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Title; Radiographic Quantifications of Joint Space Narrowing Progression by Computer-based Approach Using Temporal Subtraction in Rheumatoid Wrist

Short title; Radiographic Quantifications of JSN Progression in Rheumatoid Wrist

Abstract

Objectives. To investigate a validity of the computer-based method using temporal subtraction in carpal joints of rheumatoid arthritis (RA) patients, which can detect the difference in joint space between two images as the joint space difference index (JSDI).

Methods. The study consisted of 43 RA patients (39 women and 4 men) who underwent radiography at baseline and at 1 year. The joint space narrowing (JSN) of carpal joints on bilateral hand radiographs was assessed by our computer-based method, setting the Sharp/van der Heijde method as the standard of reference. We compared the JSDI of joints with JSN progression in the follow-up period with those without JSN progression. In addition, we examined whether there is a significant difference in JSDI in terms of laterality or topology of the joint.

Results. The JSDI of joints with JSN progression was significantly higher than those without JSN progression (Mann-Whitney U test, $P < 0.001$). There was no statistically significant difference in the JSDI between left and right carpal joints, which was analyzed for 5 different joints altogether and each joint separately (Mann-Whitney U test, $P > 0.05$ respectively). There was statistically significant difference in JSDI among different joints (Kruskal-Wallis test, $P=0.003$).

Conclusions. These results suggest that our computer-based method may be useful to

recognize the JSN progression on radiographs in rheumatoid wrist.

Advances in knowledge. The computer-based temporal subtraction method can detect the JSN progression in the wrist, which is the single most commonly involved site in rheumatoid arthritis.

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by joint swelling, joint tenderness and destruction of synovial joints, which leads to a progressive joint destruction resulting in severe disability [1]. The optimal use of disease modifying antirheumatic drugs (DMARDs) [2,3] and the clinical application of several biologic agents [4,5] were facilitated in the last decade. In this context, remission has become a realistic goal in the treatment of early rheumatoid arthritis [6]. The optimal adjustment of therapies and sensitive monitoring of the disease process are required to achieve this goal. Thus, quantifying the subtle structural changes with high sensitivity is of importance in assessment of therapeutic efficacy.

Structural damage in RA has traditionally been assessed by conventional radiography. Although radiography is extensively used in clinical trials as the primary outcome measure, it requires a relatively long duration of follow-up to evaluate therapy effectiveness because it lacks sensitivity to change. Improvement in the ability to detect the subtle structural changes would therefore be a significant advance in clinical trials. Radiography is considered the gold standard for assessment of both disease progression and the effectiveness of treatment in RA [7], although ultrasound (US) and magnetic resonance imaging (MRI) are under investigation. There are two main structural changes from RA visible on radiographs, which are bone erosion and joint space narrowing (JSN). Several visual scoring methods have been proposed to quantify the joint damage on the radiographs of RA patients. Of these, the Sharp scoring method, especially in the modified forms suggested by van der Heijde, is the most widely used to assess the bone erosion and JSN for joints of both hands and feet [8]. However, traditional scoring methods are subjective and are not able to assess subtle changes with sufficient sensitivity. In addition, these methods are time consuming, require specialized training, and suffer from inter- and intra-reader variations [9]. For routine use, ideal quantification methods would be performed by non-specialists who have not necessarily received any specialized training. In recent years, computer-based methods focusing on assessment of joint space widths have been developed to overcome the disadvantages of traditional scoring methods [10–14]. The computer-based methods provide a more sensitive, objective, quantitative, and reproducible measurement compared to assessment by visual scoring methods for JSN. However, these methods are applied to only finger joints such as metacarpophalangeal and proximal interphalangeal joints.

Recently, we have developed the computer-based method using temporal subtraction technique for assessment of JSN which can detect the difference of joint space width between two radiographs as the joint space difference index (JSDI). Although a previous study showed the relatively high sensitivity and specificity of the computer-based method for JSN progression in carpal joints as well as finger joint [15], it is unclear our computer-based method can quantify the JSN progression as is the case of Sharp/van der Heijde method in carpal joints. Our aim in this study was to investigate a validity of the computer-based method in rheumatoid wrist.

Materials and methods

Patients

Forty-three RA patients (39 women and 4 men) treated with Tocilizmab (TCZ) and/or DMARDs were included in the study. Some patients had been pretreated with biological agents (7 patients with infliximab, 3 patients with etanercept, 1 patient with adalimumab, 1 patient with abatacept, and 3 patients with combination therapy). We recruited the patients who visited the local clinic for RA patients from October, 2008 to October, 2013 and were available for baseline and follow-up bilateral hand radiographs. No pre-selection regarding severity of RA was performed. Clinical and laboratory characteristics of the patients at baseline are shown in Table 1. All patients satisfied the American College of Rheumatology revised 1987 criteria for RA [16]. A portion of our patient population has been previously reported [15].

The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee. Informed consent was obtained from all patients.

Radiograph Acquisition

Radiographs were obtained at baseline and at 1 year follow-up with a median of 12 months. All plain radiographs of the bilateral hand were acquired at anterior-posterior view by an experienced X-ray technologist using digital X-ray equipment (Shimadzu UD150L－40E, Kyoto, Japan) under the following standardized conditions: X-ray aluminum filter with 1.5 mm thickness, film focus distance 1 m, tube voltage 40 kV, tube current 200 mA, exposure 0.025 s. The X-ray beam centered on the midpoint between both hands at the level of the third metacarpophalangeal head. All radiographs were acquired by one radiological technologist under the same imaging conditions including positioning of the hand. In the computer-based analysis, all radiographs were digitized as bit-mapped images with a 1×1 mm pixel size at 8-bit grayscale.   .

Radiographic visual assessment

Each hand radiograph was scored using the Sharp/van der Heijde score (SvdH) for JSN by two experts (reader 1 and 2) who were blind to the other clinical information. The reader's professional situations were somewhat different: reader 1was experienced rheumatologist who was mainly working as a general practitioner; reader 2 was experienced radiologist who was also working as a researcher. The SvdH by reader 1 was considered as the "standard of reference" because reader 1 had more opportunity to assess radiographs using visual scoring method than reader 2. Interobserver reliability for the baseline, follow-up and delta SvdH (ΔSvdH) was assessed; here "delta" is the interval difference in the values between baseline and follow-up images. In this study, JSN for carpal joints was graded as follows: score 0 = normal; score 1 = focal or doubtful; score 2 = >50% of the original joint space; score 3 = <50% of the original joint space or subluxation; and score 4 = ankyloses or complete luxation [17]. The readers scored the radiographs in pairs, in which bilateral hand radiographs of the same patient of both points in time are presented together. The order in time was known to the readers. Distribution of chronological changes in SvdH for JSN between baseline and follow-up images by reader 1 is shown in Table 2.

Computer-based analysis for JSN progression

The computer-based method can detect the difference of joint space width between baseline and follow-up images as the joint space difference index (JSDI). This method visualized interval JSN progression between the baseline and the follow-up image as red shadow (Fig.1). If there were no changes in joint space width between the baseline and the follow-up images, the joint space in the fused image was visualized as grey shadow (Fig.2). The JSDI is defined as the average absolute value of the difference of the pixel value in each pixel for baseline and follow-up images inside the region of the interest (ROI) (Fig.3). The details of the computer-based method are presented in the previous article [15].

The computer-based method assessed the JSN progression of carpal joints (third carpometacarpal joint, fifth carpometacarpal joint, scaphoid-trapezium joint, scaphoid-capitate joint, and radius-scaphoid joint), setting the SvdH method as the standard of reference on bilateral hand radiographs. We excluded the fourth carpometacarpal joints because of the difficulty in discriminating from adjoining bone during ROI placement for JSDI. To increase the homogeneity of the study sample, severely damaged (subluxation, ankylosed, and complete luxation) joints were also excluded based on the SvdH by each reader. Computer-based analysis was performed by a non-specialist who had not received specialized training in scoring of JSN and was blinded to other clinical information. Computer-based analysis was repeated twice, and intraobserver reliability was assessed based on each reader's score.

The measurement procedure was performed as follows: First, the software read the baseline and follow-up images and fused them for every case. Second, the single reference bone of the two images was aligned visually. The chosen reference bone was as follows: third carpometacarpal joint, third metacarpal bone; fifth carpometacarpal joint, fifth metacarpal bone; scaphoid-trapezium joint, trapezium; scaphoid-capitate joint, capitate; and radius-scaphoid joint, radius. Third, the rectangular ROI sized 20×7 pixels was located manually in the center of the joint space with attention so that the edges of bones forming the joint were placed inside the ROI. At this time, the horizontal ROI borders were approximately parallel to the joint edges (Fig.1 d and Fig.2 d). Finally, information on each pixel value for the baseline and follow-up images inside the ROI was output to a text file that can be read by Microsoft Excel, and the JSDI was calculated.

We compared the JSDI of joints with JSN progression in the follow-up period (increase in SvdH) to those without JSN progression (no change in SvdH) based on each reader's score. Additionally, we examined whether there is a significant difference in JSDI in terms of laterality or topology of the joint based on each reader's score. In addition, a direct correlation of the JSDI with the ΔSvdH was evaluated. Data of the first time measurement were used for these analyses.

Statistical analysis

Statistical analyses were calculated with the use of the SPSS version 22.0 (IBM, Armonk, New York, USA), for Windows and the Excel program (Microsoft, Redmond, WA, USA). Intra- and interobserver reliabilities were estimated using calculations of intraclass correlation coefficients (ICC). The ICC ranged from −1 to +1. ICC values are interpreted as follows: <0.40, poor to fair agreement; 0.41 to 0.60, moderate agreement; 0.61 to 0.80, substantial agreement; 0.81 to 1.00, almost perfect agreement [18]. Differences between two independent samples were examined using the Mann-Whitney U test. To assess the significance of differences in terms of topology, the Kruskal-Wallis test was used. P-values less than 0.05 were considered statistically significant. Correlations between the JSDI and the Δ SvdH were examined using Spearman's rank correlation test.

Results

A total of 430 carpal joints on the bilateral hand radiographs in 43 patients were scored using SvdH method by reader 1 and 2. Interobserver reliability for baseline SvdH were in substantial agreement (ICC=0.695; 95% confidence interval [95% CI], 0.643-0.741). Interobserver reliability for follow-up SvdH were in substantial agreement (ICC=0.678; 95% CI, 0.624-0.726). Interobserver reliability for Δ SvdH was in moderate agreement (ICC=0.591; 95% CI, 0.526-0.649).

The computer-based method evaluated carpal joints twice on the bilateral hand radiographs in 43 patients, setting the SvdH method as the standard of reference. Out of 430 carpal joints, we targeted 355 and 365 carpal joints after excluding severely damaged 75 and 65 joints based on each reader's score. Intraobserver reliability for the JSDI based on the scores by reader 1 was in almost perfect agreement (ICC=0.967; 95% CI, 0.959-0.973). Intraobserver reliability for the JSDI based on the scores by reader 2 was in almost perfect agreement (ICC=0.968; 95% CI, 0.961-0.974).

Based on the reader 1’s score, the medians of the JSDI for carpal joints were 11.26 (inter-quartile range [IQR] 6.86-13.37, n=32) and 6.84 (IQR 5.33-9.04, n=323) with and without JSN progression, respectively. Both the Δ SvdH and JSDI of joints with JSN progression were significantly higher than those without JSN progression ($P < 0.001$ respectively) (Table 3). While, based on reader 2’s score, they were 8.90 (IQR 5.78-11.92, n=40) and 7.01 (IQR 5.43-9.63, n=325) with and without JSN progression in carpal joints, respectively ($P = 0.02$).

We next examined whether there is a significant difference in the JSDI and Δ SvdH in terms of laterality of the joint. There was no statistically significant difference in the JSDI and Δ SvdH between the left and right carpal joints based on reader 1’s score, which was analyzed for 5 different joints altogether and each joint separately ($P > 0.05$, respectively) (Table 4). There was no statistically significant difference in the JSDI in terms of laterality of the joints based on reader 2’s score ($P > 0.05$, respectively).

Additionally, we examined whether there is a significant difference in the JSDI and Δ SvdH in terms of topology of the joint. There was no statistically significant difference in the Δ SvdH among different joints based on reader 1’s score ($P = 0.393$). However, there was statistically significant difference in the JSDI among different joints based on reader 1's score (P = 0.003) (Table 5). The JSDI of scaphoid-capitate joint was significantly lower than that of third carpometacarpal joint and scaphoid-trapezium joint (P = 0.048 and 0.003, respectively). Based on reader 2's score, there was statistically significant difference in the JSDI among different joints (P = 0.002). The JSDI of scaphoid-capitate joint was significantly lower than that of fifth carpometacarpal joint and scaphoid-trapezium joint (P = 0.038 and 0.003, respectively).

Finally, correlations between the JSDI and the ΔSvdH were examined. The mean and standard deviation (SD) JSDI (n; the number of joints) of joints for 0, 1, 2, 3 in reader 1's ΔSvdH were 7.64±3.16 (n=323), 10.57±4.28 (n=19), 10.35±3.95 (n=10) and 11.42±0.18 (n=3), respectively. For this, the JSDI was not correlated with ΔSvdH (r = 0.877, P = 0.123) (Fig.4). The mean and SD JSDI of joints for 0, 1, 2, 3 in reader 2's ΔSvdH were 7.93±3.36 (n=325), 9.07±4.76 (n=14), 9.84±3.85 (n=23) and 9.57±5.77 (n=3), respectively. For this, the JSDI was not correlated with ΔSvdH (r = 0.870, P = 0.130).

Discussion

In this study, we investigated a validity of the computer-based method for detecting JSN progression in carpal joints by comparing the computer-based method with the SvdH method as the gold standard. The results of the computer-based method were consistent with those of the SvdH method in almost all examinations excluding assessment in terms of topology of the joints. The results indicate that our computer-based method can recognize the difference of joint space width on hand radiographs in carpal joints.

Previous computer-aided analyses were validated only in finger joints such as metacarpophalangeal, proximal interphalangeal, or distal interphalangeal joints [10,12,19]. However, assessment for JSN by traditional scoring methods such as the Sharp/van der Heijde score [17] and the Genant modified Sharp score [20] includes carpal joints. In addition, the carpal joint is a site of predilection for rheumatoid disease. Thus, it is preferred that computer-based methods are validated in not only finger joints but also in carpal joints. The advantage of our computer-based method is that it can detect JSN progression in carpal joints as well as finger joints. Furthermore, our method does not require highly trained personnel, as is the case for the traditional scoring methods.

Other modalities (i.e., US and MRI) are available that directly visualize the active disease and feature a much better sensitivity in detecting the progression of RA [21]. These modalities are thought to be better suited to monitor disease progression, and have increasingly been used as outcome measures in RA patients [18,22]. While US and

MRI allow direct visualization of early inflammatory, conventional radiography is the pivotal method for diagnosing and monitoring structural joint damage such as JSN [21,23]. Additionally, it is not only inexpensive, but also widely available and accepted. Although radiographs are usually assessed by established scoring methods, these methods suffer from intra- or inter- observer variations. Our data showed that interobserver reliability for SvdH were in substantial or moderate agreement, as assessed by ICC. In contrast, intraobserver reliability for the computer-based method was supported by high agreement. Consequently, the computer-based method could provide reproducible measurement of JSN progression.

In a previous study, Angwin et al. reported no change in Sharp scores in 47% of their 245 patients with early RA after 2 years, but a significant reduction in joint space width using a different computer-based method [24]. This report indicates that the computer-based method is more sensitive to the change in joint space width than traditional scoring methods. In this study, we cannot determine whether our computer-based method or the SvdH method is more sensitive because of the absence of a gold standard. However, our computer-based method could detect the chronological change of joint space width and is consistent with assessment by the SvdH method in almost all examinations. Additionally, our methods extracts the joint space difference between two images by superimposing the images and therefore a slight joint space difference is detected more easily than if the images were to be observed side by side. Thus, our computer-based method may be useful as a computer-aided diagnosis tool and assist the assessment of JSN by a rheumatologist.

The JSDI between progressive and stable joints revealed considerable overlap (Table 3). Although the JSDI of joints without JSN progression was expected to be 0 in theory, the median of it was 6.84 (IQR 5.33-9.04) (overall carpal joint) in practice. Additionally, the JSDI of scaphoid-capitate joints was lower than that of other joints, showing statistically significant difference among different joints. These may be explained by the influence of different hand positions during imaging, variation in the x-ray beam angle, or progression of osteopenia. This result implied the scaphoid-capitate joints should be removed from a computer-based analysis, although further analysis is need to confirm this. Furthermore, there was no statically significant correlation between the JSDI and ΔSvdH, although showing high correlation coefficient. This was due to a relatively small number of joints with changes in SvdH, especially in Δ SvdH “3” (n=3).

Several limitations of this study should be discussed. First, only a limited number of joints with JSN progression were studied (n=32 or 40). Therefore, we could validate for 5 different carpal joints altogether, but not for each joint separately. Additionally, we could not reveal the precise relationship between the JSDI and ΔSvdH. Further study, with larger numbers of joints with JSN progression, is needed to prove that the JSDI were potential marker for assessment of disease progression. Second, no pre-selection regarding steroid therapy was considered. Treatment of RA with steroid therapy may increase susceptibility to osteoporosis but also suppresses inflammatory activity, which is a risk factor for osteoporosis in RA. Therefore, steroid therapy may have an influence on the JSDI inside the ROI. Finally, our computer-based method tends to be time consuming. The analysis time is around 3 minutes per joint. We will develop an automated computer-based method that automatically aligns the joint with only minimal human intervention and can evaluate JSN progression more easily and reproducibly.

In conclusion, our computer-based method, which requires no special training or experience of traditional scoring methods, can detect the difference in joint space width between two radiographs as the joint space difference index (JSDI) in the rheumatoid wrist. Refinement of this method may enable us to obtain more sensitive, objective, quantitative, and reproducible information about JSN progression. Further study is needed to prove that this method is useful to quantify the JSN progression on radiographs in clinical trials.

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Tables

Table 1. Clinical and laboratory characteristics of patients with RA at baseline

	Value
Total no. of subjects included	43
Age, mean (range) years	58 (31-83)
Sex, no. female/male	39/4
Duration of symptoms, median (IQR) months	65 (24-108)
Follow-up time between first and second radiograph, median (IQR) months	12 (8.8-14)
ESR, median (IQR) mm/hour	50 (32-80)
CRP level, median (IQR) mg/dl	2.9 (1.6-6.8)
Swollen joint count, median (IQR)	15 (10-17)
Tender joint count, median (IQR)	13 (10-23)
VAS, median (IQR)	70 (56-77)
DMARDs, no.	
None	2
Methotrexate	23
Mizoribine	1
Bucillamine	1
Salazosulfapyridine	1
Tacrolimus	1
Combination therapy	14

ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; VAS = visual analog scale; IQR = inerquartile range; DMARDs= disease modifying antirheumatic drugs.

Table 2. Distribution of chronological changes in SvdH for JSN in carpal joints (n=355)

Chronological changes of SvdH for JSN	CM3	CM5	ST	SC	RS
0→0	55	53	33	30	27
0→1	2	2	2	2	4
0→2	1	0	1	4	2
0→3	0	0	2	1	0
1→1	6	7	13	14	8
1→2	2	0	0	0	2
1→3	0	1	0	1	0
2→2	6	7	13	9	13
2→3	0	1	1	0	1
3→3	2	4	7	5	11

SvdH=Sharp/van der Heijde score; CM3=third carpometacarpal joint; CM5=fifth carpometacarpal joint; ST=scaphoid-trapezium joint; SC=scaphoid-capitate joint; RS=radius-scaphoid joint.

Table 3. Comparison of the JSDI/ΔSvdH between joints with and without JSN progression

	Joints with JSNP(+)			Joints with JSNP(-)			*P* value
	n	median	IQR	n	median	IQR	
CM3	5	12.97 / 1.00	9.50-14.45 / 1.00-1.50	69	7.05 / 0.00	5.71-9.35 / 0.00-0.00	
CM5	4	10.02 / 1.00	5.85-11.80 / 1.00-1.75	71	7.23 / 0.00	5.70-9.51 / 0.00-0.00	
ST	6	12.39 / 1.50	11.36-16.97 / 1.00-3.00	66	7.38 / 0.00	5.57-10.76 / 0.00-0.00	
SC	8	6.34 / 2.00	5.37-11.72 / 1.25-2.00	58	5.84 / 0.00	4.87-8.13 / 0.00-0.00	
RS	9	8.29 / 1.00	6.80-13.51 / 1.00-1.50	59	6.53 / 0.00	4.84-8.47 / 0.00-0.00	
Carpal, overall	32	11.26 / 1.00	6.86-13.37 / 1.00-2.00	323	6.84 / 0.00	5.33-9.04 / 0.00-0.00	<0.001 / <0.001

JSDI=joint space difference index; ΔSvdH=change of the Sharp/van der Heijde score; JSNP(+)=joint space narrowing progression; JSNP(-)=non-joint space narrowing progression; IQR=interquartile range; CM 3=third carpometacarpal joint; CM 5=fifth carpometacarpal joint; ST=scaphoid-trapezium joint; SC=scaphoid-capitate joint; RS=radius-scaphoid joint.

Table 4. Comparison of the JSDI/ΔSvdH between left and right joints

	Left joints			Right joints			*P* value
	n	median	IQR	n	median	IQR	
CM3	38	6.89 / 0.00	5.51-9.91 / 0.00-0.00	36	7.81 / 0.00	6.65-10.10 / 0.00-0.00	0.261 / 0.673
CM5	38	6.91 / 0.00	5.21-10.57 / 0.00-0.00	37	7.67 / 0.00	6.27-9.18 / 0.00-0.00	0.641 / 0.957
ST	36	7.22 / 0.00	5.50-11.26 / 0.00-0.00	36	8.75 / 0.00	6.27-11.36 / 0.00-0.00	0.380 / 0.404
SC	33	5.42 / 0.00	4.92-7.12 / 0.00-0.00	33	6.87 / 0.00	4.98-8.85 / 0.00-0.00	0.156 / 0.973
RS	32	7.17 / 0.00	5.51-9.64 / 0.00-0.00	36	6.25 / 0.00	4.71-8.40 / 0.00-0.00	0.144 / 0.531
Carpal, overall	177	6.74 / 0.00	5.18-9.66/ 0.00-0.00	178	7.36 / 0.00	5.72-9.64 / 0.00-0.00	0.213 / 0.969

JSDI=joint space difference index; ΔSvdH=change of the Sharp/van der Heijde score; IQR=interquartile range; CM 3=third carpometacarpal joint; CM 5=fifth carpometacarpal joint; ST=scaphoid-trapezium joint; SC=scaphoid-capitate joint; RS=radius-scaphoid joint.

Table 5. Comparison of the JSDI/ΔSvdH among different carpal joints

	n	median	IQR	*P* value
CM3	74	7.26 / 0.00	5.73-10.04 / 0.00-0.00	
CM5	75	7.42 / 0.00	5.70-9.62 / 0.00-0.00	
ST	72	7.91 / 0.00	5.64-11.36 / 0.00-0.00	0.003 / 0.393
SC	66	5.84 / 0.00	4.94-8.24 / 0.00-0.00	
RS	68	6.76 / 0.00	4.97-8.86 / 0.00-0.00	

JSDI=joint space difference index; ΔSvdH=change of the Sharp/van der Heijde score; IQR=interquartile range; CM 3=third carpometacarpal joint; CM 5=fifth carpometacarpal joint; ST=scaphoid-trapezium joint; SC=scaphoid-capitate joint; RS=radius-scaphoid joint.

Figure Legends

Figure 1

The scaphoid-trapezium joint of 57-year-old woman with rheumatoid arthritis with interval change in joint space width. Radiograph images of the scaphoid-trapezium joint for the right hand at baseline (a) and follow-up (b) are shown. These images correspond to a Sharp van der Heijde Score of 0 and 1, respectively. In the fused image (c), the joint space difference is visible as a red shadow. The rectangular ROI, with a size of 20×7 pixels, was located in the center of the joint space (d), and the chronological changes in the joint space width were measured as the joint space difference index (JSDI). The JSDI for this case was 12.70.

Figure 2

The scaphoid-trapezium joint of 61-year-old man with rheumatoid arthritis without interval change in joint space width. Radiograph images of the scaphoid-trapezium joint for the right hand at baseline (a) and follow-up (b) are shown. Both of these images correspond to a Sharp van der Heijde Score of 0. In the fused image (c), the difference in the joint space between the baseline and the follow-up images is not recognizable. The rectangular ROI, with a size of 20×7 pixels, was located in the center of the joint space (d), and the chronological changes in the joint space width were measured as the joint space difference index (JSDI). The JSDI for this case was 4.10.

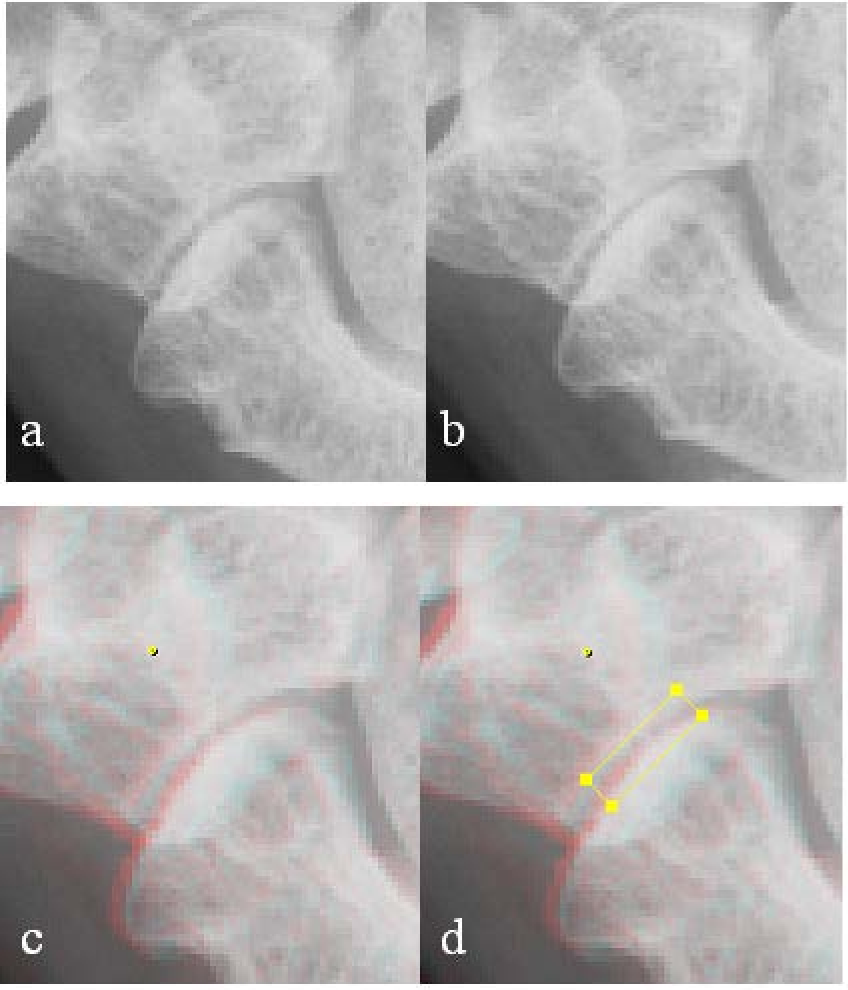
Figure 3

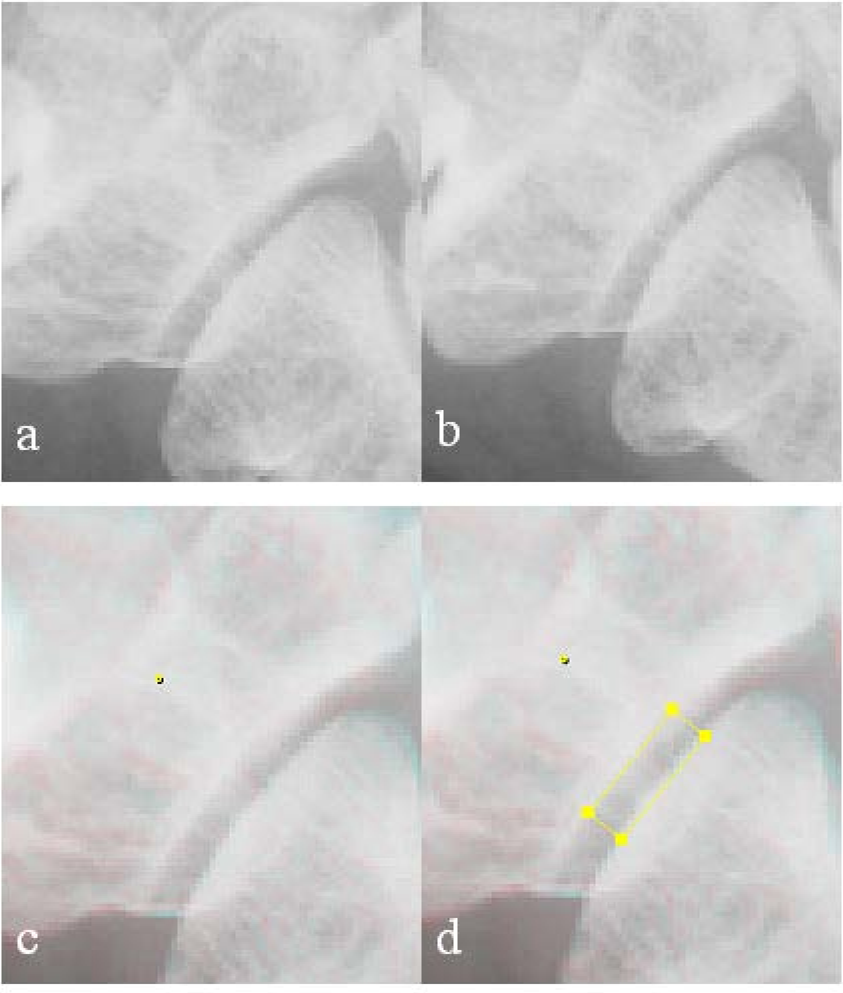
Calculation of the joint space difference index (JSDI). For each pixel with the coordinate indicated as x (column B) and y (column C), information on pixel value for the baseline and follow-up images inside region of interest (ROI) are shown in columns D and E, respectively. We subtracted the baseline pixel value from the follow-up pixel value in each pixel (column F) and calculated its absolute value (column G). Finally, we averaged these values and refer to this value as the JSDI (column I).

Figure 4

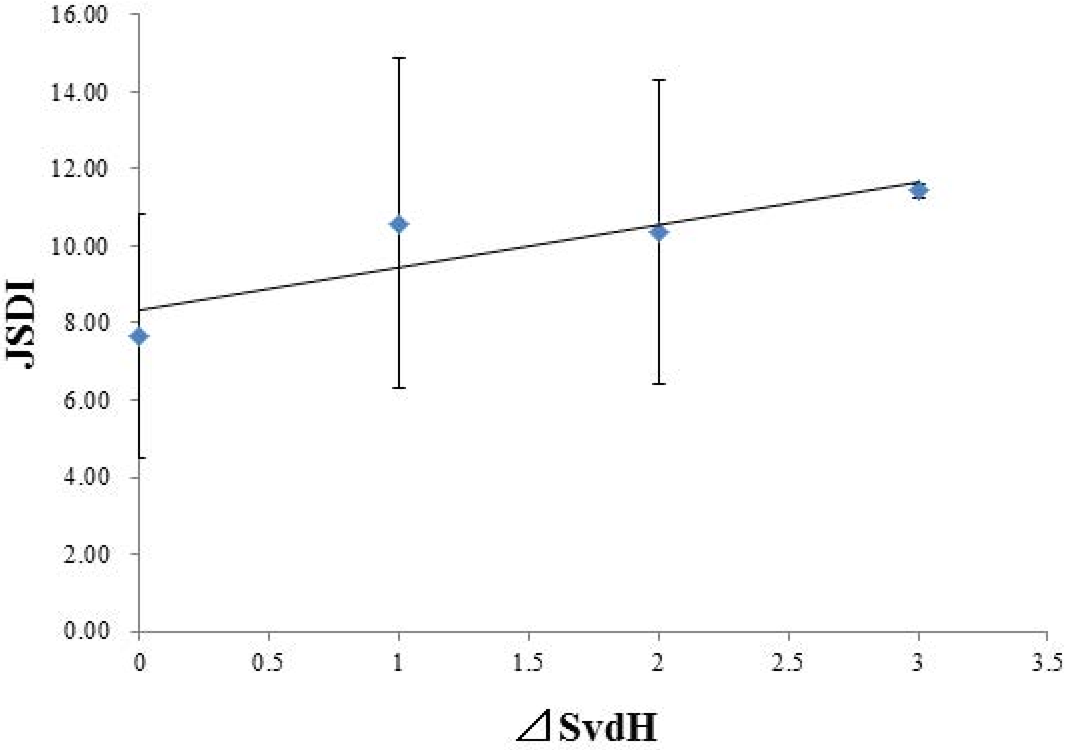
Relationship of the JSDI and ΔSvdH. The JSDI were expressed as mean and standard deviation for each ΔSvdH.

JSDI, joint space difference index; ΔSvdH, delta Sharp/van der Heijde score


a
b
c
d


a
b
c
d

	A	B	C	D	E	F	G	H	I
1	PolygonIdx	x	y	Baseline	Follow-up	Sub	Abs		JSDI
2	0	726	569	200	202	-2	2		12.70229008
3		725	570	205	204	1	1		
4		726	570	196	199	-3	3		
5		727	570	187	196	-9	9		
6		724	571	202	200	2	2		
7		725	571	198	195	3	3		
8		726	571	189	197	-8	8		
9		727	571	183	191	-8	8		
10		728	571	177	185	-8	8		
11		723	572	197	202	-5	5		
12		724	572	198	198	0	0		
13		725	572	192	196	-4	4		
14		726	572	183	190	-7	7		
15		727	572	177	190	-13	13		
16		728	572	172	199	-27	27		
17		729	572	173	202	-29	29		
18		722	573	197	209	-12	12		
19		723	573	194	202	-8	8		
20		724	573	191	197	-6	6		
21		725	573	180	196	-16	16		



16.00
14.00
12.00
10.00
8.00
6.00
4.00
2.00
0.00
JSDI
0
0.5
1
1.5
2
2.5
3
3.5
⊿SvdH