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Radiographic Temporal Subtraction Analysis Can Detect Finger Joint Space Narrowing Progression in Rheumatoid Arthritis with Clinical Low Disease Activity

Short title; Radiographic Temporal Subtraction Analysis of Finger Joint

Abstract

Background: Recent papers suggest that finger joints with positive synovial vascularity (SV) assessed by ultrasonography under clinical low disease activity (CLDA) in rheumatoid arthritis (RA) patients may cause joint space narrowing (JSN) progression.

Purpose: To investigate the performance of a computer-based method by directly comparing with the conventional scoring method in terms of the detectability of JSN progression in hand radiography of RA patients with CLDA.

Material and Methods: Fifteen RA patients (13 female, 2 male) with long-term sustained CLDA of > 2 years were included. Radiological progression of finger joints was evaluated using the computer-based method which can detect JSN progression between two radiographic images as the joint space difference index (JSDI), as well as the Genant-modified Sharp score (GSS). We also quantitatively assessed SV of these joints using ultrasonography.

Results: Out of 270 joints, we targeted 259 finger joints after excluding 9 damaged joints (4 ankylosis, 3 complete luxation, and 2 subluxation) and 2 improved joints according to the GSS results. The JSDI of finger joints with JSN progression was significantly higher than those without JSN progression ($p = 0.018$). The JSDI of finger joints with ultrasonographic SV was significantly higher than those without

ultrasonographic SV ($p = 0.004$). Progression in JSDI showed stronger associations with ultrasonographic SV than progression in GSS [OR (95% CI); 7.19 (3.37-15.36) vs 5.84 (2.76-12.33)].

Conclusions: The computer-based method was comparable to the conventional scoring method regarding the detectability of JSN progression in RA patients with CLDA.

Keywords:

Rheumatoid arthritis, Radiograph, Joint space narrowing, Clinical low disease activity, Synovial vascularity, Computer-based analysis

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic inflammation of the synovial joints. The resulting joint pain and stiffness cause impaired function, and for the majority of cases progressive synovitis will lead to permanent damage of the articular cartilage and bone (1, 2). In the last decade, treatment of RA has been significantly improved by treat to target strategies and the introduction of biological agents (3). Remission has been recognized for the management of early RA as a goal of treatment, achieved by halting radiographic progression at an early stage of the disease (4). Consequently, at early stages of RA, precise and quantitative assessment of joint damage progression is critical to induce and maintain clinical remission of disease.

Plain radiography is considered the imaging modality gold standard for assessing RA as it is inexpensive, simple and fast to use, and radiographic measurement is used in clinical trials as the major outcome criteria (5). Radiographic evaluation in RA currently relies on several semi-quantitative scoring methods such as the van der Heijde-modified Sharp score (vdHSS) and the Genant-modified Sharp score (GSS), that grade joint space narrowing (JSN) and bone erosion of individual joints using a

categorical scale (6-8). These categorical scoring methods, however, include several limitations such as disagreement between readers caused by the difficulty of standardized scoring and requiring specialized training (9).

Over the past decade various computer-based techniques have been developed and introduced for standardized measurement of joint space width (JSW) in finger joints (10-13). Computer-based techniques for measurement of JSW could provide substantial advantages in comparison with conventional scoring methods. This is attributed to high sensitivity and reproducibility of computer-based techniques as well as their objective and quantitative nature (14-16). Although these computer-based techniques perform assessment of JSN by measuring JSW on a radiograph cross-sectionally, it is not thoroughly studied whether these methods can evaluate longitudinal and temporal changes in joint space accurately.

A computer-based quantification method of JSW difference using temporal subtraction was recently developed which can detect JSN progression between two radiographic images as the joint space difference index (JSDI) (17, 18)

. Ichikawa et al. were successful in showing that JSDI can detect interval change of joint space in hand joints of active RA patients using vdHSS as the gold standard. However, further validation is needed to prove that this method is also valid in broader situations;

for example, expected interval JSN progression is subtle in RA patients with inactive disease. Direct comparison of the sensitivity of detection of JSN progression between conventional scoring methods such as vdHSS and computer-based methods like JSDI is also desirable. In search for a cohort of RA patients which meets the conditions that JSN progression is subtle and predictable, recent papers suggest that finger joints with positive synovial vascularity (SV) assessed by ultrasonography (US) under clinical low disease activity (CLDA) in RA patients may cause progression of JSN on the GSS (19-22).

We therefore determined to reuse the data (21) to investigate the performance of our software to detect the difference in interval JSN progression in the single cohort of RA patients with CLDA retrospectively. The validity of the software assessment of JSN progression was first examined by the semi-quantitative scoring method as a gold standard. We then directly compared the software with the conventional scoring method in terms of the detectability of JSN progression taking the observation into consideration that there is an association between JSN progression and the presence of ultrasonographic SV.

Material and Methods

Patients

Fifteen patients with RA and long-term (> 1 year) sustained CLDA (disease activity score with 28 joints - erythrocyte sedimentation rate (DAS28-ESR) < 3.2) were analyzed retrospectively. The demographic and laboratory characteristics of patients are shown in Table 1. The patients had been treated with non-biologic DMARDs [8 patients with methotrexate (MTX), 3 patients with MTX + tacrolimus] or with biologics [1 patient with MTX + adalimumab, 2 patients with MTX + tocilizumab (TCZ) and 1 patient with TCZ monotherapy]. Our patients population (15/15, 100%) has been previously reported (21). The purpose of this reported study was to investigate the relationship between synovial vascularity and structural alternation assessed with conventional radiographic scoring of finger joints in rheumatoid patients with low disease activity. The current study investigated the performance of a computer-based radiographic method by directly comparing with the conventional radiographic scoring method using the relationship between synovial vascularity and future structural alternation. This study was conducted in accordance with the Declaration of Helsinki (23). The study was approved by the local ethics committee and informed consent was obtained from all patients.

Ultrasonography

Ultrasonography was performed at baseline and at the 8th, 20th and 52nd weeks by one of three US experts (M.H., F.S. and A.N.) who specialize in musculoskeletal ultrasonography and were blinded to other clinical information. A 13-MHz linear array transducer and US machine were used (EUP-L34P, HI VISION Avius; Hitachi, Tokyo, Japan). Power Doppler settings and reliability of the US experts are described in previous studies (24, 25). First to fifth metacarpophalangeal (MP) and second to fifth proximal interphalangeal (PIP) joints were scanned in the longitudinal plane over the dorsal surface. A SV value was determined by counting the number of vascular flow pixels in the region of interest (ROI).

Radiography

Plain radiographs of the hands were obtained at the baseline and at the 52nd week. All plain radiographs were acquired by Radnext 32 (Hitachi, Tokyo, Japan) under the following standard conditions: X-ray aluminum filter thickness 0.5 mm, film focus distance 100 cm, tube voltage 50 kV, tube current 100 mA, exposure 0.025 sec, and center of exposure MP joint of the 2nd finger. All X-ray images were displayed as digital imaging and communications in medicine (DICOM) images with 0.15×0.15 mm

pixel size at 10-bit grayscale resolution.

JSN was scored using the GSS according to a 9-point scale from 0 to 4, with 0.5 increments (6, 26). Radiological assessments were examined according to the GSS by an expert rheumatologist (J.F.) with more than 15 years of experience who was blinded to other clinical information (6). Temporal hand radiographs of each patient were displayed side by side chronologically.

Computer-based method for JSN progression

We used an original software application for this study. The software is equipped with a temporal subtraction function which can detect JSN progression between two radiographic images to compute the JSDI. The software first reads in baseline and follow-up images and fuses them into a single color image by assigning cyan to the baseline and red to the follow-up images. The distal bone of each joint is then aligned by shifting and rotating the follow-up image. Finally, a rectangular ROI with size 25 × 7 pixels is located in the center of joint space so that the horizontal border of the ROI is approximately parallel to the joint space, and the JSDI is calculated (Fig. 1). The principle of the software has been described in a previous article (17, 18).

JSN progression of MP and PIP joints was assessed according to our software

operated by a radiological technologist (T.O.) who was blinded to other clinical information in this study. Interphalangeal (IP) joints were not included because of high variability in JSDI values due to misregistration possibly caused by different manner of positioning during image acquisition. Computer-based measurement was performed twice to assess the intraobserver reliability. The JSDI data from the first measurement were used for this analysis; the second measurement was only used for the reliability analysis.

Statistical analysis

Statistical analyses were calculated with the use of Excel (Microsoft, Redmond, WA, USA) and IBM SPSS 22 (IBM, Armonk, New York, USA). Quantitative variables were given as median and interquartile range (IQR) or mean and standard deviation (SD). P-value < 0.05 was considered to indicate a significant difference.

Intraobserver reliability levels were assessed by using intraclass correlation coefficients (ICC) (one-way random). Agreement strengths for ICC values have been classified as follows: < 0.40 = poor to fair agreement; 0.41-0.60 = moderate agreement; 0.61-0.80 = substantial agreement; and 0.81-1.00 = almost perfect agreement (27).

We compared the JSDI between the progressive and non-progressive finger

joints according to the ΔGSS to ascertain that the JSDI can detect interval JSN progression in the visual assessment. Here, "Δ (delta)" indicates the interval difference in the values between baseline and follow-up images. We then compared the ΔGSS and JSDI in the positive and negative SV finger joints in terms of the ultrasonographic findings. Joints with positive SV [SV (+)] were defined as those with positive SV detected at least once in the ROI at baseline and during the follow-up period. Otherwise, joints were defined as negative SV [SV (-)]. This analysis was performed to demonstrate that finger joints with positive SV under CLDA cause structural destruction, especially JSN, in RA. Differences in parameters were examined using the Mann-Whitney U test.

In the target JSDI, a cut-off level for JSN progression was determined by the discriminant analysis method. This method, which is also referred to as Otsu' method, is a parameterless global thresholding binarization method. It calculates a threshold value in such a way as to maximize the separation metrics which are determined by the variances between the two distributions. The principle of the method has been described in detail by Otsu (28).

Associations of progression in the GSS or the JSDI with ultrasonographic SV on joint level were examined by cross-tabulation analyses with chi-square tests. Odds

ratios (ORs) with 95% confidence intervals (CIs) were estimated by linear regression, with JSN progression in the GSS or the JSDI as the outcome and ultrasonographic SV as the determinant. Joints without ultrasonographic SV served as reference.

Results

Out of 270 joints (10 MP and 8 PIP joints in 15 patients), we targeted 259 finger joints after excluding 9 damaged joints (4 ankylosis, 3 complete luxation, and 2 subluxation) in 3 patients and 2 improved joints in 1 patient according to the GSS results. Images of 259 joints in 15 patients in terms of GSS, JSDI and SV of the finger joints were evaluated. The medians of GSS at baseline, at follow-up and ΔGSS were 1 (IQR 1-2, n; the number of joints = 259), 1 (IQR 1-2, n = 259) and 0 (IQR 0-0, n =259), respectively. Out of 259 joints, ΔGSS (+) was assigned to joints with positive ΔGSS according to the GSS results (n = 37, 14.29%). Otherwise, ΔGSS (-) was assigned to the others (n = 222, 85.71%). The median of JSDI was 54.09 (IQR 38.14-74.20, n = 259). The medians of SV at baseline, the 8th week, the 20th week and the 52nd week were the same values [0 (IQR 0-0, n = 259)]. The percentages of joints with positive SV and negative SV were 18.92% (n = 49) and 81.08% (n = 210). In Fig. 2, representative radiographic images

with non-progressive (Fig. 2a) and progressive (Fig. 2b) joints are shown.

Intraobserver reliability for baseline GSS and follow-up GSS was in substantial agreement (ICC = 0.730; 95% CI, 0.668-0.782 and ICC = 0.718; 95% CI, 0.653-0.772, respectively). Intraobserver reliability for ΔGSS was in moderate agreement (ICC = 0.490; 95% CI, 0.392-0.577). Intraobserver reliability for JSDI was in almost perfect agreement (ICC = 0.963; 95% CI, 0.953-0.971).

The JSDI of finger joints with JSN progression for finger joints [ΔGSS (+)] was significantly higher than those without JSN progression for finger joints [ΔGSS (-)] ($p = 0.018$). The median JSDI of ΔGSS (-) and ΔGSS (+) were 52.68 (IQR 36.79-70.63, n = 222) and 59.75 (IQR 46.50-102.86, n = 37), respectively.

The ΔGSS of finger joints with positive SV were significantly higher than those with negative SV ($p < 0.001$). The median ΔGSS of SV (-) and SV (+) were 0 (IQR 0-0, n = 210) and 0 (IQR 0-0.5, n = 49), respectively. The JSDI of finger joints with positive SV was significantly higher than those with negative SV ($p = 0.004$). The median JSDI of SV (-) and SV (+) were 52.84 (IQR 37.41-68.93, n = 210) and 66.99 (IQR 42.75-139.24, n = 49), respectively (Table 2).

In the computer-based analysis, JSN progression was defined as the JSDI more than the threshold value (JSDI = 99.78) by the discriminant analysis method. As a result,

36 finger joints (13.9%) were classified as JSN progression [JSDI (+)] and 223 joints (86.1%) as JSN non-progression [JSDI (-)] according to the computer-based analysis.

The efficacy of progression, defined by the two methods (based on GSS or JSDI), was assessed by associating the finger joint analyses with ultrasonographic SV findings. Positive associations were found between SV and progression of GSS and JSDI (Pearson's chi-square test, $p < 0.001$, respectively). Moreover, these associations were stronger for JSDI than for GSS [OR (95% CI); 7.19 (3.37-15.36) vs 5.84 (2.76-12.33)] (Table 3).

Discussion

Early and accurate detection of joint destruction in RA patients is essential in clinical practice. Rheumatologists need to be equipped with reliable monitoring tools to assess joint damage so that they can select adequate therapy for RA patients.

Evaluation of JSN progression on X-ray images of the hands and feet using semi-quantitative scoring methods (e.g. vdHSS and GSS) are widely accepted for this purpose (11, 29, 30). However, the disadvantages of these methods include the steep learning curve and time required to analyze the images. Another shortcoming of these methods is that the evaluation can only be done by a medical expert such as a

rheumatologist and radiologist. We therefore developed an original software application which can perform computer-based analysis to quantify interval JSN progression using clinical X-ray images of the hand (17, 18).

In this study we examined the detectability of our software for quantitative measurement of the interval JSN change in rheumatoid patients with long-term sustained CLDA, by comparing with a conventional semi-quantitative scoring method. In a previous study Ichikawa et al. indicated that the computer-based method can detect the difference in JSW between two radiographs with an index named JSDI in the rheumatoid wrist (18). However, they could not demonstrate the superiority of the computer-based method over the conventional scoring method for sensitive detection of the destructive change progression.

We therefore searched for a reliable risk factor for JSN progression, so that we could compare the quantification methods in a “head-to-head” manner. Our choice of the risk factor for JSN progression was synovitis shown with positive power Doppler signal of the finger joint (19-22). In addition, in patients with long-term sustained CLDA, progression of JSN is limited as the disease activity is suppressed. Thus, we considered that RA patients with CLDA would be suitable as a target group of patients to examine whether the software can assess slight changes of JSN. We hypothesized

that we can directly compare the JSDI with the semi-quantitative scoring methods in terms of detectability in slight JSN progression with or without ultrasound findings. The results of this study indicate that the computer-based method is comparable to the conventional scoring method regarding detectability of interval JSN change.

To our knowledge, this is the first attempt to verify the usefulness of the computer-based method for quantifying JSN progression using the relationship between US synovitis and JSN progression in RA. In an osteoarthritis population, Damman et al. studied the validity of semi-automatic JSW measurements using US findings and reported that progression in both semi-automatic JSW and conventional scoring methods showed associations with inflammatory US features at baseline (31). In the current study, we also found association between US findings and progression of semi-quantitative JSN scoring and semi-automated JSW measurements. Furthermore, progression measured with semi-automated JSW measurements outperformed compared to progression assessed by semi-quantitative JSN scoring.

The aforementioned successful results are due largely to the unique technology implemented in our software; a method of fusing the baseline and follow-up images by superimposing the radiographs. Most of the existing software methods for JSN assessment have been developed to measure the distance of joint space using one

cross-sectional radiograph, in which the degree of human intervention is somewhat different (10-13). We believe our software can accurately extract slight JSN changes of two images obtained chronologically. The advantage of this method lies in the fact that the distal margin of the MP/PIP joints need not be strictly determined, which has been a technical challenge due to its vague osseous margin delineated manually or automatically. The software mainly detects the magnitude of topological difference of the proximal edge of the MP/PIP joints which is well-defined and easily delineated.

In spite of the favorable results in this preliminary study, we cannot replace the conventional semi-quantitative scoring methods with our semi-automated JSW measurement software in clinical trials at this point. We need further validation of this software in various conditions which includes the difference of the imaging device and systems utilized, the radiological technological aspect to obtain the images, the medications which may affect the radiographic appearance of the bone and joint, experience of personnel who obtain and analyze the images, and so on. In addition, the overlap of the JSDI value observed between the JSN progression and JSN non-progression finger joints suggests that further refinement in its accuracy is required in future work.

Limitations of this study include its small scale and retrospective nature; a

prospective study with larger scale is needed to confirm our observations. Technically, image acquisition with reproducible positioning of the hands may improve the quality of the assessment by reducing misregistration during post-processing of image fusion. In addition, time required to analyze the joints with the software should be shortened; currently it takes a few minutes to analysis a single joint. We are preparing to develop an automated computer-based method that can align joints for fusion/subtraction, with minimal human intervention.

In conclusion, our computer-based method was comparable to the conventional human scoring method regarding detectability of interval JSN change in RA patients with low disease activity. Although further validation and refinement are needed, this computer-based method may be a promising approach to quantitatively and objectively assess the interval structural destruction in RA patients.

References

1. Schellekens GA, Visser H, de Jong BA, et al. The diagnostic properties of rheumatoid arthritis antibodies recognizing a cyclic citrullinated peptide. Arthritis Rheum 2000;43:155-163.

2. van der Heijde DM. Radiographic imaging: the 'gold standard' for assessment of disease progression in rheumatoid arthritis. Rheumatology (Oxford) 2000;39 Suppl 1:9-16.

3. Smolen JS, Aletaha D, Bijlsma JW, et al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis 2010;69:631-637.

4. van der Heijde D. Radiographic progression in rheumatoid arthritis: does it reflect outcome? Does it reflect treatment? Ann Rheum Dis 2001;60 Suppl 3:iii47-50.

5. Bridges SL, Jr., Causey ZL, Burgos PI, et al. Radiographic severity of

rheumatoid arthritis in African Americans: results from a multicenter observational study. Arthritis Care Res (Hoboken) 2010;62:624-631.

6. Genant HK, Jiang Y, Peterfy C, et al. Assessment of rheumatoid arthritis using a modified scoring method on digitized and original radiographs. Arthritis Rheum 1998;41:1583-1590.

7. Ravindran V, Rachapalli S. An overview of commonly used radiographic scoring methods in rheumatoid arthritis clinical trials. Clin Rheumatol 2011;30:1-6.

8. van der Heijde D. How to read radiographs according to the Sharp/van der Heijde method. J Rheumatol 2000;27:261-263.

9. Sharp JT, Wolfe F, Lassere M, et al. Variability of precision in scoring radiographic abnormalities in rheumatoid arthritis by experienced readers. J Rheumatol 2004;31:1062-1072.

10. Bottcher J, Pfeil A, Rosholm A, et al. Digital X-ray radiogrammetry combined with semiautomated analysis of joint space widths as a new diagnostic approach in rheumatoid arthritis: a cross-sectional and longitudinal study. Arthritis Rheum 2005;52:3850-3859.

11. Finckh A, de Pablo P, Katz JN, et al. Performance of an automated computer-based scoring method to assess joint space narrowing in rheumatoid arthritis:

a longitudinal study. Arthritis Rheum 2006;54:1444-1450.

12. Pfeil A, Bottcher J, Seidl BE, et al. Computer-aided joint space analysis of the metacarpal-phalangeal and proximal-interphalangeal finger joint: normative age-related and gender-specific data. Skeletal Radiol 2007;36:853-864.

13. Peloschek P, Langs G, Weber M, et al. An automatic model-based system for joint space measurements on hand radiographs: initial experience. Radiology 2007;245:855-862.

14. Neumann G, dePablo P, Finckh A, et al. Patient repositioning reproducibility of joint space width measurements on hand radiographs. Arthritis Care Res (Hoboken) 2011;63:203-207.

15. Pfeil A, Oelzner P, Bornholdt K, et al. Joint damage in rheumatoid arthritis: assessment of a new scoring method. Arthritis Res Ther 2013;15:R27.

16. Sharp JT, Angwin J, Boers M, et al. Computer based methods for measurement of joint space width: update of an ongoing OMERACT project. J Rheumatol 2007;34:874-883.

17. Ichikawa S, Kamishima T, Sutherland K, et al. Performance of computer-based analysis using temporal subtraction to assess joint space narrowing progression in rheumatoid patients. Rheumatol Int 2016;36:101-108.

18. Ichikawa S, Kamishima T, Sutherland K, et al. Radiographic quantifications of joint space narrowing progression by computer-based approach using temporal subtraction in rheumatoid wrist. Br J Radiol 2016;89:20150403.

19. Brown AK, Conaghan PG, Karim Z, et al. An explanation for the apparent dissociation between clinical remission and continued structural deterioration in rheumatoid arthritis. Arthritis Rheum 2008;58:2958-2967.

20. Fukae J, Isobe M, Kitano A, et al. Positive synovial vascularity in patients with low disease activity indicates smouldering inflammation leading to joint damage in rheumatoid arthritis: time-integrated joint inflammation estimated by synovial vascularity in each finger joint. Rheumatology (Oxford) 2013;52:523-528.

21. Fukae J, Isobe M, Kitano A, et al. Structural deterioration of finger joints with ultrasonographic synovitis in rheumatoid arthritis patients with clinical low disease activity. Rheumatology (Oxford) 2014;53:1608-1612.

22. Nguyen H, Ruyssen-Witrand A, Gandjbakhch F, et al. Prevalence of ultrasound-detected residual synovitis and risk of relapse and structural progression in rheumatoid arthritis patients in clinical remission: a systematic review and meta-analysis. Rheumatology (Oxford) 2014;53:2110-2118.

23. World Medical A. World Medical Association Declaration of Helsinki: ethical

principles for medical research involving human subjects. JAMA 2013;310:2191-2194.

24. Fukae J, Isobe M, Kitano A, et al. Radiographic prognosis of finger joint damage predicted by early alteration in synovial vascularity in patients with rheumatoid arthritis: Potential utility of power doppler sonography in clinical practice. Arthritis Care Res (Hoboken) 2011;63:1247-1253.

25. Fukae J, Kon Y, Henmi M, et al. Change of synovial vascularity in a single finger joint assessed by power doppler sonography correlated with radiographic change in rheumatoid arthritis: comparative study of a novel quantitative score with a semiquantitative score. Arthritis Care Res (Hoboken) 2010;62:657-663.

26. Peterfy CG WC, Szechinski J, et al. Comparison of the Genant-modified Sharp and van der Heijde-modified Sharp scoring methods for radiographic assessment in rheumatoid arthritis. Int J Clin Rheumtol 2011 6:15–24.

27. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-174.

28. Otsu N. A threshold selection method from gray-level histograms. . IEEE Trans Syst Man Cybern 1979;9:62–66.

29. McQueen FM. Imaging in early rheumatoid arthritis. Best Pract Res Clin Rheumatol 2013;27:499-522.

30. Ostergaard M, Pedersen SJ, Dohn UM. Imaging in rheumatoid arthritis--status and recent advances for magnetic resonance imaging, ultrasonography, computed tomography and conventional radiography. Best Pract Res Clin Rheumatol 2008;22:1019-1044.

31. Damman W, Kortekaas MC, Stoel BC, et al. Sensitivity-to-change and validity of semi-automatic joint space width measurements in hand osteoarthritis: a follow-up study. Osteoarthritis Cartilage 2016;24:1172-1179.

Tables

Table 1. Demographic and laboratory characteristics of patients

	baseline	52nd week
Age, median (range) years	54 (32 - 69)	
Sex, female/male	13 / 2	
Duration of disease, median (range) months	50 (26 - 196)	
Duration of CLDA, median (range) months	15 (12 - 19)	
Swollen joint count, range	0-2	0-3
Tender joint count, range	0-2	0-3
DAS28-ESR, mean (SD)	2.03 (0.55)	1.96 (0.57)

CLDA, clinical low disease activity; DAS28, disease activity score with 28 joints;

ESR, erythrocyte sedimentation rate; SD, standard deviation

Table 2. Comparison of progression in GSS and JSDI between finger joints with positive and negative synovial vascularity

Group	SV(-)			SV(+)			p-value
	n	median	IQR	n	median	IQR	
ΔGSS	210	0	0-0	49	0	0-0.5	< 0.001
JSDI	210	52.84	37.41-68.93	49	66.99	42.75-139.24	0.004

GSS, Genant-modified Sharp score; JSDI, joint space difference index; SV, synovial vascularity; IQR, interquartile range

Table 3. Association of progression in GSS or JSDI with ultrasonographic synovial vascularity

		GSS			JSDI		
		ΔGSS(+)	ΔGSS(-)	OR (95% CI)	JSDI(+)	JSDI(-)	OR (95% CI)
SV	SV(+)	18	31	5.84 (2.76-12.33)	19	30	7.19 (3.37-15.36)
	SV(-)	19	191	1	17	193	1

GSS, Genant-modified Sharp score; JSDI, joint space difference index; SV, synovial vascularity;

OR, odds ratio; CI, confidence interval







