

Clinical Significance of Wrist Joint Synovial Blood-Flow Signals on Doppler Ultrasonography in Patients with Rheumatoid Arthritis

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ABSTRACT

The clinical significance of power Doppler ultrasonography signal scores of synovial blood flow in the wrist joint was investigated in 40 patients with rheumatoid arthritis meeting the diagnostic criteria established by the American College of Rheumatology. Synovial blood-flow signals of the wrist joint were given scores according to Neuman's method. The sum of the bilateral wrist signal scores was regarded as the total wrist signal score. The blood-flow score in each wrist and the total score in both wrists were significantly correlated with serum levels of C-reactive protein and the 28-Joint Disease Activity Score-C-reactive protein index. This study suggests that blood-flow signals in the wrist joint reflect the systemic activity of rheumatoid arthritis.

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Key words : rheumatoid arthritis, power Doppler ultrasonography, angiogenesis

INTRODUCTION

Rheumatoid arthritis is a chronic inflammatory disease with the main inflammatory lesions in the articular synovial membrane¹. Marked vascularization and inflammatory cell infiltration are present in hyperplastic inflammatory synovial tissue, called pannus². New blood vessels present in pannus are essential for supplying nutrients to the proliferative synovial membrane. Pannus invades and induces the destruction of cartilage and bone. A method of measuring synovial vascular blood flow with Doppler ultrasonography has recently been developed³⁻⁷. Synovial vascular blood flow is visualized as red and yellow signals on Doppler ultrasonography^{8,9}.

Our previous study found that blood-flow signal scores in the right wrist joints of 21 patients with

rheumatoid arthritis were correlated with the serum level of vascular endothelial growth factor, a vascularization-related factor, but not with the serum level of C-reactive protein (CRP) or the 28-Joint Disease Activity Score (DAS28)-CRP, a rheumatoid arthritis activity index¹⁰. Because rheumatoid arthritis is characterized by symmetric arthritis, we investigated blood-flow signal scores in each wrist joint and the total score in both wrist joints in a larger number of cases.

PATIENTS AND METHODS

This study involved 40 outpatients (28 women and 12 men) who fulfilled the diagnostic criteria of the American College of Rheumatology¹¹. The mean (\pm SD) age was 57.8 ± 12.6 years (range, 31-85 years).

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Table 1. Scores of blood flow signals and clinical date

Patient	Age (years)	Sex	Disease duration (years)	Drug	Right wrist SG	Right wrist swelling or pain	Left wrist SG	Left wrist swelling or pain	Total wrist SG	CRP	DAS28-CRP
1	69	F	7	PSL 15 mg	2	(+)	2	(+)	4	1.44	4.52
2	51	F	0.2	—	2	(-)	1	(-)	3	6.87	5.29
3	34	F	3	PSL 4 mg MTX 8 mg	0	(-)	2	(+)	2	0.12	2.78
4	60	F	1	—	2	(+)	2	(+)	4	5.58	5.61
5	55	F	22	PSL 6 mg	1	(+)	1	(+)	2	0.98	4.02
6	69	F	3	PSL 12.5 mg MTX 12.5 mg infliximab	1	(+)	1	(-)	2	0.07	5.34
7	31	M	0.4	—	1	(-)	0	(-)	1	0.53	2.18
8	49	F	1	—	0	(-)	1	(-)	1	0.94	3.9
9	57	F	4	PSL 6 mg MTX 8 mg infliximab	0	(-)	0	(-)	0	0.04	>
10	85	M	1	—	2	(+)	1	(+)	3	11.49	6.54
11	84	M	1	—	2	(-)	2	(-)	4	5.42	4.6
12	74	F	0.5	—	0	(-)	0	(-)	0	0.57	3.3
13	73	F	3	PSL 5 mg MTX 4 mg	0	(-)	0	(-)	0	8.86	3.28
14	48	M	4	MTX 8 mg	0	(-)	0	(-)	0	0.04	>
15	52	F	2	—	0	(-)	2	(+)	2	0.11	2.77
16	64	F	4	infliximab	0	(-)	0	(-)	0	0.04	>
17	64	F	0.1	PSL 8 mg MTX 8 mg	0	(+)	0	(-)	0	0.12	3.38
18	35	F	0.1	—	2	(+)	0	(+)	2	0.07	3.04
19	61	F	6	PSL 6 mg MTX 10 mg	1	(-)	0	(-)	1	1.25	3.44
20	55	F	7	etanercept	2	(+)	0	(-)	2	0.26	3.09
21	71	F	7	PSL 2 mg MTX 8 mg	1	(+)	0	(-)	1	0.11	3.33
22	49	M	1	PSL 4 mg	1	(+)	1	(+)	2	1.57	4.46
23	56	F	1	PSL 6 mg MTX 8 mg	1	(-)	0	(-)	1	0.17	2.58
24	49	M	1	infliximab	1	(-)	1	(-)	2	1.08	2.55
25	66	M	4	PSL 10 mg	1	(+)	0	(-)	1	0.86	3.3
26	59	M	2	PSL 5 mg MTX 8 mg	0	(-)	0	(-)	0	0.34	2.19
27	58	M	8	PSL 7 mg MTX 12.5 mg	1	(+)	1	(-)	2	0.77	3
28	48	M	2	PSL 6 mg MTX 10 mg	0	(+)	0	(-)	0	0.3	3.06
29	41	F	2	MTX 6 mg	1	(-)	0	(-)	1	0.04	>
30	37	F	16	PSL 6 mg MTX 8 mg	0	(-)	0	(-)	0	0.22	2.75
31	50	F	9	PSL 5 mg	1	(+)	1	(-)	2	0.43	2.82
32	68	F	5	PSL 5 mg MTX 4 mg	1	(-)	0	(-)	1	0.82	2.19
33	42	F	0.5	PSL 8 mg MTX 10 mg	0	(-)	0	(-)	0	3.9	2.99
34	54	F	5	PSL 12.5 mg MTX 7.5 mg	1	(+)	2	(+)	3	1.64	3.67
35	73	F	17	—	1	(-)	0	(-)	1	0.18	2.03
36	75	M	3	PSL 10 mg MTX 4 mg	1	(+)	0	(+)	1	0.78	4.54
37	58	F	15	PSL 4 mg	2	(+)	1	(-)	3	0.39	3.07
38	64	M	1	PSL 5 mg MTX 8 mg	0	(-)	0	(-)	0	2.33	2.81
39	62	F	12	MTX 6 mg	0	(-)	0	(-)	0	0.08	1.87
40	62	F	5	MTX 6 mg	0	(-)	0	(-)	0	0.04	>

CRP : C-reactive protein (mg/dl); DAS28 : 28-Joint Disease Activity Score ; SG : microvascular power Doppler signal grade of right wrist ; PSL : prednisolone ; MTX : methotrexate

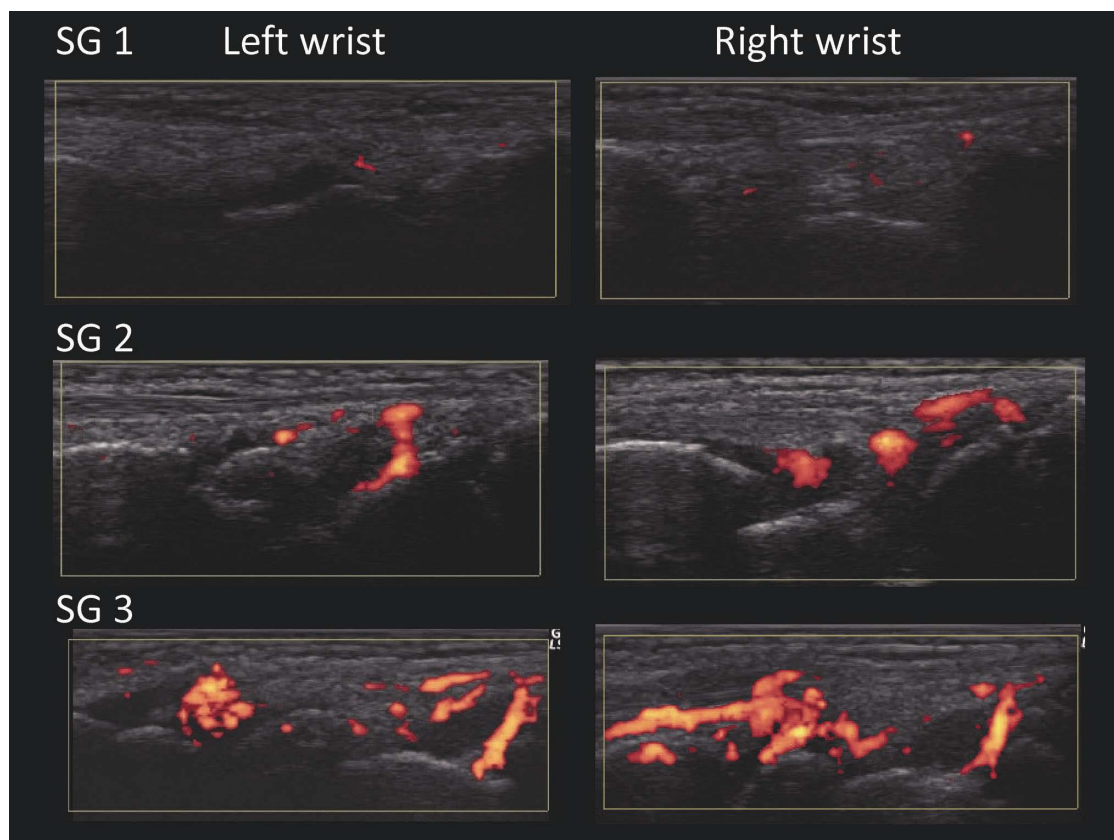


Fig. 1. Grading of synovial blood-flow signals in the wrist joint. Blood-flow signals in the articular synovial membrane were classified into: grade 1, no flow; grade 2, mild or moderate flow; and grade 3, intense flow.

This study was approved by the Ethics Committee of The Jikei University, and informed consent was obtained from all patients. Table 1 shows the clinical findings of the patients.

Power Doppler ultrasonography (PDUS) was performed with a linear array transducer (10 MHz; GE Healthcare, Waukesha, WI, USA). Both wrist joints were longitudinally scanned with ultrasonography. Synovial blood flow was evaluated with PDUS in each of the intra-articular synovial sites. The synovial blood-flow scores corresponded to the maximum score for synovitis. One rheumatologist and one radiologist analyzed recorded video clips without information on the clinical conditions and laboratory test data of the patients. Neuman's method was used to evaluate synovial blood-flow signals^{12,13}: grade 1, no flow (0 points); grade 2, mild or moderate flow (1 point); and grade 3, intense flow (2 points) (Fig. 1). The total of the signal scores of both wrist joints was

designated as the total wrist blood-flow signal score (0–4 points).

For statistical analysis, the Spearman rank correlation test was used, and $p < 0.05$ was regarded as indicating significance.

RESULTS

Clinical conditions of the patients

The mean (\pm SD) disease duration was 4.67 ± 5.19 years: <1 year in 6 patients, ≥ 1 year and <5 years in 20 patients, ≥ 5 years and <10 years in 9 patients, and ≥ 10 years in 5 patients. Oral prednisolone doses were 0 mg in 17 patients, >0 mg and <5 mg in 4 patients, ≥ 5 mg and <10 mg in 14 patients, and ≥ 10 mg in 5 patients, and oral methotrexate doses were 0 mg in 19 patients, >0 mg and ≤ 4 mg in 3 patients, >4 mg and ≤ 8 mg in 13 patients, and >8 mg in 5 patients. Five patients were treated with biological

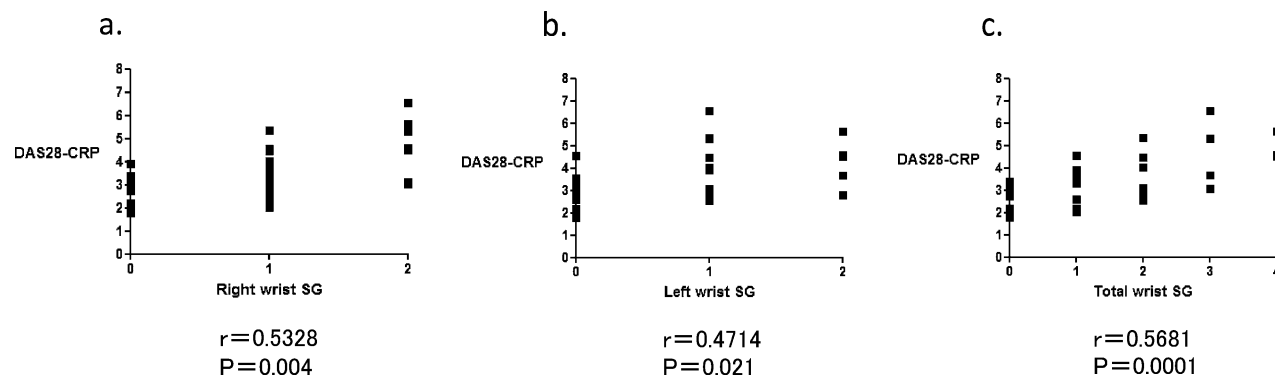


Fig. 2. Relationship between the wrist blood-flow signals and serum CRP level
 a. Relationship between the right wrist blood-flow signals and serum CRP level
 b. Relationship between the left wrist blood-flow signals and serum CRP level
 c. Relationship between the total wrist blood-flow signals and serum CRP level

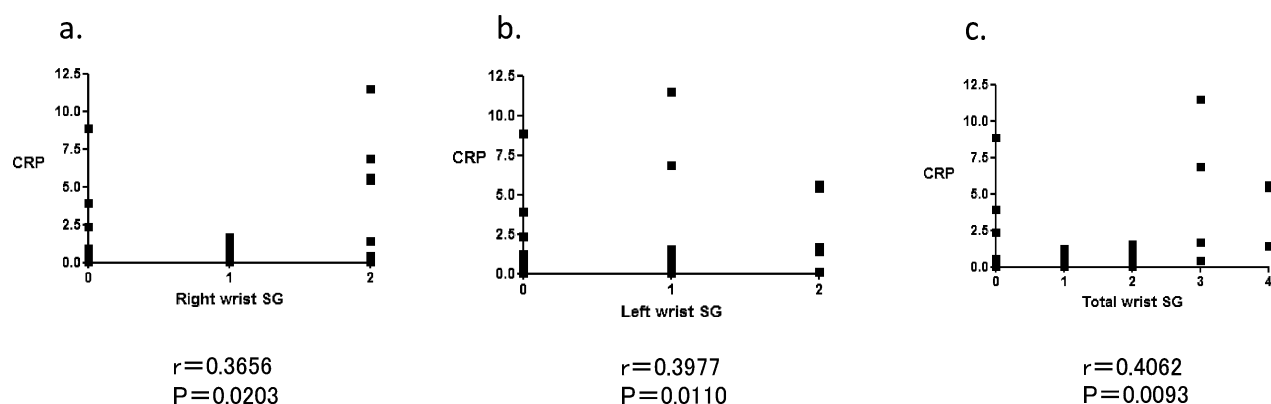


Fig. 3. Relationship between the wrist blood flow signals and DAS28-CRP
 a. Relationship between the right wrist blood-flow signals and DAS28-CRP
 b. Relationship between the left wrist blood-flow signals and DAS28-CRP
 c. Relationship between the total wrist blood-flow signals and DAS28-CRP

products, and 10 patients were untreated.

Relationship between the wrist joint blood-flow signal score and DAS28-CRP

The mean (\pm SD) DAS28-CRP score was 3.3 ± 1.1 : it was <2 in 4 patients, ≥ 2 and <3 in 3 patients, ≥ 3 and <4 in 14 patients, ≥ 4 and <5 in 5 patients, ≥ 5 and <6 in 3 patients, and ≥ 6 in 1 patient. The right, left, and total wrist signal scores were correlated with DAS28-CRP (Fig. 2a-c).

Relationship between the wrist joint blood-flow signal score and serum CRP level

The mean (\pm SD) serum CRP level was 1.73 ± 2.7 mg/dl. The right, left, and total wrist blood-flow

signal scores were correlated with the serum CRP level (Fig. 3a-c).

DISCUSSION

Our previous study showed that the blood flow-signal score in the right wrist joints of 21 patients with rheumatoid arthritis was correlated with the serum level of vascular endothelial growth factor but not with the serum CRP level or the DAS28-CRP¹⁰. As described in the classification criteria established by the American College of Rheumatology, a characteristic of rheumatoid arthritis is symmetric articular swelling¹⁴. Therefore, we investigated scores in each wrist and the total score in both wrists in a larger

number of cases.

Blood-flow signal scores in the right and left wrists and the total score in both wrists were significantly correlated with the serum CRP level and with the DAS28-CRP. Although our previous study found no significant correlation between the right wrist signal score and serum CRP level, the correlation coefficient ($r=0.4186$) and the probability value ($P=0.590$) showed a tendency toward correlation¹⁰. That a correlation was demonstrated in the present study might be due to the larger number of patients.

In rheumatoid arthritis, arthritis develops throughout the entire body. Thus, the systemic findings—the DAS28-CRP and the serum CRP level—are not necessarily correlated with the local findings in the hands. There have been various reports on the association of clinical findings with the synovial blood flow-signal score in a single joint. Qvistgaard et al.¹⁵, Shio et al.¹⁶, and Klauser et al.¹⁷ have investigated the association in the fingers. Qvistgaard et al. have investigated the association of metacarpophalangeal (MCP) joint blood-flow signals with clinical findings but identified no correlation with the serum CRP level¹⁵. Shio et al. have investigated the association of MCP synovial blood-flow signals with the DAS28 and serum CRP level but observed no correlation with the DAS28 or the serum CRP level¹⁶. Filippucci et al. have investigated the wrist joint¹⁷; although they found no significant correlation between wrist blood-flow signals and the DAS28, they did find a tendency ($r=0.382$ and $P=0.067$). In contrast, Kasukawa et al. have investigated the knee joint and noted a correlation between the knee joint blood-flow signals and the serum CRP level¹⁸. Therefore, no consensus has been reached with regard to the relationship between clinical findings and synovial blood-flow signals in a single joint.

However, when data in previous reports and the present study were combined, there may have been a certain tendency regarding the relationship between synovial blood-flow signals in single joints and clinical findings; however, no correlation with systemic findings was noted in small joints, such as the MCP joint, but a correlation may have been present in large joints, such as the knee.

The wrist joint is intermediate in size between finger joints and large joints, such as the knee. Single wrist joints were previously investigated by us ($n=21$) and by Filippucci et al. ($n=24$); both studies obtained similar findings. We could not demonstrate the presence of a significant correlation, but a tendency was noted; the findings of Filippucci et al were similar. Thus, the type of joint may be important in evaluating the correlation between blood-flow signals and clinical findings.

Arthritis most frequently develops in the wrist joint in rheumatoid arthritis, as described in the American College of Rheumatology criteria. Accordingly, certain findings are present in the wrist joint in many patients with rheumatoid arthritis. In fact, 19 of our 40 patients showed symptoms in the wrist joint. In contrast, in the knee joint, swelling or tenderness was noted only in 9 patients, and 5 of them also had these symptoms in the wrist joint, revealing that only a few patients showed abnormalities in the knee joint alone without abnormalities in the wrist joint. Similarly, of 9 patients with swelling or tenderness of the elbow joint, 4 also had these symptoms in the wrist joint, and of 7 patients with swelling or tenderness in the shoulder joint, 4 also had these symptoms in the wrist joint. Therefore, these results suggest that the wrist joint is more suitable than the large joint such as the knee or elbow joint for evaluating the correlation between blood flow signals and clinical findings.

In the present study, we investigated the correlation between clinical findings and blood-flow signals in the both wrists and in each wrist in a larger number of patients. We found that the total blood flow signal score in both wrists and the scores in each wrist were correlated with clinical findings. Although the total score in both wrists was correlated more strongly with clinical findings than were the scores in each wrist, the total score in both wrists and the scores in each wrist were also significantly correlated with clinical findings.

Associations between the total synovial blood-flow signals in all joints of the body and various clinical findings have recently been reported. Narredo et al. have reported that the total synovial blood-flow signal score of 44 joints was correlated with the

serum CRP level and the DAS28¹⁹. However, because of the time required, it is difficult to examine all joints in the body with Doppler ultrasonography in routine clinical practice. In contrast, the wrist joints alone can be examined within a relatively short time. This study suggests that blood-flow signals in the wrist joint reflect the systemic activity of rheumatism.

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