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ORIGINAL ARTICLE

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Power Doppler and spectral Doppler measurements of knee-joint synovitis in rheumatoid arthritis patients with superficial pattern signals and in those with deep pattern signals

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Abstract Power Doppler and spectral Doppler ultrasonography were used to scan 127 knee joints of 72 patients with rheumatoid arthritis (RA). Synovial effusion thickness and synovial proliferation (pannus) thickness, as well as the flow signal diameter, were measured on ultrasonogram prints of the power Doppler using digital calipers. In addition, color-flow signal grades on power Doppler and the resistance index (RI) values on spectral Doppler were evaluated. The values of these five variables were compared among 58 joints with superficial pattern flow signals and 69 joints with deep pattern flow signals. Compared with the joints with deep pattern signals, the joints with superficial pattern signals had significantly higher mean values of effusion thickness ($P < 0.0001$) and flow signal grades ($P < 0.0001$), and significantly lower mean RI ($P < 0.0001$). On the other hand, the joints with deep pattern signals had a significantly higher value of signal diameter ($P = 0.0125$) and had a trend to higher value of pannus thickness ($P = 0.079$) as well. Significant correlations were observed between effusion thickness and signal grades ($P < 0.0001$); effusion thickness and RI ($P < 0.0001$); signal diameter and pannus thickness ($P = 0.0102$); signal diameter and RI ($P < 0.0001$); and signal grades and RI ($P < 0.0001$). The ultrasonographic measurements of synovitis in RA patients provide valuable information on synovial inflammation.

Key words Effusion thickness · Flow signal diameter · Flow signal grades · Pannus thickness · Resistance index

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Introduction

Ultrasonographic evaluation of synovitis in rheumatoid arthritis (RA) patients has been successfully done using gray scale, and power and spectral Doppler in assessing synovial effusion,[1] synovial proliferation,[2] blood flow signals,[3] and vascular resistance.[4] Most of the approaches used to evaluate these findings have been semiquantitative and involve the use of grading scores. In the present study, we used digital calipers to measure synovial effusion thickness and synovial proliferation thickness, as well as diameter of the flow signals on ultrasonogram prints. The values of these three variables, along with flow signal grades and the synovial vascularity resistance index (RI), were compared with joints with superficial pattern signals and joints with deep pattern signals. Subsequently, correlations between pairs of these five variables were evaluated.

Patients and methods

Patients

Seventy-two patients with RA were enrolled in the present study. The subjects (60 women and 12 men) had a mean age of 48.7 years (range 24–85 years) and a mean disease duration of 7.1 years (range 0.5–25 years). All patients satisfied the American College of Rheumatology 1987 revised criteria.[5] The patients' primary treatments included methotrexate alone in 30 patients; other disease-modifying antirheumatic drugs in 15 patients; infliximab and methotrexate in 24 patients, and etanercept and methotrexate in 3 patients.

Power Doppler and spectral Doppler ultrasonography

A Toshiba Aplio 80 system (Toshiba, Tochigi, Japan) with standard settings (treatment power, <5000 W/cm^2, low-pass wall filter no. 3, medium persistence) was used. Power Doppler assessments were performed using a pulse repeti-

tion frequency of 1170–1220 Hz. Pulsed-wave spectral Doppler was performed using the lowest filter setting (125 Hz). A multidimensional linear scanner (PLT-704 AT) was used as a transducer at 5.3 MHz. The suprapatellar recess of the knee, in 20° flexion under a supine position, was scanned longitudinally and transversely.

Measurements of signal diameter, synovial effusion thickness, and synovial proliferation thickness

The measurements (mm) of the thickness of synovial effusion and synovial proliferation (pannus), as well as flow signal diameters, were obtained using digital calipers (E-PITA 10, Nakamura MFC, Tokyo, Japan) on the ultrasonogram prints of the power Doppler ultrasonography instead of using the internal measurements on the ultrasonography screen. Because the ultrasonograms were automatically enlarged 1.3 times by the machine to facilitate visualization, the measurements obtained from the pictures were divided by 1.3 to obtain the real length. The thickness of the synovial effusion was measured as the width of the low echogenic layer that was present between the surface of the anterior (capsular) pannus and the surface of the posterior (cortical) pannus. The thickness of the capsular pannus was measured as the width between the moderately echogenic lineal articular capsule and the surface of the moderately echogenic anterior pannus. Ultrasonographic differentiation of the articular capsule from the extra-capsular connective tissue is somewhat difficult because of a similar echogenicity of two tissues. The color-flow signals present in the deep layer of the capsular pannus may be a useful marker to delineate the border between the two tissues. The thickness of the cortical pannus was measured as the width between the high echogenic lineal cortex of the femur and the surface of the moderately echogenic posterior pannus. Measurements of flow signal diameter were obtained using the signal selected for obtaining a velocity wave on spectral Doppler. Whenever the image of the selected signal on the spectral Doppler was unclear because of the "gates" mark (=), the corresponding signal on the power Doppler was used to measure the diameter. To facilitate the diameter measurements, a magnifier was used to adjust the insides of the caliper jaws to the ends of the signal diameter.

Color-flow signals and RI

The intensity of the color flow signals taken on power Doppler was graded using the modified Klauser's method:[6,7] grade 0, no color-flow signal; grade 1, one to four color-flow signals; grade 2, five to eight color-flow signals; grade 3, more than nine color-flow signals. The RI was calculated by the following formula:

$$\frac{\text{maximum velocity} - \text{minimum velocity}}{\text{maximum velocity}},$$

in tracing the velocity wave obtained on the spectral Doppler. A single signal to make the velocity wave on the spectral Doppler was selected as the signal corresponding to the signal pattern of the joints from among several signals, if present, on the power Doppler, as well as an appropriate signal for providing a velocity wave.

For all five variables, effusion thickness, pannus thickness, signal diameter, signal grades, and RI, as well as the mean of the two values obtained on the longitudinal and transverse scans of each knee joint were used in the analysis.

Statistical analysis

The statistical analysis was done using the J-Stat software package for Windows. Differences between the groups were evaluated using the Mann–Whitney *U* test. Correlations between two values were obtained by a linear regression coefficient or Spearman's rank correlation coefficient. *P* values of less than 0.05 were considered to be statistically significant. Inter-observer agreement was calculated by *k* value (Bonferroni).

Results

The color-flow signals on the power Doppler in the proliferated synovium (pannus) of RA patients could be seen anywhere in the pannus. Nevertheless, the locations of the flow signals could be divided into four layers: the deep and superficial layers of the capsular pannus as well as the superficial and deep layers of the cortical pannus. The typical signals for each of the four layers are presented in Fig. 1: capsular deep signal (Fig. 1A), capsular superficial signals (Fig. 1B), cortical superficial signals (Fig. 1C), and cortical deep signal (Fig. 1D). In the legends of these figures, the data on effusion thickness, capsular pannus thickness, cortical pannus thickness, and the signal grades on the power Doppler, as well as the signal diameter and the RI values of the selected signals on the spectral Doppler are presented.

In our previous study,[8] we measured the RI values of 167 flow signals in 97 knee joints from 52 RA patients and compared the RI values of 43 capsular deep (aD) signals, 87 capsular superficial (aS) signals, 15 cortical superficial (oS) signals, and 22 cortical deep (oD) signals. Significant differences in the mean RI value were observed between the aD and the aS RI ($P < 0.0001$), as well as between the oS and the oD RI ($P = 0.0002$), but not between the aD and the oD RI ($P = 0.4526$), or between the aS and the oS RI ($P = 0.0929$) (unpublished data). On the basis of these observations, the knee joints were classified into joints with superficial pattern signals (located in the superficial half of the capsular and cortical pannus) and joints with deep pattern signals (located in the deep half of the capsular and cortical pannus). Thus, in the present study, the ultrasonographic measurements of effusion thickness (mm), capsular

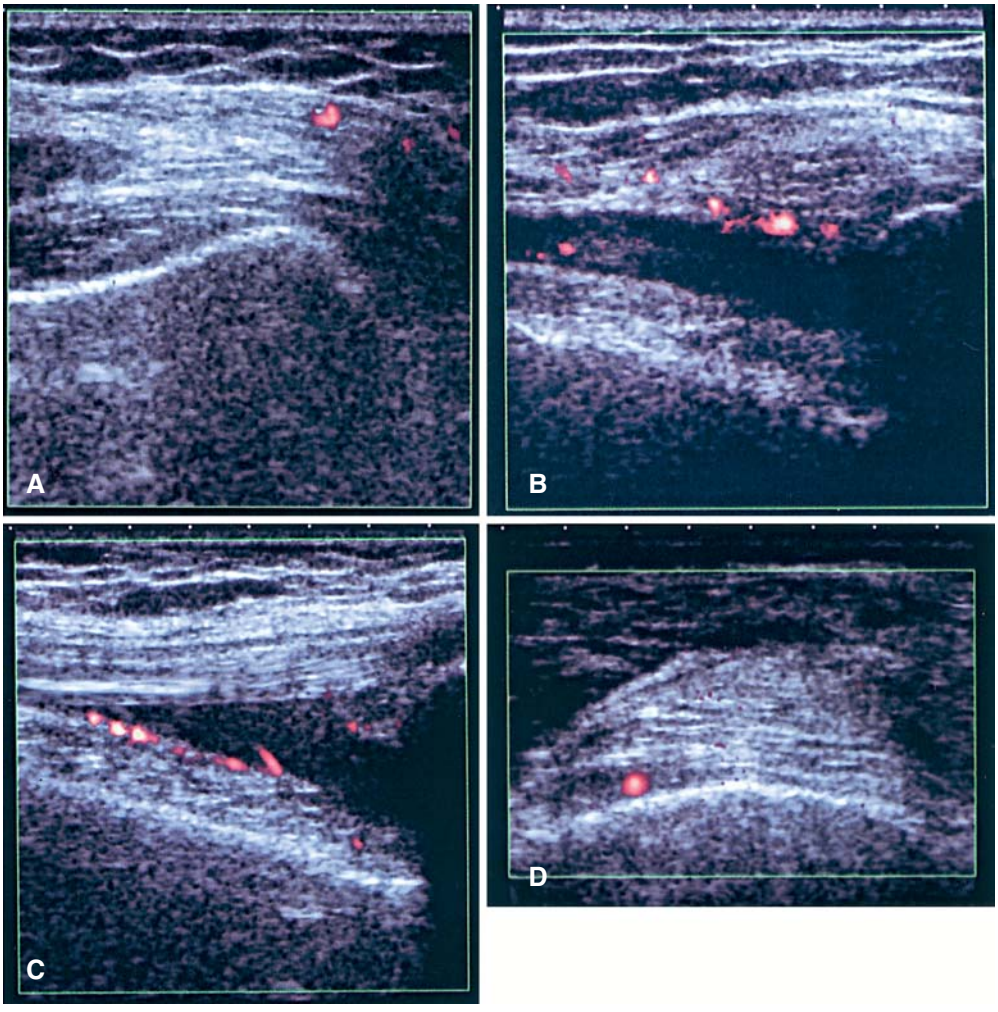

Fig. 1. **A** Grade 1 capsular deep signal on a power Doppler ultrasonogram of the right knee joint of an rheumatoid arthritis (RA) patient, scanned transversely at the suprapatellar recess. Effusion thickness 0.78 mm, capsular pannus thickness 10.0 mm, cortical pannus thickness 6.78 mm, diameter of the signal located under the articular capsule line 1.97 mm, and resistance index (RI) of the same signal used for the diameter measurement 0.82. The *scale* on the top of the figure is marked in 5 mm. **B** Grade 2 capsular superficial signals on power Doppler ultrasonogram of the left knee joint of an RA patient, scanned longitudinally at the suprapatellar recess. Effusion thickness 5.66 mm, capsular pannus thickness 10.80 mm, cortical pannus thickness 6.77 mm, diameter of the second larger signal from the right on the surface of the capsular pannus 2.23 mm, RI of the same signal used for the diameter measurement 0.73. The *scale* on the top of the figure is marked in 5 mm. **C** Grade 2 cortical superficial signals on power Doppler ultrasonogram of the left knee joint of an RA patient, scanned longitudinally at the suprapatellar recess. Effusion thickness 4.21 mm, capsular pannus thickness 7.88 mm, cortical pannus thickness 5.79 mm, diameter of the third signal from the left on the surface of the cortical pannus 1.46 mm, RI of the same signal used for diameter measurement 0.69. The *scale* on the top of the figure is marked in 5 mm. **D** Grade 1 cortical deep signal on power Doppler ultrasonogram of the right knee joint of an RA patient, scanned transversely at the suprapatellar recess. Effusion thickness 0.75 mm, capsular pannus thickness 7.89 mm, cortical pannus thickness 3.06 mm, diameter of the signal located above the femoral cortex line 1.88 mm, RI of the same signal used for the diameter measurement 0.85. The *scale* on the top of the figure is marked in 5 mm

pannus thickness (mm), cortical pannus thickness (mm), flow signal grades, signal diameter (mm), and RI values of the selected signals were compared among 58 joints with superficial pattern signals and 69 joints with deep pattern signals. Inter-observer agreement in flow signal grades and flow signal patterns was 0.78 for k values. The mean values of these six variables in the two groups are summarized in Table 1. As shown in Table 1, when compared with the joints with deep pattern signals, the joints with superficial pattern signals had significantly higher mean values of synovial effusion thickness ($P < 0.0001$) and flow signal grades ($P < 0.0001$), and significantly lower mean RI values ($P < 0.0001$). On the other hand, when compared with the joints with superficial pattern signals, the joints with deep pattern signals had a significantly higher mean value of signal diameter ($P = 0.0125$) and had a trend to higher mean value of total pannus (capsular plus cortical) thickness ($P = 0.0789$). Furthermore, as compared with the cortical pannus thickness, the capsular pannus thickness was significantly higher in the superficial signal joints ($P = 0.0017$), in the deep signal joints ($P = 0.0101$), and in all the joints (both superficial and deep signal joints; $P < 0.0001$).

Using 127 values, the correlation between pairs of five variables (total pannus thickness was used instead of cap-

Table 1. Power Doppler and spectral Doppler measurements of knee-joint synovitis in 58 joints with superficial pattern signals and 69 joints with deep pattern signals from 72 rheumatoid arthritis patients

Ultrasonographic variables	Knee-joint flow signals		Mean of (a) + (b)
	Superficial pattern (a) (n = 58)	Deep pattern (b) (n = 69)	
Effusion thickness (mm)	6.23 ± 2.00***	3.91 ± 2.46	4.97 ± 2.53
Pannus thickness (mm)			
Capsular (c)	7.90 ± 1.57^{ns},**	8.53 ± 2.45*	8.25 ± 2.11***
Cortical (d)	6.80 ± 1.91^{ns}	7.52 ± 2.58	7.19 ± 2.31
Total of (c) + (d)	14.71 ± 2.82^{ns}	16.05 ± 4.21	15.44 ± 3.67
Flow signal diameter (mm)	1.18 ± 0.32*	1.35 ± 0.36	1.27 ± 0.35
Flow signal grades	1.58 ± 0.66***	1.14 ± 0.37	1.34 ± 0.51
Resistance index	0.73 ± 0.11***	0.86 ± 0.12	0.82 ± 0.11

Values are given as mean ± SD
ns, not significant; *P < 0.05, **P < 0.01, ***P < 0.0001

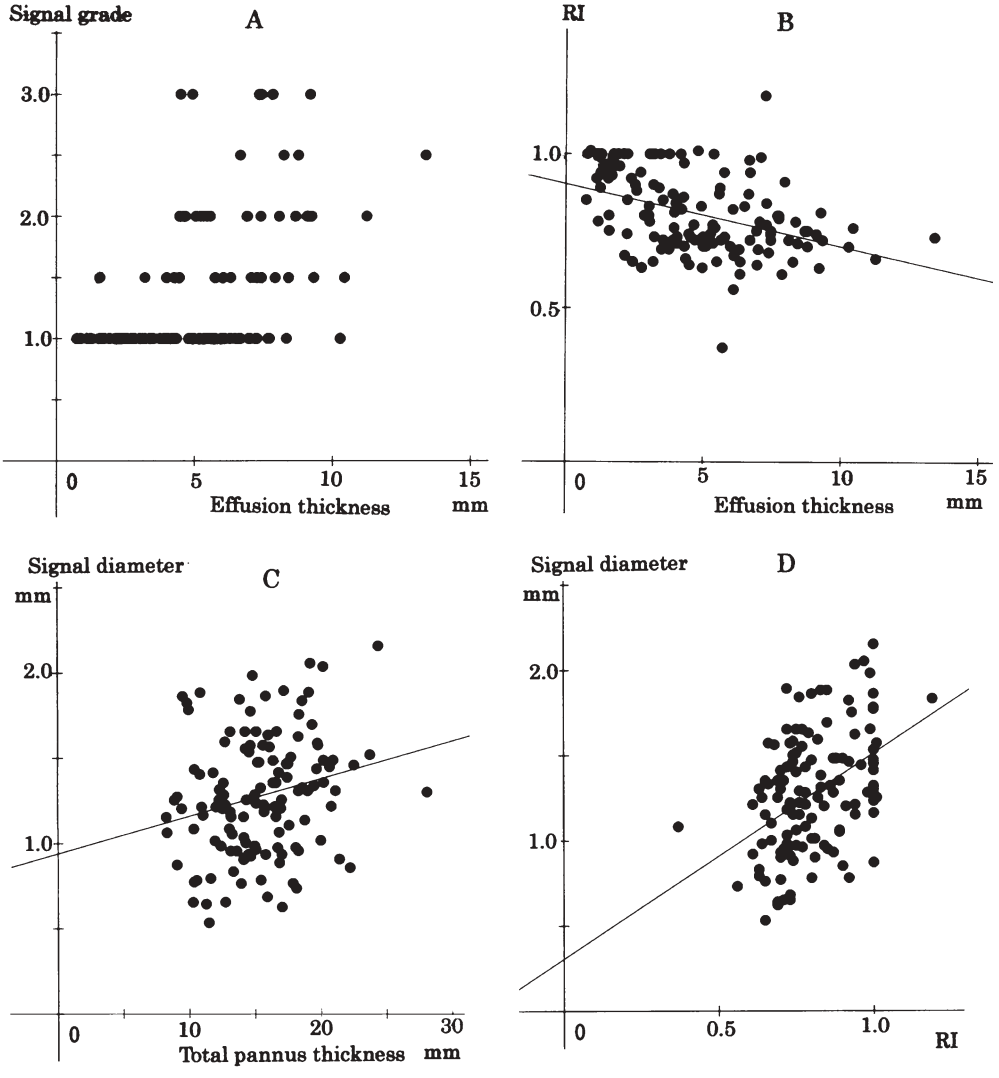

Fig. 2. The correlations between pairs of the five Doppler ultrasonographic variables obtained from 127 knee joints of 72 RA patients. Significant correlations were observed between signal grades and effusion thickness (r = 0.537, P < 0.0001, in **A**), RI and effusion thickness (r = –0.398, P < 0.0001, in **B**), signal diameter and total pannus thickness (r = 0.227, P = 0.0102, in **C**), and signal diameter and RI (r = 0.444, P < 0.0001, in **D**)

sular and cortical pannus thickness) was studied. As shown in Fig. 2, significant correlations were observed between signal grades and effusion thickness (r = 0.537, P < 0.0001, in Fig. 2A), RI and effusion thickness (r = –0.398, P < 0.0001, in Fig. 2B), signal diameter and total pannus thickness (r = 0.227, P = 0.0102, in Fig. 2C), signal diameter and RI (r = 0.444, P < 0.0001, in Fig. 2D), and signal grades and RI (r = –0.388, P < 0.0001, not shown). No significant correlations were observed between any of the other pairs of variables.

Discussion

The results obtained in the present measurement study using the digital calipers on ultrasonogram prints were quite similar to those reported in the earlier semiquantitative study;[8] both studies found significant differences between the superficial signal joints and the deep signal joints with respect to effusion thickness ($P < 0.0001$ in both), signal grades ($P < 0.0001$ in both), and RI values ($P < 0.0001$ in both), although the differences in the present study were not significant, between the two groups of joints with respect to pannus thickness ($P = 0.0789$ and $P = 0.0096$, respectively). A finding that was observed in the present study that the capsular pannus thickness was significantly greater than the cortical pannus thickness in both the superficial signal joints and the deep signal joints could be reevaluated when considering the validity of the measurement method used in the present study for the capsular pannus thickness. With respect to the different localization of flow signals in knee-joint synovitis, Fiocco et al.[9] first identified a difference between the superficial and the deep flow signals in the pannus: they found that there was an earlier reduction of the superficial signals than the deep signals in response to etanercept therapy in RA and psoriatic arthritis patients. However, no other differences between the two types of signals in the pannus have been reported earlier. In our previous study,[10] 10 RA patients with joints that had cortical pattern signals had significantly higher levels of C-reactive protein than 17 RA patients with joints that had capsular pattern signals. To the best of our knowledge, the measurement of the flow signal diameter on the power Doppler in the pannus of RA patients has not been reported earlier. It is of great interest to know the diameter of the vessels in the pannus and to determine its correlation with the other variables on power Doppler to further our understanding of the pathogenesis of synovitis. In the present study, the flow signal diameter in the pannus was significantly greater in the deep signal joints than in the superficial signal joints, and the diameter significantly correlated with the total pannus thickness and RI values, which provides valuable information on pannus formation in RA synovitis. A study comparing the ultrasonography findings with the histopathology of the pannus in the knee joints is needed to confirm the relationship of the signal diameter with pannus thickness or with vascular resistance in the synovial vasculature on power Doppler. With respect to this point, Walther et al.[11] reported a significant correlation between the flow signal intensity on power Doppler and the extent of histological vascularity present in knee-joint synovitis of 10 RA and 13 osteoarthritis patients. In contrast, Schmidt et al.[12] reported no significant correlation between the number of synovial vessels on histology and the flow signal intensity or the extent of synovial proliferation on power Doppler in the knee-joint pannus of 10 RA and 10 osteoarthritis patients. However, in these two studies, vessel diameter, pannus thickness, and relationship between these two variables were not considered. An increase in RI values on spectral Doppler with etanercept therapy[13] and infliximab therapy[14,15] was reported in RA patients. However, the present study and our previous study[8] are the only studies that have found a significant difference in RI values between the superficial signal joints and the deep signal joints. Furthermore, the present results show that the RI values correlated with effusion thickness and signal diameter. These findings are of interest as they shed new light on the role of the vessels in the synovitis of RA patients. This study also found a significant inverse correlation between RI and flow signal intensity, which others and we have previously reported.[16–20]

Taken together, the results of the present study suggest that the degree of synovial effusion had a stronger association with the increased grades of flow signals which have higher perfusion (lower RI values) and are located in the superficial layer of the pannus, whereas pannus thickness had a stronger association with the larger vessels which have lower perfusion (higher RI values) and are located in the deep layer of the pannus.

In conclusion, the Doppler ultrasonographic measurements of synovial effusion, synovial thickness, and signal diameter, as well as signal intensity and RI values, could be useful indicators for evaluating and analyzing synovial inflammation in RA patients.

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