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Type of the article; Letter

Title; Relationship between Power Doppler Grade and the Pathological Blood Vessel Features in Long Standing Rheumatoid Arthritis

Sir,

In spite of the fact that Power-Doppler (PD) ultrasonography is currently used in the analysis of inflammatory activity of rheumatoid arthritis (RA), little is known about pathological condition where positive PD signal is visualized in synovitis. We tried to elucidate the relationship between PD signal and the size of the capillary vessel in the pannus utilizing surgical specimen of the joints in long standing RA patients.

In rheumatoid arthritis (RA), providing direct/indirect evidence of synovial inflammation is of clinical importance. Pathological examination is able to observe the pannus and proliferated blood vessel directly. However, it is not easily carried out due to its harmfulness. The abnormal bloodstream in the synovial lesion may be caught by PD ultrasonography. Thereby ultrasonography is useful in the observation of the disease activity and treatment response. There are a few studies on correlations between PD ultrasonography and pathology, which conclude positive correlations between PD signal count and inflammation activity [1]. However, there are few studies to elucidate the relationship between PD signal positivity and the blood vessel features on pathological specimen. Walther M, et al showed, by analyzing the biopsy specimen, that PD signal is related to the blood vessel area but not influenced by the number of the blood vessels in the knee joint of the early RA patients [2]. Here, we determined to examine this using surgical specimen from joints with long standing RA.

Synovial tissue was resected from 10 joints (7 metacarpophalangeal joints of the finger, 2 wrist joints, and

1 metatarsophalangeal joint of the big toe) of 10 female RA patients who underwent synovectomy and joint reconstructive surgery, with an average (range) age and disease duration of 61.5 (34-75) and 16 (3-46) years, respectively. Preoperative PD revealed grade 0 (absence of signal) in 3 joints, grade 2 (agglutination of less than half of the whole hypertrophic synovium) in 4 joints and grade 3 (agglutination of more than half of the whole hypertrophic synovium) in 3 joints. The maximum score obtained from the synovial sites was evaluated in each joint [1]. Preoperative ultrasound evaluations of the affected joints were performed using a TOSHIBA Xario (Tokyo, Japan) and a HITACHI AVIUS (Tokyo, Japan), with transducers of 10-16 MHz. The PD signal was assessed with a pulse repetition frequency of 750 Hz and medium wall filter. Gain was adjusted by turning it up until random noise is encountered and then lowering it until the noise disappears. The blood vessel area measurement was performed for 10 representative pathological slices with Rooney sub-score of 9 or 10 for the proliferating blood vessels. Rooney sub-score is the index that is used for a histologic evaluation, which includes the degree of synovial hyperplasia, the degree of fibrosis, the number of blood vessels, perivascular infiltrates of lymphocytes, focal aggregates of lymphocytes and diffuse infiltrates of lymphocytes [3]. Total number of the analyzed blood vessels was 139. The area measurement was performed using ImageJ [4]. First, the part including blood vessel was magnified and separated a blood vessel and a background by using the threshold. Then ROI was set to surround the blood vessel and the number of pixels were calculated. Blood vessels with area of more than 10,000 μm2 (or about 100 μm in diameter) were excluded because

we are interested in vessels exclusively related with neovascularization.

Although statistical analysis could not be performed because of small number of the samples,, PD-grade reflected to the vascular flow in larger blood vessel area (Fig. 1). Larger blood vessel area may implicate more blood flow amounts and/or faster vascular flow. Therefore, high PD-grade may indicate the presence of fast vascular flow. Furthermore, it may not be useful to increase the sensitivity of PD, when we consider the number of the capillary vessels in the joint is not necessarily related with disease activity [1] . This study is limited by the fact that there was small number of target patients and that it may be difficult to distinguish between mixed image of several blood vessels and dilated blood vessel, due to blooming artifact which affects blood vessel outline.

In conclusion, we examined the relationship between PD grade and blood vessel area by using surgical specimen from joints of long standing RA. Larger blood vessel area or presumably faster capillary flow may reflect the positive PD signal in the joints of patients with long standing RA.

Compliance with Ethical Standards:

Funding:None.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964

Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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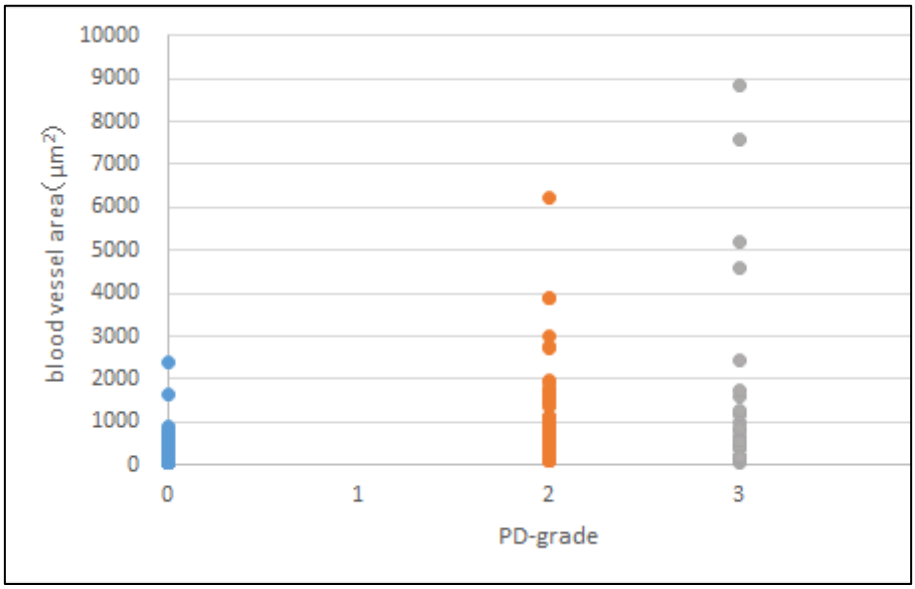


Fig. 1 Relationship between PD grade and blood vessel area

Three blood vessels with area of more than 10,000 μm2 were excluded in PD-grade 0 and 2. In joints with PD grade 0, the area of all the blood vessels (n = 64) was less than 4,000 μm2 without exception. In joints with PD of grade 2, a blood vessel had areas of more than 4,000 μm2. In joints with PD of grade 3, 4 blood vessels had areas of more than 4,000 μm2. Statistical analysis could not be performed because of small number of the samples.