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Normative Reference Values of Joint Space Width Estimated by Computer-aided Joint Space Analysis (CAJSA): The Distal Interphalangeal Joint

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Purpose: **The study introduces reference data for a computer-aided analysis. The semiautomated computer-aided diagnostic system provides the estimation of joint space width at the distal interphalangeal joints, considering gender-specific and age-related changes.** ***Patients and methods:*** **869 subjects (351 female/518 male) with hand x-rays were included and underwent measurements of joint space distances at the distal interphalangeal articulation (JSD-DIP) of the second to the fifth finger using computer-aided joint space analysis (CAJSA).** ***Results:*** **Data showed a notable age-related decrease of CAJSA parameters, and an accentuated age-related joint space narrowing in women. Males showed a significantly wider JSD-DIP (+ 16.7%) compared to the female cohort for all age groups. Both men and women revealed an accentuated decrease of JSD-DIP (total) in the age group from 10 to 15 years (for men −10.5% and for women −17.6%). After the age of 21 years a continuous decline of the JSD-DIP (total) is observed.** ***Conclusion:*** **Our data present gender-specific and age-related normative reference data for computer-aided joint space analysis, which provide a valid and reliable differentiation between disease-related joint space narrowing and age-related joint space narrowing, particularly in patients with osteoarthritis of the fingers.**

KEY WORDS: Computer-aided diagnosis, distal interphalangeal joint, joint space distance, normative reference value, osteoarthritis, rheumatoid arthritis

Abbreviations:

CAD	Computer-aided diagnosis
CAJSA	Computer-aided joint space analysis
CV	Coefficient of variation
JSD	Joint space distance
JSD-MCP	Joint space distance of the metacarpal–phalangeal joint
JSD-DIP	Joint space distance of the distal–interphalangeal joint
SD	Standard deviation
JSD-PIP	Joint space distance of the proximal-interphalangeal joint

INTRODUCTION

The hand is a common site of peripheral osteoarthritis, which is underestimated as a cause of disability and, in addition, its effect on quality of life may be considerable.[1] The most common sites for finger osteoarthritis are the distal interphalangeal joints (DIP), proximal interphalangeal joints (PIP), and the base of the thumb.[2–5] Osteoarthritis of the hand has an incidence rate of approximately 100/100,000 person per year.[6] Cross sectional studies have estimated the prevalence of radiographic hand osteoarthritis in those patients over 65 years as ranging from 64 to 78% in men and 71 to 99% in women.[7–10]

Conventional radiography is a widely available and cost-effective method, and remains the standard

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of diagnosis for the detection and quantification of joint alteration in the course of finger osteoarthritis.[11] The assessment of disease is performed by visualization of changes in joint space width as an indirect sign of cartilage loss. The disadvantage of conventional imaging is the limited sensitivity in detecting an early narrowing of the joint space.[12] The conventional assessment of joint space width is influenced by the subjective scoring depending on the experience of the clinician, and is characterized by a remarkable interobserver variation of the measurements.[13]

Computer-aided diagnosis (CAD) has been consequently refined and improved, and is increasingly accepted in the field of radiological diagnostics.[14–16] Although early measurements of joint space widths were carried out only on large joints, especially at the hip and knee,[17–20] the new computer-aided joint space analysis (CAJSA, Version 1.3.6; Sectra; Sweden) is a recently developed approach, which conducts semiautomated measurements of joint space distances at the distal interphalangeal articulation of the second to the fifth finger. In recent studies, CAJSA have been able to detect and quantify disease-related joint-space narrowing of the metacarpal–phalangeal joint (MCP) caused by the course and severity of rheumatoid arthritis, which is accelerated in early RA.[21,22]

The aim of this study is to introduce reference data for computer-aided joint space analysis (CAJSA), a semiautomated computer-aided diagnostic system for the measurements of joint space distances, and to quantify gender-specific and age-related differences regarding the distal interphalangeal articulation.

PATIENTS AND METHODS

Patients

This prospective study enrolled 869 subjects (351 female, 518 male). All subjects underwent measurements of the joint space distance of the distal interphalangeal articulation (JSD-DIP in centimeters) using CAJSA technology.

Mean age was 35.5 years with a standard deviation of 19.2 years and an age range of 6.1 to 95.3 years (females: mean age 37.9 ± 20.8 years, males: 33.2 ± 17.5 years). Digital radiographs of the hand were taken from each subject between 2001 and 2005 who were admitted to the University clinic because of fracture exclusion. Each hand radiograph was read by two musculoskeletal radiologists for evidence of osteoarthritis using the Kellgren–Lawrence grading system with a standard atlas[23]: grade 0 = normal joint; grade 1 = small osteophyte of doubtful significance; grade 2 = definite osteophyte; grade 3 = osteophyte and joint space narrowing; grade 4 = severe joint space narrowing. In cases of ambiguity, a third musculoskeletal radiologist reviewed the radiographs.

Exclusion criteria were determined by an extensive questionnaire, and included: visible metallic material (ie, splints and material after osteosynthesis; $n = 899$), signs of fracture ($n = 4{,}867$), amputation ($n = 38$), endocrinological diseases known to affect bone metabolism (eg, hyper/hypoparathyroidism, Cushing disease; $n = 245$), rheumatic diseases (eg, rheumatoid arthritis; $n = 1{,}237$), renal disorders ($n = 1{,}084$), genetic diseases ($n = 23$), oncological diseases ($n = 1{,}255$), medication with bone-influencing drugs (eg, steroids, vitamin D, or calcium intake; $n = 182$), Kellgren–Lawrence grade higher than 1 ($n = 534$) and incorrect hand positioning ($n = 103$).

Methods

Measurement of Joint Space Width (By Computer-aided Joint Space Analysis)

The computer-aided joint space analysis (Version 1.3.6; Sectra; Sweden) was used to determine JSD-DIP based on radiographs of the hand (Fig. 1). All digital plain radiographs of the hand were acquired by a Siemens Multix device (Siemens, Erlangen, Germany) under the following standardized conditions: filter 1.0, film focus distance 1 m, aluminum 80, tube voltage 42 kV, exposure level 4 mAs, AGFA Scopix Laser 2 B 400 (Agfa, Cologne, Germany).

The system performs a continual self-checking to maintain quality of the digital imaging, stopping the process when imaging becomes inferior (ie, consecutively incorrect depictions of anatomical structures).

The technique analyzes a finger joint by detection of the joint edges within a rectangular region of interest as defined by the user. Each region of interest was drawing around the joint by the same musculoskeletal radiologist. The positioning of the region of interest to specify a

Fig. 1. Semiautomatic measurement of the distal interphalangeal joint space (II–V) by the computer-aided joint space analysis (CAJSA, Version 1.3.6; Sectra; Sweden). The region of interest (ROI) is semiautomatic positioning by the operator. In the figure, the ROIs are in projection of the distal interphalangeal joint II to V. The software causes a filtering of the edge of the ROI and the distance between the bones is defined as the average distance between the two involved edges.

particular joint is the only operator-dependent interaction during the entire measurement process. The software causes a filtering of the edge of the ROI and automatically detects the tips of the two specified bones. A 1.5-cm-long edge path across each bone is further determined and the distance between the two edges is measured as a function of the horizontal position. The mean average and standard deviation of the distance over a moving interval of 0.8 cm is calculated. The distance between the bones is defined to be over the edge interval for which the standard deviation is minimal. In our investigations, the measurement of the joint spaces was methodically established for the distal interphalangeal joint II–V and distances were given in centimeters.

Short-term Precision of Joint Space Measurement (By Computer-aided Joint Space Analysis)

The intraradiograph reproducibility (measurements of 10 images of the same hand with repositioning) for the CAJSA parameters showed the following coefficients of variation, where the notation II through V denotes the second through fifth fingers, respectively:

JSD – DIP II : 1.57% JSD – DIP III : 1.59%

JSD – DIP IV : 1.32% JSD – DIP V : 1.47%

Ethics

All examinations were performed in accordance with the rules and regulations of the local human research and ethics committee. As a special note, the authors emphasize that all radiographs used for CAJSA-calculations were performed as part of routine clinical care (eg, exclusion of fractures caused by relevant trauma); no additional radiographs were obtained only for study purposes.

Data Analysis

The objective of the statistical analysis was to establish normative reference values of the joint space distance for the distal interphalangeal joint of the second to fifth digit. Comparison of CAJSA parameters versus age were done via regression analysis. The significance of sex-dependent changes was calculated with the Mann–Witney *U* test. The significance of differences between the age group under 10 years and above 86 years were also calculated with the Mann–Witney *U* test. Statistical analysis was performed using SPSS version 10.13® (SPSS, Chicago, Illinois, USA) for Windows.

RESULTS

CAJSA Parameters Depend on Age-related Changes

For all individuals, the CAJSA system reliably recognized the distal interphalangeal articulations. This study revealed a close relationship between

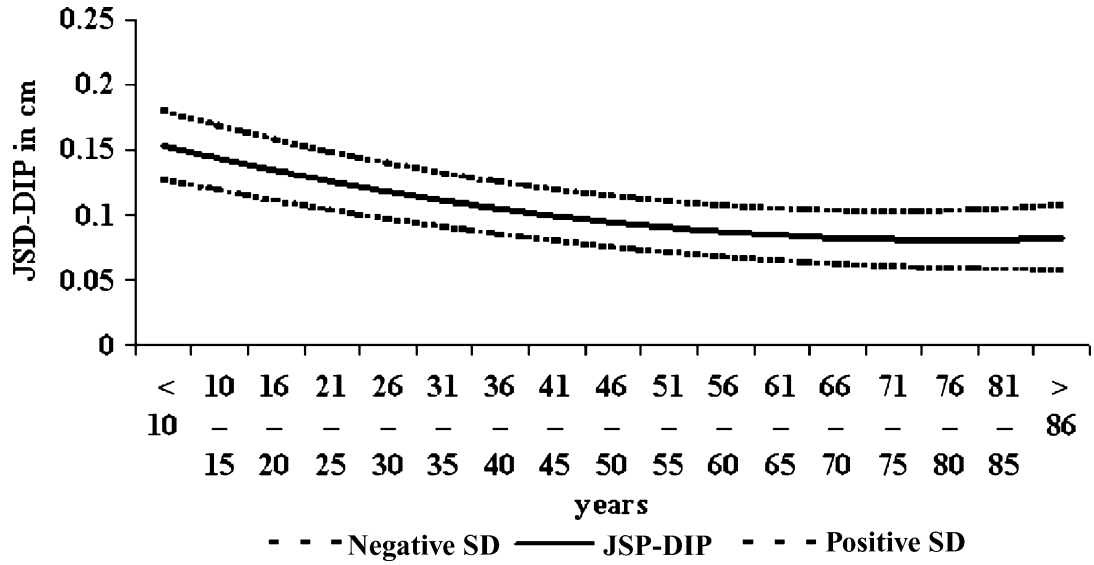

Fig. 2. Age-related normative values of Joint Space Distance of the Distal-Interphalangeal joint (JSD-DIP total) and standard deviations (SD) determined on women (n = 351).

age and all established parameters. Therefore all correlations between age and parameters of CAJSA were significant negative for women ($-0.54 < r < -0.63$, $p < 0.001$) as well as for men ($-0.46 < r < -0.57$, $p < 0.001$) whereas JSD-DIP for the female subjects (Fig. 2) continuously showed a closer association to age compared with the JSD-DIP in men (Fig. 3). The highest correlation was observed for JSD-DIP III versus age ($r = -0.63$, $p < 0.001$) in the female group.

In men JSD-DIP (total) significantly decreased (-57.9%; $p < 0.001$) from 0.19 ± 0.03 cm (age < 10 years) to 0.08 ± 0.02 cm (age > 86 years) in a continuous manner (Tables 2 and 3). In women, JSD-DIP (total) also presented a significant and continuous reduction (-52.9%; $p < 0.001$) from

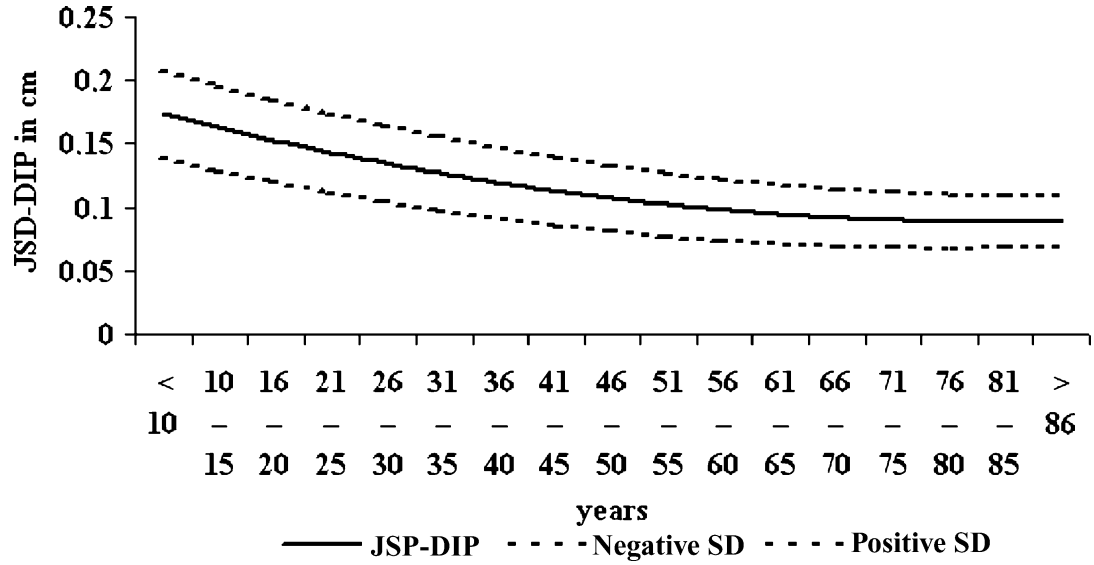

Fig. 3. Age-related normative values of Joint Space Distance of the Distal-Interphalangeal joint (JSD-DIP total) and standard deviations (SD) determined on men (n = 518).

Table 1. Mean and Standard Deviation for Joint Space Distance of the Distal Interphalangeal Joint (Women, *n* = 351)

		JSD, in Centimeters				
Age in Years	*N*	DIP[a] II Mean (SD)	DIP[a] III Mean (SD)	DIP[a] IV Mean (SD)	DIP[a] V Mean (SD)	DIP[a] Total Mean (SD)
<10	12	0.16 (0.03)	0.18 (0.03)	0.18 (0.03)	0.16 (0.04)	0.17 (0.03)
10–15	16	0.14 (0.02)	0.15 (0.03)	0.14 (0.02)	0.12 (0.02)	0.14 (0.02)
16–20	42	0.13 (0.02)	0.13 (0.03)	0.12 (0.02)	0.10 (0.02)	0.12 (0.02)
21–25	45	0.12 (0.02)	0.12 (0.02)	0.12 (0.01)	0.10 (0.01)	0.12 (0.02)
26–30	35	0.12 (0.03)	0.12 (0.03)	0.11 (0.03)	0.10 (0.02)	0.11 (0.03)
31–35	32	0.12 (0.02)	0.12 (0.02)	0.11 (0.02)	0.10 (0.02)	0.11 (0.02)
36–40	22	0.12 (0.02)	0.11 (0.02)	0.10 (0.02)	0.10 (0.01)	0.11 (0.02)
41–45	22	0.11 (0.03)	0.11 (0.02)	0.10 (0.02)	0.09 (0.01)	0.10 (0.02)
46–50	24	0.11 (0.02)	0.11 (0.02)	0.10 (0.02)	0.09 (0.01)	0.10 (0.02)
51–55	24	0.10 (0.02)	0.09 (0.02)	0.09 (0.01)	0.08 (0.01)	0.09 (0.02)
56–60	16	0.10 (0.02)	0.09 (0.02)	0.08 (0.02)	0.08 (0.02)	0.09 (0.02)
61–65	11	0.10 (0.02)	0.09 (0.02)	0.08 (0.01)	0.08 (0.02)	0.09 (0.02)
66–70	14	0.09 (0.02)	0.09 (0.02)	0.08 (0.02)	0.07 (0.02)	0.08 (0.02)
71–75	7	0.08 (0.02)	0.09 (0.02)	0.08 (0.01)	0.07 (0.02)	0.08 (0.02)
76–80	9	0.08 (0.03)	0.09 (0.03)	0.08 (0.02)	0.07 (0.01)	0.08 (0.02)
81–85	12	0.08 (0.03)	0.09 (0.02)	0.08 (0.02)	0.07 (0.01)	0.08 (0.02)
>86	8	0.08 (0.03)	0.09 (0.02)	0.08 (0.02)	0.07 (0.03)	0.08 (0.03)
Total	351	0.11 (0.02)	0.11 (0.02)	0.10 (0.02)	0.09 (0.02)	0.10 (0.02)

[a]DIP = Distal Interphalangeal joint
SD = Standard deviation
JSD = Joint Space Distance

0.17 ± 0.03 cm (age < 10 years) to 0.08 ± 0.03 cm (age > 86 years; Tables 1 and 3). A similar decline was observed for JSD-DIP III in males (−57.9%; $p < 0.001$). In females, JSD-DIP (II to IV) revealed a significant reduction of −50.0% ($p < 0.001$) between ages <10 and >86 years. A maximal decrease for JSD-DIP V in men (−61.1%; $p < 0.001$) from 0.18 ± 0.02 cm (age < 10 years) to 0.07 ± 0.01 cm (age > 86 years) and in women (−56.3%; $p < 0.001$) from 0.16 ± 0.04 cm (age < 10

Table 2. Mean and Standard Deviation for Joint Space Distance of the Distal Interphalangeal Joint (Men, *n* = 518)

		JSD, in Centimeters				
Age in Years	*N*	DIP[a] II Mean (SD)	DIP[a] III Mean (SD)	DIP[a] IV Mean (SD)	DIP[a] V Mean (SD)	DIP[a] Total Mean (SD)
<10	15	0.17 (0.05)	0.19 (0.02)	0.20 (0.04)	0.18 (0.02)	0.19 (0.03)
10–15	26	0.17 (0.03)	0.18 (0.04)	0.17 (0.04)	0.15 (0.03)	0.17 (0.04)
16–20	96	0.14 (0.02)	0.15 (0.03)	0.14 (0.03)	0.12 (0.02)	0.14 (0.03)
21–25	82	0.13 (0.03)	0.13 (0.03)	0.13 (0.03)	0.11 (0.02)	0.13 (0.03)
26–30	60	0.13 (0.02)	0.13 (0.03)	0.12 (0.03)	0.11 (0.02)	0.12 (0.03)
31–35	46	0.13 (0.03)	0.13 (0.03)	0.12 (0.03)	0.11 (0.02)	0.12 (0.03)
36–40	38	0.13 (0.03)	0.13 (0.03)	0.12 (0.03)	0.10 (0.02)	0.12 (0.03)
41–45	36	0.12 (0.02)	0.12 (0.03)	0.12 (0.03)	0.10 (0.02)	0.12 (0.03)
46–50	28	0.12 (0.03)	0.12 (0.03)	0.11 (0.03)	0.10 (0.03)	0.11 (0.03)
51–55	20	0.12 (0.02)	0.12 (0.02)	0.11 (0.03)	0.10 (0.01)	0.11 (0.02)
56–60	14	0.11 (0.02)	0.11 (0.02)	0.09 (0.03)	0.08 (0.02)	0.10 (0.02)
61–65	15	0.11 (0.03)	0.10 (0.02)	0.09 (0.02)	0.08 (0.02)	0.10 (0.02)
66–70	12	0.10 (0.02)	0.10 (0.02)	0.09 (0.02)	0.08 (0.02)	0.09 (0.02)
71–75	8	0.10 (0.03)	0.10 (0.03)	0.09 (0.02)	0.08 (0.04)	0.09 (0.03)
76–80	11	0.10 (0.02)	0.10 (0.02)	0.09 (0.02)	0.08 (0.01)	0.09 (0.02)
81–85	3	0.09 (0.2)	0.10 (0.02)	0.09 (0.02)	0.08 (0.03)	0.09 (0.02)
>86	8	0.09 (0.03)	0.08 (0.01)	0.08 (0.01)	0.07 (0.01)	0.08 (0.02)
Total	518	0.13 (0.03)	0.12 (0.03)	0.12 (0.03)	0.10 (0.02)	0.12 (0.03)

[a]DIP = Distal Interphalangeal joint
SD = Standard deviation
JSD = Joint Space Distance

Table 3. Changes of Joint Space Distances Between the Age Groups <10 and >86 Years

	Reduction Between Groups <10 and >86 Years, in Percent	
	Men (n = 518)	Women (n = 351)
JSD-DIP[a] II	−47.1% ($p<0.001$)	−50.0% ($p<0.001$)
JSD-DIP[a] III	−57.9% ($p<0.001$)	−50.0% ($p<0.001$)
JSD-DIP[a] IV	−60.0% ($p<0.001$)	−50.0% ($p<0.001$)
JSD-DIP[a] V	−61.1% ($p<0.001$)	−56.3% ($p<0.001$)
JSD-DIP[a] total	−57.9% ($p<0.001$)	−52.9% ($p<0.001$)

[a]JSD-DIP = Joint Space Distance of the Distal Interphalangeal joint, in centimeters

years) to 0.07 ± 0.03 cm (age > 86 years) was documented. For JSD-DIP II and IV, similar results with −47.1% ($p < 0.001$) versus −60.0% ($p < 0.001$) were obtained for men.

An accentuated decrease of JSD-DIP (total) in the age group from 10 to 15 years (for men −10.5% with $p < 0.05$, and for women −17.6% with $p < 0.01$) and in the age group from 16 to 20 years (for men −17.6% with $p < 0.01$ and for women −14.3% with $p < 0.01$) was found for both genders. The annual joint space narrowing up to the age of 20 years (annual joint space narrowing between the age of 10 up to 20 years, given as percentage per year) was −1.9% ($p < 0.05$) for men and −2.1% ($p < 0.05$) for women. Beginning with the age of 21 years (annual joint space narrowing between the ages of 21 up to 90 years, given as percentage per year) males revealed a decrease of −0.4% ($p < 0.05$) and females showed a reduction of −0.5% ($p < 0.05$).

Gender-related Differences of CAJSA Parameters

The results showed that women had a significantly smaller total JSD-DIP (mean −16.7%; $p < 0.01$; Table 4), compared to men. The female JSD-DIP II, JSD-DIP III, and JSD-DIP V are significantly decreased with −15.4% ($p < 0.01$), −8.3% ($p < 0.05$), and −10.0% ($p < 0.05$) in comparison to males. The pronounced difference was observed for JSD-DIP IV with a change of −16.7% ($p < 0.01$).

DISCUSSION

The aim of this study is to establish normative gender-specific and age-related reference values for computer-aided joint space analysis (CAJSA), to establish CAJSA into the clinical routine. Our data evaluated age-related and gender-specific changes of the distal interphalangeal joint space width in a normal population.

Short-term Precision of Different Articulations

CAJSA technology now provides measurements of the JSD-MCP, which may be published for patients with rheumatoid arthritis. Böttcher et. al.[24] has shown an excellent short-term precision regarding the metacarpal–phalangeal articulation between 0.59% (the metacarpal–phalangeal joint II) to 0.99% (the metacarpal–phalangeal joint IV). Measurements of JSD at the proximal and distal interphalangeal joints are more complex, because these joints have a bicompartmental configuration which results in a varied width of each compartment

Table 4. Comparison of Normative Values (JSD-DIP) Between Men and Women

	Men	Women		
	Mean (SD)	Mean (SD)	Relative Difference Between Men and Women (%)	Significance (Mann–Witney U Test)
JSD-DIP[a] II (in cm)	0.13 (0.03)	0.11 (0.02)	15.4	$p<0.01$
JSD-DIP[a] III (in cm)	0.12 (0.03)	0.11 (0.02)	8.3	$p<0.05$
JSD-DIP[a] IV (in cm)	0.12 (0.03)	0.10 (0.02)	16.7	$p<0.01$
JSD-DIP[a] V (in cm)	0.10 (0.02)	0.09 (0.02)	10.0	$p<0.05$
JSD-DIP[a] total (in cm)	0.12 (0.03)	0.10 (0.02)	16.7	$p<0.01$

[a]JSD-DIP = Joint Space Distance of the Distal Interphalangeal joint

following minor rotations of the hand. A minor rotation during x-ray imaging results in impaired reproducibility for the proximal interphalangeal articulation and distal interphalangeal articulation. Böttcher et al documented a limited intraradiograph reproducibility of JSD of the proximal interphalangeal joint using the CAJSA version 1.3.5.[24] After improvement of contour-finding procedures based on the new CAJSA software version (1.3.6), the actual results revealed a moderate short-term precision ranging from 1.32% (JSD-DIP IV) to 1.59% (JSD-DIP III).

Influence of Gender and Age on JSD-DIP

Present theories of the pathogenesis of osteoarthritis suggest that both systemic and local factors affect the likelihood of osteoarthritis onset in the small hand joints.[25,26] Local factors such as higher grip strength and hand trauma have been associated with the development of hand osteoarthritis.[27,28] Obesity is also reported to be a significant risk factor for the development of knee osteoarthritis,[29,30] but its association with hand osteoarthritis is less clear. Some studies have reported no association between high body mass index and hand osteoarthritis in the elderly subjects, whereas other studies have found a positive association, particularly with carpometacarpal osteoarthritis.[31–33] It is thought that systemic factors such as age, sex, race, and genetics predispose for hand osteoarthritis.[34] Age and sex have well described effects on the prevalence of hand osteoarthritis.[35] Jones et al[36] presented a high prevalence of hand osteoarthritis with manifestation at the distal interphalangeal articulation in women (70%), as compared to men (57%). Furthermore, age and sex have well described effects on the severity of hand osteoarthritis,[35] but there is less information as to whether the age gradient is different between the sexes.[37] Our results reveal a remarkable impact of the occurrence of finger osteoarthritis in women. The JSD-DIP (total) for women is considerably smaller (−16.7%) than in the male cohort.

JSD Measurement in Clinical Practice

Hand radiography has been claimed to be the best method for clinical determination of hand osteoarthritis.[7–9,38,39]

However, precise verification of hand osteoarthritis remains problematic,[39] because no absolute clinical, radiological, or pathological standard for the diagnosis exists.[40] Using the normative values estimated by CAJSA, a radiological standard of JSD for affected distal interphalangeal joints is now available. Consecutive cutoff values based on these normative data can improve the detection of initial cartilage destruction in early osteoarthritis; the narrowing of JSD-DIP may now be measured and evaluated in detail.

The reference values established by this technology allow the detection and quantification of cartilage dissolution in the early stages of joint-affecting disorders (ie, osteoarthritis and rheumatoid arthritis) based on a direct comparison between normative values and the data of the patient. Further studies should focus on the applicability to other articulations and determine the influence on therapeutic strategies in patients with osteoarthritis.

CONCLUSION

Computer-aided techniques have shown remarkable potential in the measurement of several radiogeometrical features; in particular CAJSA has provided a cost-effective approach for the quantification of joint space distances using digital radiographs of the hand. The present study provides normative reference values for both women and men, revealing significant gender-specific differences in joint space width for the two sexes in all age groups. Additionally, this new CAD method allows an excellent overview of the narrowing of JSD-DIP during aging. Therefore, multicenter studies with larger gender-specific age groups will be required to confirm the age-associated joint space narrowing. These normative values are expected to enhance the process of identification of patients suffering from osteoarthritis. Further prospective studies are required to determine the predictive value of CAJSA to detect patients with early onset of joint osteoarthritis and to introduce the CAJSA technique as a cost-effective, widely available, and precise method in the clinical routine.

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