Mod Rheumatol (2005) 15:33–36
DOI 10.1007/s10165-004-0353-y

ORIGINAL ARTICLE

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Doppler sonographic analysis of synovial vascularization in knee joints of patients with rheumatoid arthritis: increased color flow signals and reduced vascular resistance

Received: June 1, 2004 / Accepted: September 29, 2004

Abstract Synovial vascularization was analyzed by power Doppler and spectral Doppler sonography in 42 knee joints of 28 patients with rheumatoid arthritis. The synovial vessels with greater intensity of color flow signals demonstrated significantly lower indicators of vascular resistance – resistive index ($P < 0.01$) and pulsatility index ($P < 0.01$) – than those with lesser intensity. Consequently, an inverse correlation was observed between intensity of color flow signals and both resistive index ($P < 0.01$) and pulsatility index ($P < 0.01$).

Key words Doppler sonography · Knee joint · Rheumatoid arthritis (RA) · Synovial vascularization · Vascular resistance

Introduction

Increased vascularization in the inflammatory synovium of patients with rheumatoid arthritis (RA) has been successfully evaluated by power Doppler sonography.[1–5] Vascular resistance of the peripheral vessels has been quantitatively demonstrated by pulse-waved spectral Doppler sonography and a decreased resistance of synovial vessels in RA patients has recently been reported,[3,6,7] However, a correlation between increased vascularization and decreased vascular resistance in the inflammatory synovium has not been clearly demonstrated. In the present study, power Doppler and spectral Doppler sonography were used to assess 56 knee joints from 28 RA patients. We were able to analyze intensity of color flow signals and vascular resistance of synovial vessels and also to determine the correlation between these two variables in 42 joints.

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Patients and methods

Patients

Twenty-eight RA patients were enrolled in the present study. Subjects were 26 women and 2 men with a mean age of 56.9 years (ranging from 29 to 84 years). Fifty-six knee joints were examined. All patients satisfied the American College of Rheumatology 1987 revised criteria for RA.[8]

Gray-scale sonography and Doppler sonography

Gray-scale sonography (GSS) and power and spectral Doppler sonography were performed using a Toshiba Aplio 80 system (Toshiba, Tochigi, Japan) following the standard method described previously.[5] Briefly, standard apparatus settings (transmit power, $<5000\,mW/cm^2$; low-pass wall filter No. 3; medium persistence) were used. B-Mode gray-scale frequency was 11.0 MHz. Power Doppler gain was optimized at 60%–70% with a pulse repetition frequency (PRF) of 11.7–12.2 kHz. Pulsed-wave spectral Doppler imaging was performed using the lowest filter setting (125 Hz). Spectral Doppler tracing of the color flow signals was performed to confirm true arterial or venous flow and also to calculate resistive index (RI) and pulsatility index (PI) of the vessels. A multidimensional linear scanner (PLT-704 AT) was used as the transducer, at 5.3 MHz. The suprapatellar region of the knee was scanned longitudinally and transversely. Intensity of both synovial effusion and synovial proliferation were determined by GSS according to

the method of Rubaltelli et al.:[9] grade 0, less than 1 mm thickness; grade 1, 2–4 mm thickness; grade 2, 5–7 mm thickness; grade 3, over 8 mm thickness. Synovial vasculature was identified as the color flow signals on power Doppler sonography (PDS) in the proliferated synovium located between those of the highly echogenic cortical surface of the femur and those of the moderately echogenic articular capsule. Intensity of color flow signals obtained by PDS was graded according to the modified Klauser method:[5,10] grade 0, no color flow signal; grade 1, 1–4 color flow signals; grade 2, 5–8 color flow signals; grade 3, more than 9 color flow signals. One area of color flow signals obtained on PDS was randomly selected and pulse waves were demonstrated by pulsed-wave spectral Doppler sonography (SDS). Analysis of vascular resistance was performed by tracing the margin of the sonographic waves obtained by SDS using a dotted line, allowing automatic computerized calculation of resistive index (RI) and pulsatility index (PI). Resistive index and PI were obtained by the following formula: RI = peak systolic (maximum) velocity–end diastolic (minimum) velocity/peak systolic (maximum) velocity; PI = maximum velocity–minimum velocity/mean velocity. Mean values of two readings obtained on longitudinal and transverse scanning of the knee joint were calculated to represent intensity of synovial effusion, synovial proliferation and color flow signal, RI, and PI.

Statistical analysis

Statistical analysis was performed using the J-Stat software package for Windows. Differences between groups were evaluated using Student's unpaired *t*-test. Correlation between two values was obtained by Spearman's rank correlation coefficient. *P* values of less than 0.05 were considered to indicate significance.

Results

Fifty-six knee joints were examined by Doppler sonography. However, only 42 joints were used for

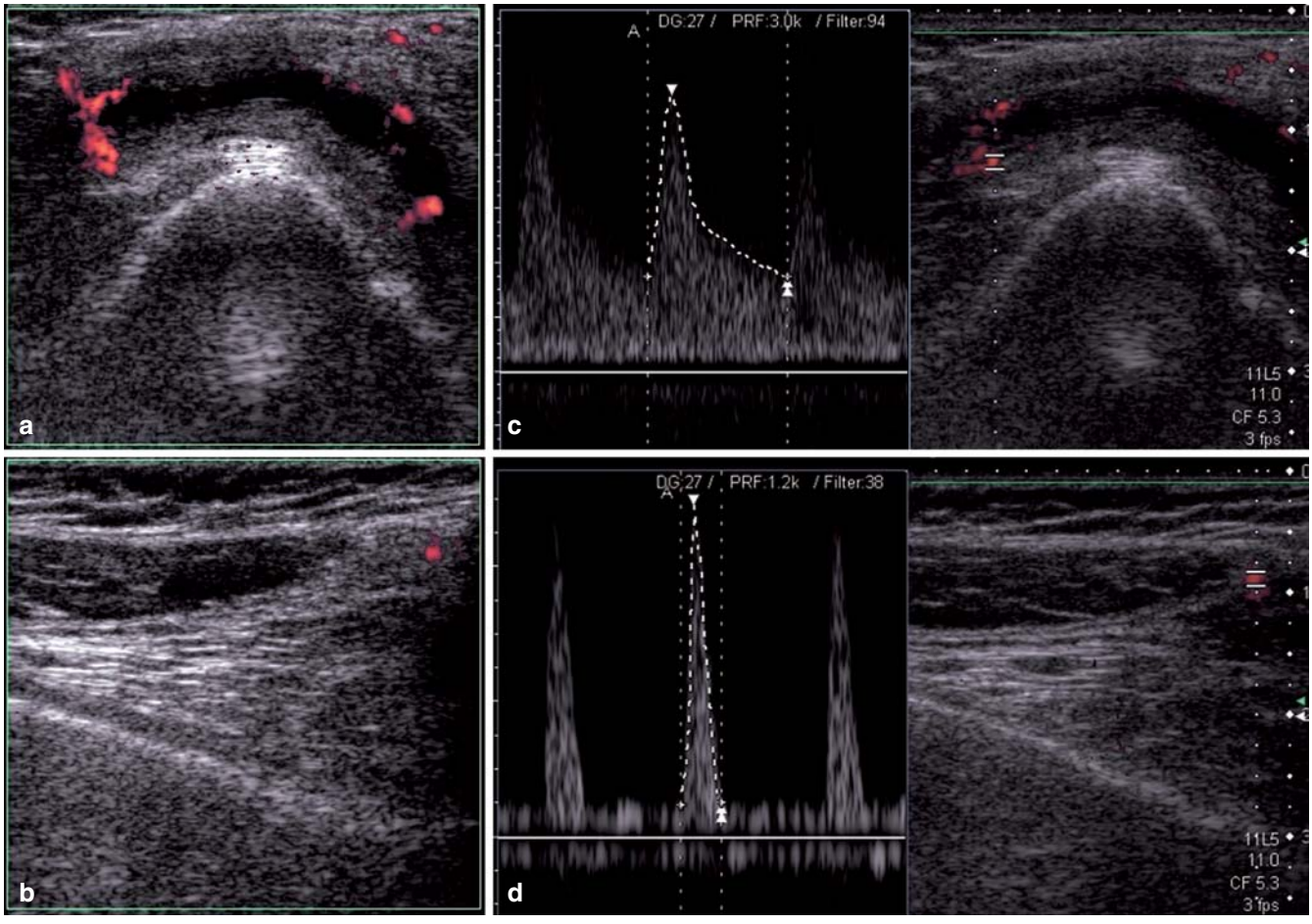

Fig. 1. Power Doppler sonograms (**a**,**c**) and spectral Doppler sonograms (**b**,**d**) of patients MI (**a**,**b**) and TK (**c**,**d**). **a** Grade 3 color flow signals were demonstrated on supracapsular transverse imaging of the right knee. **b** Lower vascular resistances, resistive index (RI) (0.67) and pulsatility index (PI) (1.25), were demonstrated on the same view of the right knee. **c** Grade 1 color flow signals were demonstrated on supracapsular longitudinal imaging of the left knee. **d** Higher vascular resistances, RI (1.00) and PI (2.30), were demonstrated on the same view of the left knee

Table 1. Correlation between intensity of color flow signals and synovial effusion or synovial proliferation demonstrated by power Doppler sonography, and vascular resistance demonstrated by spectral Doppler sonography

Grade of color flow signals	No. of joints	Grade of synovial effusion (mean ± SD)	Grade of synovial proliferation (mean ± SD)	Vascular resistance (mean ± SD) Resistive index	Pulsatility index
1	32	0.69 ± 0.54	1.31 ± 0.47	0.85 ± 0.14	1.88 ± 0.51
1.5	2				
2	5				
3	3				
1.5 + 2 + 3	10	1.40 ± 0.70	1.30 ± 0.48	0.64 ± 0.06	1.20 ± 0.22
P value		<0.01*	ns	<0.01*	<0.01*

Ten joints exhibiting combined grades [1.5 + 2 + 3] and 32 joints with grade 1 were compared
*, significant; ns, not significant

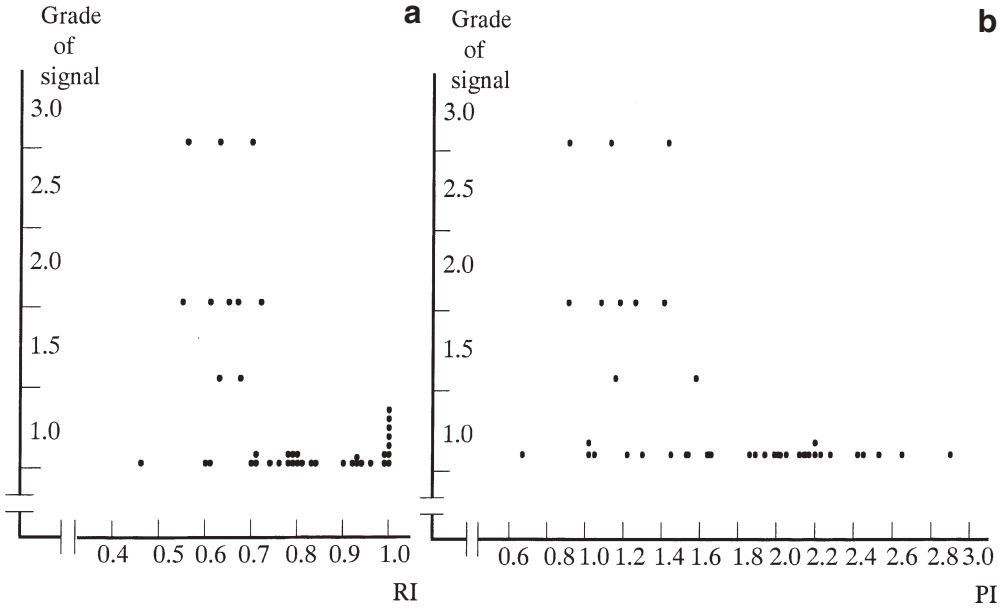

Fig. 2. Correlation between intensity of color flow signals and **a** resistive index (*RI*); **b** pulsatility index (*PI*). **a** $r = -0.592$, $P = 0.0001$. **b** $r = -0.563$, $P = 0.0003$

sonographic analysis in the present study, since 14 joints demonstrated either no color flow signals or a flat pattern on spectral Doppler sonography that did not enable calculation of vascular resistance. Representative power Doppler and spectral Doppler sonographic images of synovial vascularization in knee joints of RA patients are shown in Fig. 1. Figure 1a and b demonstrate sonographic appearances for patient MI; grade 3 color flow signals (Fig. 1a) and lower RI (0.67) and PI (1.25) values (Fig. 1b) are apparent. Figure 1c and d demonstrate the sonographic appearance for patient TK; grade 1 color flow signals (Fig. 1c) and higher RI (1.00) and PI (2.30) values (Fig. 1d) are observed.

Frequencies of each grade of color flow signals were as follows: grade 1, $n = 32$; grade 1.5, $n = 2$; grade 2, $n = 5$; grade 3, $n = 3$. Ten joints exhibiting combined grades (1.5 + 2 + 3) and 32 joints with grade 1 were compared for intensity of synovial effusion and synovial proliferation, and values of RI and PI. The results obtained are summarized in Table 1. The higher vascularization group (grades 1.5 + 2 + 3) demonstrated a significantly higher grade of synovial effusion (1.40 ± 0.70 vs 0.69 ± 0.54, $P < 0.01$) but not of synovial proliferation (1.30 ± 0.48 vs 1.31 ± 0.47) than the lower vascularization group (grade 1). Conversely, the higher vascularization group demonstrated significantly lower values of both RI (0.64 ± 0.06 vs 0.85 ± 0.14, $P < 0.01$) and PI (1.20 ± 0.22 vs 1.88 ± 0.51, $P < 0.01$) than the lower vascularization group. Consequently, a significant inverse correlation was observed between the grade of color flow signal and both RI ($r = -0.592$, $P = 0.0001$) (Fig. 2a) and PI ($r = -0.563$, $P = 0.0003$) (Fig. 2b).

Discussion

Power Doppler sonographic demonstration of hypervascularization in the synovium of RA patients has been reported by many investigators[1–4] as well as by the present authors,[5,11] and an association of synovial vascularization with clinical disease activity has been discussed.

Spectral Doppler sonography demonstrates peak systolic (maximum) velocity and end diastolic (minimum) velocity of the peripheral vasculature. In normal tissues, diastolic velocity of the peripheral vasculature has been considered to be zero, indicating adequate vessel resistance in the diastolic phase of blood flow. However, it has been reported that normal kidney, brain, and umbilical cord exhibit markedly higher arterial diastolic flow.[3] In addition, diastolic velocity increases in inflammatory tissues such as synovial tissues in RA patients, indicating increased permeability (reduced vascular resistance) of the vessels and leakage to the tissue.[3] In the present study of RA patients, significantly reduced resistance indicated by RI ($P < 0.01$) and PI ($P < 0.01$) was observed in hypervascular synovium when compared with less vascular synovium. Similarly reduced resistance of synovial vessels in RA patients has been reported by Qvistgaard et al.,[3] Shahin et al.,[6] and Terslev et al.[7,12] In addition, a significant correlation was found between intensity of color flow signals and values of RI ($P < 0.01$) or PI ($P < 0.01$). From these observations we considered RI or PI to be qualitative indicators in the evaluation of synovial hypervascularity in RA synovium and inflammatory activity of arthritis as well as color flow signals, since the grade of the color flow signals correlated with the grade of synovial effusion as was described in the present study and the previous one.[5] Both RI and PI values and color flow signals will be useful indicators for evaluating the therapeutic effect of antirheumatic drugs in RA patients. In conclusion, in the knee joints of RA patients, synovial vessels with greater intensity of color flow signals revealed lower vascular resistance. A significant inverse correlation was observed between the intensity of color flow signals and indicators of vascular resistance.

Acknowledgment We express our sincere thanks to Mr. K. Nihei of the Library Unit of Ohta Nishinouchi Hospital for his technical help with sonographic images.

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