.

RESULTS

Study population
In one of the 236 eligible patients JSW measurement was not possible due to technical problems with the radiograph. Characteristics of 235 hand OA patients included in the analyses are shown in table 1. The mean age was 64.8 years and the majority was female. JSW was measured in 5631 joints. JSN score was not applicable in 9 joints due to technical problems and were therefore excluded.

In one of the 471 controls the JSW measurement was not available. The mean age of the controls was 46.1 years (SD 11.4) and 195 persons (42%) were female. JSW was measured in 11280 joints.

Quantification of JSW in OA patients and controls
Most of the DIPJs (56%) and PIPJs (62%) in OA patients were classified in JSN=1. For the MCPJs, the majority of the joints (81%) in OA patients were normal (classified as JSN=0). The mean JSW for all joints in hand OA patients was 0.98 mm (SD 0.21), being the smallest for the DIPJs and largest for the MCPJs with 0.70 mm (SD 0.25)

Table 1. Characteristics of 235 patients with hand osteoarthritis (OA).

Age, years	64.8 (6.9)
Women, no (%)	194 (83)
Postmenopausal women, no (%)	184 (95)
Body mass index, kg/m^2	28.3 (5.8)
ACR criteria hand OA, no (%)	205 (87)
Right handed, no (%)	186 (79)
Additional OA sites, no (%)	
Knee	94 (40)
Hip	69 (29)
Spine	174 (74)
AUSCAN pain	7.3 (4.8)
AUSCAN function	13.9 (8.7)
No. self-reported painful joints*	6.0 (6.3)
No. painful joints on pressure*	4.7 (5.3)
Grip strength, kg	21.4 (10.4)
HAMIS	4.0 (2.9)

Values are means (SD) unless stated otherwise.
*DIPJs 2-5, PIPJs 2-5, MCPJs 2-5 both hands.
Abbreviations: ACR: American College of Rheumatology; AUSCAN: Australian/Canadian Osteoarthritis Hand Index; HAMIS: Hand Mobility in Scleroderma.

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and 1.40 mm (SD 0.25), respectively (table 2). The mean JSW for all joints in controls from the KART study was 1.18 mm (SD 0.41), for MCPJs 1.61 mm (SD 0.23), for PIPJs 0.96 mm (SD 0.20) and for DIPJs 0.90 mm (SD 0.26). The JSW of KART-controls was significantly larger than the JSW in hand OA patients (p-value <0.001). The significance remained the same if EAC-controls were included in the analyses.

JSW in relation with age, sex (in controls and OA patients) and JSN scores (in OA patients only)
The quantification of JSW in relation to the JSN score according to OARSI atlas is also shown in table 2. The largest JSW was seen in the JSN=0 group, the smallest JSW in the JSN=3 group. No estimation for the JSW in the MCPJs with JSN=3 is given, since only two MCP joints were present in this group.

In hand OA patients, being female was associated with a smaller JSW of the finger joints only after adjustment for presence of osteophytes (adjusted β -0.08 (95%CI -0.15 to -0.01)). In controls, being female was also associated with a smaller JSW, when adjusted for the mean width of phalanges of the hands only (adjusted β -0.08 (95%CI -0.12 to -0.05)), and not statistically significant for hand OA patients (adjusted β -0.04 (95%CI -0.12 to 0.05)). Age was not associated with a smaller JSW in hand OA patients (with or without adjustment for presence of osteophytes), but older age was associated with smaller JSW in controls (table 3). The associations of JSW (as dependent variable) and female sex, with additional adjustment for age, remained the same in both control and patient populations (data not shown).

Table 2. A. Distribution of number of joints (%) in the visual grading method for joint space narrowing (JSN) graded 0-3 according to the OARSI scoring method. **B.** Mean joint space width in millimetres (SD) in relation to JSN according to the OARSI scoring method.

A.

	JSN=0	JSN=1	JSN=2	JSN=3
All joints (n=5631)	2574 (46)	2529 (45	405 (7)	123 (2)
DIPs (n=1878)	454 (24)	1048 (56)	284 (15)	92 (5)
PIPs (n=1873)	588 (31)	1156 (62)	100 (5)	29 (2)
MCPs (n=1880)	1532 (81)	325 (17)	21 (1)	2 (0.1)

B.

	Controls	Hand OA	JSN=0	JSN=1	JSN=2	JSN=3
All joints	1.15 (0.17)	0.98 (0.21)	1.28 (0.34)	0.80 (0.23)	0.42 (0.28)	0.17 (0.23)
DIPs	0.89 (0.23)	0.70 (0.25)	0.95 (0.23)	0.72 (0.20)	0.39 (0.27)	0.16 (0.23)
PIPs	0.95 (0.15)	0.84 (0.22)	1.05 (0.25)	0.79 (0.19)	0.47 (0.30)	0.18 (0.24)
MCPs	1.61 (0.23)	1.40 (0.27)	1.47 (0.27)	1.12 (0.23)	0.54 (0.34)	*

All joints = DIP 2-5, PIP 2-5 and MCP 2-5 in both hands, DIPs = DIP 2-5 in both hands, PIPs = PIP 2-5 in both hands, MCPs = MCP 2-5 in both hands.
*No estimation since only 2 joints were present.

Table 3. Association of joint space width in millimetres with age and sex in the control group (11280 joints) and in patients with hand osteoarthritis (5631 joints), expressed as β-coefficient with 95%CI and p-value.

	Control group	Hand OA	
	Crude	Crude	Adjusted*
Female	-0.17 (-0.20 to -0.14), <0.01	-0.07 (-0.15 to 0.01), 0.08	-0.08 (-0.15 to -0.01), 0.02
Age	-0.001 (-0.003 to 0.00), 0.04	0.001 (-0.003 to 0.01), 0.77	0.003 (0.000 to 0.006), 0.09

*Adjustment for osteophytes

Associations of JSW and JSN with clinical determinants at joint level

On the joint level, decreased JSW was associated with presence of osteophytes, self-reported pain, nodes, pain on palpation and erosions (table 4). The unstandardised β-coefficient can be interpreted as the mean difference in JSW between the presence and absence of the determinant in that joint. For example, if an erosive lesion was present in a joint, the mean JSW is -0.61 mm smaller in that joint. If a joint was scored as an osteophyte grade 1 or grade 3 according to the OARSI atlas, the mean JSW is -0.20 or -0.62 mm smaller than in a joint without an osteophyte, respectively.

For the JSN score, associations with clinical determinants showed that an increase in JSN score is related to the presence of each of the determinants named above (table 4). These associations were similar to those with JSW. For example, if an erosive lesion was present, the mean JSN score is 1.43 higher than for a joint without an erosion. Since the JSN score is not a continuous outcome measure, but a graded scoring method, the β-coefficient cannot be interpreted as an exact mean difference in this table.

Table 4. Association of joint space width (JSW) and joint space narrowing (JSN) with clinical determinants in hand osteoarthritis patients, at joint level, expressed as β-coefficient with 95%CI and p-value

	JSW (5631 joints)	JSN (5631 joints)
Osteophytes (OARSI)		
Osteophyte=0	0	
Osteophyte=1	-0.20 (-0.23 to -0.17), <0.001	0.36 (0.31 to 0.41), <0.001
Osteophyte=2	-0.54 (-0.61 to -0.48), <0.001	1.24 (1.11 to 1.38), <0.001
Osteophyte=3	-0.62 (-0.74 to -0.51), <0.001	1.31 (1.12 to 1.50), <0.001
Self-reported pain		
No pain	0	0
Pain present	-0.21 (-0.27 to -0.16), <0.001	0.39 (0.30 to 0.48), <0.001
Presence of nodes		
No nodes	0	0
Nodes present	-0.37 (-0.40 to -0.34), <0.001	0.48 (0.42 to 0.55), <0.001
Pain on palpation		
No pain	0	0
Pain present	-0.25 (-0.29 to -0.21), <0.001	0.37 (0.29 to 0.44), <0.001
Erosions*		
No erosion	0	0
Erosion present	-0.61 (-0.68 to -0.54), <0.001	1.43 (1.31 to 1.54), <0.001

β-coefficient adjusted for age, sex, BMI, family effect within sibling pairs and mean width of the phalanx.
*Erosion defined as an erosive joint or joint with a remodeled irregular sclerotic surface.

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Associations of summed JSW and JSN with clinical determinants at patient level

Lower total JSW was associated with a higher osteophyte scores and a higher number of joints with self-reported pain, pain on palpation and nodes (table 5). The presence of more pain and functional limitations measured with the AUSCAN and worse hand mobility according to the HAMIS were also associated with lower total JSW. JSW was positively associated with grip strength, meaning that a higher JSW is related to more grip strength.

Similar to JSW, a higher JSN score was associated with higher osteophyte scores and a higher number of joints with self-reported pain, pain on palpation and nodes (table 5). Again more JSN was related to the presence of more pain and functional limitations measured with the AUSCAN and worse hand mobility according to the HAMIS. JSN was not related to grip strength. The crude estimates for both JSW and JSN did not differ from the adjusted estimates.

DISCUSSION

This paper compares the JSW in millimeters of finger joints in a large population of patients with hand OA with visual grading score for JSN and JSW measurements of controls. We showed that quantitative JSW measurements and the visual grading method for JSN are both associated with self-reported pain and functional ability, pain on palpation and the

Table 5. Association of summed joint space width (JSW) and summed joint space narrowing (JSN) with clinical determinants in hand osteoarthritis patients, at patient level, expressed as β-coefficient with 95%CI and p-value.

	Summed JSW	Summed JSN
Summed osteophytes	-0.27 (-0.34 to -0.19), <0.001	0.75 (0.62 to 0.88), <0.001
No. joints self-reported pain	-0.14 (-0.23 to -0.05), 0.003	0.30 (0.12 to 0.48), 0.001
No. joints nodes	-0.28 (-0.42 to -0.14), <0.001	0.76 (0.50 to 1.03), <0.001
No. joints pain on palpation	-0.12 (-0.23 to -0.01), 0.03	0.27 (0.06 to 0.49), 0.01
AUSCAN pain	-0.13 (-0.25 to -0.01), 0.03	0.25 (0.02 to 0.49), 0.04
AUSCAN function	-0.11 (-0.17 to -0.05), 0.01	0.21 (0.08 to 0.34), 0.002
Grip strength left hand	0.05 (-0.02 to 0.12), 0.14	-0.06 (-0.19 to 0.08), 0.44
Grip strength right hand	0.07 (0.00 to 0.13), 0.07	-0.07 (-0.21 to 0.08), 0.36
HAMIS both hands	-0.46 (-0.68 to -0.24), <0.001	1.08 (0.64 to 1.52), <0.001

β-coefficient adjusted for age, sex, BMI, family effect within sibling pairs and mean width of the phalanx.
Abbreviations: see table 1.

presence of osteophytes, nodes and erosions. This implies that JSW measurement is a valid method to evaluate loss of joint space in finger joints of hand OA patients.

The expectation was that the mean JSW in patients with hand OA would be smaller than in controls without hand complaints. We confirmed this hypothesis. The radiographs and JSW measurements of these controls were judged by the same expert and measured in the same hospital with identical semi-automated method as in the present study minimising confounding factors.

The present study showed that females had smaller JSW than men in hand OA patients after adjustment for the presence of osteophytes, since this is another feature of OA. Additional adjustment for age did not change these results. In controls, females also have smaller JSW than men after adjustment for the size of the hand (reflected by the mean width of phalanges of the hand), so partly this effect can be contributed to the fact of having smaller hands. These results that females have smaller JSW are in accordance to data from patients with rheumatoid arthritis and healthy controls, showing that JSW in females were smaller than in males (without adjustments).[19-21] The study in healthy controls showed an age-dependent decrease of the JSW in both males and females.[20,21] In patients with rheumatoid arthritis (94 females, 34 males), only in females an association between age and JSW was seen.[19] In the present study, older age was associated with a lower JSW in controls, but no association between age and JSW was seen in hand OA patients. This could be explained by the small age range between 50 and 85 years in hand OA patients which could lead to a biased (positive) association of age and JSW in this population. Alternatively, the positive association between age and JSW in hand OA patients could be explained by thickening of the cartilage in early stages of OA reflecting a larger JSW on radiographs.[22]

We show that JSW measurements are a valid method to measure the joint space, since it is related to clinical features. In the past it was shown that the quantitative method itself is accurate and reproducible.[10,23-25] The visual grading method for

JSN showed the same relation with clinical features. An additional advantage of JSW measurements performed by the computer software is that it is not subject to interpretation differences which can be present amongst human observers. The expectation is that quantifying loss of joint space with this method will give fewer mistakes in interpretation compared to the grading of joint space narrowing. In addition, the JSW can be more easily compared with other JSW in other studies. Unfortunately, the present study did not measure the mistakes made by the computer where the expert reviewer need to interrupt and should be investigated in the future.

Results shown in table 4 and 5, where same associations of JSW and JSN with clinical determinants were found, indicate that the JSW method is not superior to the visual grading method to measure joint space. An argument to choose for one of these methods could be that one method is easier or more feasible to use than the other (e.g. less time-consuming). For example, the positioning of the hand in the JSW method is important to derive the most precise joint space width measurements. The study of Angwin et al. showed that if the hand was positioned in six different arranged positions, the JSW of the MCPJs varied.[23] In the visual grading method, the effect of positioning could be less important than in the JSW method. In longitudinal studies it could be that the JSW method is more sensitive to measure subtle changes where the visual grading method is not able to detect these changes and whether they are relevant in clinical practice. Bijsterbosch et al. showed that the changes in the visual grading method were not related with clinical determinants.[5] It could be that changes in the JSW method would be related with clinical determinants, but this hypothesis needs further investigation. In a longitudinal study in early rheumatoid arthritis it was shown that a change in JSW was a more sensitive outcome measure than a visual grading method (total Sharp score).[26]

Several limitations of this study can be addressed. Since radiographs are still two-dimensional representations it is not possible to measure joint space width as a measure of volume which can more accurately describe the three-dimensional structure of a joint. The mean JSW remains the best estimate of the cartilage of the joint. The mean JSW could be influenced by other structures such as osteophytes if these are projected in the frontal plane. The automatic measurements were reviewed by an expert in order to confirm that the joint space width between the true contours of the interphalangeal bones was measured. In hand OA, no studies are known where the volume of the joint space or cartilage was quantified. In knee OA joints, Duryea et al. performed a comparison between quantitative magnetic resonance imaging (MRI) (volume and thickness measurements in mm^3) with radiography (JSW in mm) in a longitudinal study where a relatively weak correlation was found.[27] Furthermore, hand OA patients in the present study are not representative for the general population, since they were selected on familial OA at multiple sites. Previous studies showed that these hand OA patients were less affected by their hand complaints than hand OA patients in the rheumatology practice.[1,28] Bias in the selection of hand joints in controls is possible, since patients selected from the cohort with knee complaints may be not fully comparable with a randomly selected population. However, since the knee complaints were sub-acute (and not chronic), they should not have a higher risk

of the presence of hand OA at the moment of their study inclusion than a random selected control group. This is supported by the finding that the JSW of controls is higher than the hand OA patients in our population. Finally, the hand radiographs were obtained with the same study protocol and technician in the majority of subjects. Since the knee population consisted mostly of males, hand radiographs of EAC-controls were included, however their radiographs were not obtained according to the study protocol. This could also lead to a bias in the mean JSW.

In conclusion, automated quantitative analyses of the JSW are a valid method to measure JSN in relation with clinical features, such as pain and the presence of nodes. The role of measuring the JSW in hand OA patients needs to be investigated in longitudinal studies to determine if it can discriminate progression in hand OA in an earlier stage than the JSN scoring and to assess its relationship to change in symptoms over time.

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