Ultrasound *versus* clinical joint level assessment to predict structural damage in rheumatoid arthritis patients receiving biological therapy: a prospective study

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Little is known about the predictive value of bone deterioration, as assessed by comparing ultrasound (US) and clinical findings, particularly in patients treated with biological agents (1-4). In this prospective joint level analysis, we aimed to determine the predictive ability of US and clinical assessment for joint structural damage in rheumatoid arthritis (RA) patients receiving biologics.

Twenty-three consecutive patients with RA (median age: 51 [range: 33–80] years, 19 females, 4 males) starting treatment with biologics (tocilizumab, adalimumab, and infliximab administered to 14, 4, and 5 patients, respectively) were prospectively enrolled, and clinical joint assessments (tender, swollen, painful) and US evaluations of articular synovitis were performed at baseline and at 12, 24, and 52 weeks. We examined 230 metacarpophalangeal, 230 proximal interphalangeal, 46 wrist, and 230 metatarsophalangeal joints. The US condition was graded semiquantitatively (0–3) in the grey-scale (GS) and power Doppler (PD) mode at each assessment. Structural radiographic progression was assessed using the Genant-modified Sharp score at baseline and 52 weeks. All study participants provided informed consent. The enrolled patients showed significant improvement in the clinical disease activity index from baseline to weeks 12, 24, and 52 (mean at baseline: 12.31, week 12: 5.46, week 24: 4.31, and week 52: 3.90; $p<0.001$). Out of 736 joints, structural damage was observed in 80 (10%) joints. In order to evaluate which variables measured could predict structural damage in individual joints at 52 weeks, we focused on the odds ratio (OR) of each variable. All of the baseline clinical, GS, and PD findings showed a statistically significant OR, and the highest OR was shown in joints with PD grade ≥2 (OR: 7.09, $p<0.001$), followed by joints with PD grade ≥1 (OR: 6.51, $p<0.001$). Joints with PD grade ≥2 persisting for 12 weeks showed a higher risk of structural damage (OR: 12.38, $p<0.001$), followed by joints with PD grade ≥1, which persisted for 52 weeks (OR: 11.57, $p<0.001$). Although the clinical findings that persisted for 12 weeks showed a statistically significant OR, the 24- and 52-week persistent findings were not predictive of structural damage unlike US findings. In the combined clinical and US assessments, the 12-week persistent coupled findings of tenderness and PD grade ≥1 increased the risk for structural damage (OR: 25.52, $p<0.001$), and damage in the joints progressed when there was tenderness and the PD grade was ≥2 (Table I). The double-positive joints in clinical and PD findings showed a higher risk of damage than joints with only clinical findings at both baseline and follow-up time points. Although one potential limitation of this study is the relatively small sample size, the analysis based on the joint condition was successfully conducted, showing statistically significant differences. In conclusion, both examination techniques were predictive of structural damage; however, the baseline findings, particularly with regard to persistent findings, of the US examination were more predictive of structural damage than those of the clinical examination. To the best of our knowledge, this is the first study to show the superior predictive power of double-positive clinical and US findings of the joints for bone deterioration via coupled assessment compared to those of single examination techniques. Therefore, utilising both clinical and US examination to ensure accurate estimation of structural damage could be useful in clinical settings for precise RA progression monitoring, even in patients treated with biological agents.

This study was conducted in accordance with the 2008 Declaration of Helsinki and received ethical approval (no. 12-060) from the institutional ethics committee of Juntendo University. All study participants provided informed consent.

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Table I. Predictive ability of coupled findings.

Combined variable	OR (95% CI), *p*-value					
	Baseline		*p*-value	Baseline to 12 weeks		*p*-value
Clinical findings, no. (%) of joints						
Tender and swollen joint	4.78	(1.95–11.59)	0.001	8.38	(1.16–60.36)	0.06
Tender, swollen, and painful joint	6.57	(2.22–19.4)	0.002	4.14	(0.37–46.2)	0.292
Clinical and ultrasound findings, no. (%) of joints						
Tender and PD* grade ≥1	8.38	(3.44–20.42)	<0.001	25.52	(2.62–248.36)	0.004
Tender and PD grade ≥2	10.30	(3.63–29.24)	<0.001	∞	–	0.001
Swollen and PD grade ≥1	7.33	(3.79–14.17)	<0.001	10.39	(3.39–31.74)	<0.001
Swollen and PD grade ≥2	6.75	(3.26–13.98)	<0.001	6.85	(1.80–26.09)	0.01
Painful and PD grade ≥1	5.82	(2.98–11.38)	<0.001	6.35	(1.40–28.91)	0.031
Painful and PD grade ≥2	5.61	(2.63–11.98)	<0.001	8.38	(1.16–60.36)	0.06

*Power Doppler; OR: odds ratio; CI: confidence interval.