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Original article

Predictive value of Doppler ultrasound-detected synovitis in relation to failed tapering of biologic therapy in patients with rheumatoid arthritis

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Abstract

Objective. To investigate the predictive value of synovitis detected by Doppler US in relation to failed tapering of biologic therapy (BT) in RA patients in sustained clinical remission.

Methods. A total of 77 RA patients (52 women, 25 men) in sustained clinical remission, treated with a stable dosage of BT were prospectively recruited. BT was tapered according to an agreed strategy implemented in clinical practice (i.e. increasing the interval between doses for s.c. BT and reducing the dose for i.v. BT). BT tapering failure was assessed at 6 and 12 months. Doppler US investigation of 42 joints for the presence and grade (0–3) of B-mode synovial hypertrophy and synovial power Doppler signal (i.e. Doppler synovitis) was performed at baseline by a rheumatologist blinded to clinical and laboratory data. Hand and foot radiographs were obtained at baseline and at 12-month follow-up.

Results. Of the 77 patients, 46 (59.7%) were on s.c. BT and 31 (40.3%) on i.v. BT. At 12 months, 35 patients (45.5%) presented BT tapering failure, 23 of them (29.9% of all patients) in the first 6 months of BT tapering. In logistic regression analysis, the baseline DAS28 and the global score of Doppler synovitis were identified as independent predictors of BT tapering failure at 12 and 6 months. The presence of Doppler synovitis was the strongest predictor for BT tapering failure. No patient showed radiographic progression.

Conclusion. Our results suggest that the presence of Doppler-detected synovitis may predict BT tapering failure in RA patients in sustained clinical remission.

Key words: ultrasound, Doppler, synovitis, rheumatoid arthritis, biologic therapy.

CLINICAL SCIENCE

Rheumatology key messages

- Doppler US predicted biologic therapy tapering failure in RA patients.
- Doppler US may contribute in improving the appropriate selection for biologic therapy tapering among RA patients.

Introduction

In recent years, the high economic impact of biologic therapy (BT) on health care systems has promoted a great interest in optimizing BT by either withdrawing or tapering these drugs in RA patients in sustained clinical remission [1, 2]. Several studies have shown the capability of US to detect B-mode synovitis and synovial Doppler activity in a high percentage of RA patients in clinical remission

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treated with either synthetic or biologic DMARDs [3–7]. However, the most important capability aspect is that US-detected subclinical synovitis, mainly synovial Doppler signal, has shown predictive value in relation to both radiographic damage progression [8, 9] and disease flare or relapse [5, 9, 10].

The primary objective of this prospective observational longitudinal study was to investigate the predictive value of synovitis detected by Doppler US (DUS) in relation to failed tapering of BT at 6 and 12 months in RA patients in sustained clinical remission. The secondary objectives were as follows: to investigate the predictive value of clinical and laboratory biomarkers in relation to failed tapering of BT at 6 and 12 months in these patients; to establish the minimal joint count that should be assessed by DUS to discriminate between an RA patient with successful BT tapering and BT tapering failure at 6 and 12 months.

Methods

Patients

A total of 80 consecutive RA patients (54 women, 26 men) [11] treated with BT were prospectively recruited from the BT Unit of our centre. Inclusion criteria were the following: being in sustained clinical remission as judged by their usual consultant rheumatologist in clinical visits every 3 months in the previous 12 months and being in remission according to either the DAS in 28 joints (DAS28) criterion (i.e. DAS28 < 2.6) or the Simplified Disease Activity Index (SDAI) criterion (i.e. SDAI < 3.3) and in remission or low disease activity (i.e. DAS28 < 3.2; SDAI < 11) according to the other criterion at baseline; being in treatment with stable dosage of BT and, if administered, with stable dosage of synthetic DMARDs at least in the previous 6 months; being in treatment with $\leqslant 5$ mg/day of prednisone in the previous 6 months; having received neither NSAIDs for >1 week nor local CS injections in the previous 6 months. Patients treated with rituximab were not included.

At inclusion, patients could receive either full dosage (i.e. labelled dosage) or tapered dosage of BT according to a one-step BT tapering strategy (i.e. increase of 50% in the interval between doses for s.c. BT or reduction of 25% of the dose for i.v. BT) implemented in clinical practice in our centre before the study [12]. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee of the Hospital GU Gregorio Marañón (Madrid, Spain). Informed consent was obtained from all patients before study enrolment.

BT tapering strategy

In patients on full dosage, BT was tapered at baseline according to the BT tapering strategy previously implemented in our centre (Table 1). At 6 months, BT was tapered again in patients who had not needed BT, synthetic DMARDs or systemic CS dosage increase from baseline and were in remission according to either the DAS28 or the SDAI criterion and in remission or low disease activity according to the other criterion (Table 1). In patients with tapered dosage prior to the study, BT was tapered only at baseline according to the strategy applied to the labelled-dosage patients at 6 months.

Clinical, laboratory and radiographic assessment

Patient demographics and RA features were recorded at study entry. A standardized clinical and laboratory assessment was performed at baseline, and at 6 and 12 months by two of the investigators (I.D.L.T. and L.V.) who were not the patients' consultant rheumatologists and were not involved in therapeutic decisions except for baseline and 6-month BT tapering strategy. These investigators were blinded to the DUS findings. At each visit, patients were evaluated for disease activity according to the DAS28 and SDAI criteria. During the study period, the patients were routinely assessed by their consultant rheumatologists every 3 months and at any time in between the clinical visits in cases of RA worsening. Therapeutic decisions between the standardized assessments were taken by the patients' consultant rheumatologist, according to their clinical practice, without knowledge of the DUS findings.

Radiographs of the patients' hands and feet were obtained at baseline and at 12 months. The radiographs were read by an independent investigator (N.B.) using

Table 1 Biologic therapy tapering strategy

Biologic agent	Pre-inclusion dosage	Baseline tapering	6-month tapering
Adalimumab	40 mg/2 weeks	40 mg/21 days	40 mg/4 weeks
Etanercept	50 mg/week	50 mg/10 days	50 mg/2 weeks
Golimumab	50 mg/month	50 mg/45 days	50 mg/2 months
Abatacept	500 mg (weight $<$ 60 kg), 750 mg (weight $\geqslant$ 60 kg and $\leqslant$ 100 kg) or 1000 mg (weight $>$ 100 kg)/4 weeks	Reduction of 25% of the pre-inclusion dose	Reduction of 50% of the pre-inclusion dose
Infliximab	3–5 mg/kg/8 weeks	Reduction of 25% of the pre-inclusion dose	Reduction of 50% of the pre-inclusion dose
Tocilizumab	8 mg/kg/4 weeks	Reduction of 25% of the pre-inclusion dose	Reduction of 50% of the pre-inclusion dose

van der Heijde and colleagues' modification of the Sharp method [13] (see supplementary data, radiographic assessment section, available at *Rheumatology* Online).

DUS assessment

The patients underwent a baseline US assessment consisting of a systematic examination on B-mode and power Doppler mode of 36 joint regions (42 joints) according to a described standardized scanning technique [7, 14]. This assessment was performed by a rheumatologist experienced in musculoskeletal US (E.N.) who was unaware of the clinical, laboratory and radiographic findings and was not involved in the treatment decisions.

The following bilateral joints/joint regions were investigated for the presence of IA B-mode synovial hypertrophy (SH) and synovial power Doppler signal: glenohumeral (i.e. posterior and axillary recesses and biceps sheath), elbow (i.e. anterior and posterior recesses), wrist (i.e. radiocarpal, midcarpal and distal radioulnar joints, dorsal recesses), second through fifth MCPs (i.e. dorsal and palmar recesses), second through fifth PIPs of the hands (i.e. dorsal and palmar recesses), hip (i.e. anterior recess), knee (i.e. suprapatellar and parapatellar recesses), ankle joints (i.e. tibiotalar joint, dorsal recess and subtalar joint, medial and lateral recesses), and second through fifth MTP joints (i.e. dorsal recess). These joints were investigated for the presence and score [0–3] of IA B-mode SH and synovial power Doppler signal, according to the OMERACT definitions [15] and published scoring systems [7, 14], using a real-time scanner (Mylab 70 XVG; Esaote, Genoa, Italy) equipped with two multifrequency linear array transducers, a 6- to 18-MHz transducer for superficial areas and a 4- to 13-MHz transducer for deep areas. B-mode and power Doppler machine settings were optimized before the study and standardized for the whole study. These settings were as follows: B-mode frequency of 10–18 MHz, B-mode gain of 56–62%, Doppler frequency of 6.3–14.3 MHz, Doppler gain of 45–62%, low-wall filters and pulse repetition frequency of 500–750 Hz, depending on the depth of the anatomical area.

At each IA synovial recess, SH was scored semi-quantitatively on a scale of 0–3 (0, absent; 1, mild; 2, moderate; 3, marked). The synovial power Doppler signal was also scored on a semi-quantitative scale of 0–3 (0, no synovial power Doppler signal); 1, mild ($\leqslant$3 power Doppler signals within the SH); 2, moderate ($>$ 3 power Doppler signals in less than half of the SH); 3, marked (power Doppler signals in more than half of the SH). Each joint/joint region was scored for B-mode SH and synovial power Doppler signal on a scale from 0 to 3. These scores corresponded to the maximum score for SH and power Doppler signal, respectively, obtained from any one of the synovial sites (i.e. recess or joint) evaluated at each joint/joint region.

A global index for SH (SHI) (the sum of the SH scores obtained for each evaluated joint/joint region; 0–108) and a global index for Doppler synovitis (DSI) (the sum of synovial power Doppler signal scores obtained for each evaluated joint/joint region; 0–108) were calculated for each patient. In addition, we calculated SHI and DSI for a 12-joint DUS scoring model [14] and a wrist–MCP–ankle–MTP DUS scoring model [7]. The 12-joint DUS scoring model included bilateral elbow, wrist, second and third MCP joints, knee and ankle joints. The wrist–MCP–ankle–MTP DUS scoring model included 20 joint regions as follows: bilateral wrist, second through fifth MCP joints, ankle and second through fifth MTP joints.

BT tapering failure criteria

BT tapering failure was assessed at the 6-month and 12-month standardized assessment and was defined as: a reinstatement of pre-inclusion BT dosage or previous step dosage according to the time or an increase in synthetic DMARD dosage or systemic CS dosage $\geqslant$5 mg/day of prednisone by their usual consultant rheumatologist during the follow-up period or the presence of non-remission disease according to both DAS28 (i.e. DAS28 $\geqslant$2.6) and SDAI (i.e. SDAI $\geqslant$3.3) criteria and/or the presence of moderate or high disease activity according to either the DAS28 (i.e. DAS28 $\geqslant$ 3.2) or SDAI (i.e. SDAI $\geqslant$ 11) criterion. The time to BT tapering failure was recorded. Patients who fulfilled the second criterion of failure BT pre-inclusion dosage or previous step dosage were reinstated. Peri-articular or IA steroid injections were not considered failure but were recorded.

Statistical analysis

Statistical analysis was performed using SPSS, version 15.0 (SPSS, Chicago, IL, USA). Comparison between two independent groups was analysed using the *t*-test or the Mann–Whitney test for quantitative variables, depending on the assumption of normality, and Fisher's exact test was used for qualitative variables.

Multivariate logistic regression was used to identify (from among all baseline clinical, laboratory and DUS variables) independent predictors of BT tapering failure at 6 and 12 months. Only variables reaching a *P*-value of $<$ 0.10 in bivariate models were used in multivariate models. Forced introduction as well as forwards and backwards stepwise procedures were used for variable selection. Receiver operating characteristic curves were used to determine the best cut-off value to classify patients as BT tapering success/failure for quantitative variables retained in the final models. $P < 0.05$ was considered significant.

Results

Demographics and baseline data

The data from 77 patients [52 women, 25 men; mean (S.D., range) age, 58.2 (13.1, 25–86) years] who completed the study were analysed. Three patients dropped out of the study within 3 months after inclusion due to BT withdrawal because of infection, stroke and patient's desire, respectively. The mean (S.D., range) disease duration was 13.1 (6.8, 3–31) years. The mean (S.D., range) remission duration at baseline was 35.7 (28.4, 12–144) months. Of the 77 patients, 46 (59.7%) were on s.c. BT and 31 (40.3%) on

i.v. BT. Of these, 23 (29.9%) patients were treated with adalimumab, 21 (27.3%) with etanercept, 18 (23.4%) with infliximab, 7 (9.1%) with tocilizumab, 6 (7.8%) with abatacept and 2 (2.6%) with golimumab. At inclusion, 59 patients (76.6%) were on a labelled dosage of BT. Forty-seven patients (61%) were taking a concomitant synthetic DMARD, 80.9% of them MTX. Nine patients (11.7%) were taking oral prednisone ($\leqslant$5 mg/day).

The baseline DAS28 criterion of remission was fulfilled in 77 patients (100%), and the SDAI criterion of remission was fulfilled in 51 patients (66.2%). The mean (S.D., range) DAS28 was 1.82 (0.61, 0.49–2.58) and the mean (S.D., range) SDAI was 2.55 (2.33, 0.1–8.2). The mean (S.D., range) baseline total radiographic score was 43.0 (43.9, 2–205).

At baseline, 73 patients (94.8%) showed an SHI $>$ 0, and 26 patients (33.8%) showed a DSI $>$ 0. The mean (S.D., range) SHI was 6.36 (5.05, 0–22) and the mean (S.D., range) DSI was 1.13 (2.05, 0–11). A representative DUS images of synovitis in an RA patient in clinical remission on BT is shown in supplementary Fig. S1, available at *Rheumatology* Online.

BT tapering failure

Of the 77 patients, 35 (45.5%) [14 (30.4%) patients on s.c. BT and 21 (67.7%) patients on i.v. BT; 29 (49.2%) patients on BT full dosage at baseline and 6 (33.3%) patients on BT tapered dosage at baseline] presented BT tapering failure within the 12-month follow-up, 23 of them (29.9% of all patients) in the first 6 months of BT tapering. The patients with tapering failure during the follow-up period were on the following therapies: 5 patients (14.3%) on adalimumab, 9 (25.7%) on etanercept, 12 (34.7) on infliximab, 7 (20%) on tocilizumab and 2 (5.7%) on abatacept.

Of the 23 patients who had BT tapering failure at 6 months, in 14 (60.9%) the pre-inclusion dosage of BT had been reinstated by their usual consultant rheumatologist because of disease activity worsening at a mean (S.D., range) of 4 (1.5, 1–6) months since baseline, and 9 (39.1%) met the DAS/SDAI-determined failure criteria at the 6-month assessment. Of the 12 patients who had BT tapering failure between 6 and 12 months, in 11 (91.7%) the previous step dosage of BT had been reinstated by their usual consultant rheumatologist at a mean (S.D., range) of 10.9 (1.3, 8–12) months since baseline and 1 (8.3%) fulfilled the DAS/SDAI-determined failure criteria at the 12-month assessment. Three patients (3.9%) required an IA steroid injection during follow-up; two of them in addition fulfilled tapering failure criteria, while in one patient BT was successfully tapered at 12 months.

Comparison between patients with successful and failed BT tapering at 12 and 6 months

Table 2 displays the baseline clinical, laboratory and DUS parameters in patients with successful and failed BT tapering. Patients who presented BT tapering failure had significantly longer disease duration, a greater number of synthetic DMARDS and a higher baseline DAS28 and SDAI than patients with successful BT tapering at 6 and 12 months. All baseline Doppler variables were significantly higher in patients with BT tapering failure as compared with patients with BT tapering success at 6 and 12 months. Baseline and final radiographs were available for 62 patients (80.5%); 58 (93.5%) of them showed erosions at baseline. No patient showed radiographic progression.

Predictor factors of BT tapering failure

In logistic regression analysis, the baseline DAS28 and DSI for the 42-joint, 12-joint and wrist–MCP–ankle–MTP DUS assessments were identified as independent predictors of BT tapering failure at 6 and 12 months in both the total population and the group who received labelled-dosage BT at baseline. These variables were dichotomized using receiver operating characteristic curves. The cut-off values for baseline DAS28 and DSI that showed the highest sensitivity and specificity for BT tapering outcome were 2.2 and 0.5, respectively. Table 3 shows the odds ratios with 95% CIs for BT tapering failure for these variables in the final multivariate logistic models. The presence of Doppler synovitis was the strongest predictor for BT tapering failure in all models.

The odds and probability of BT tapering failure at 6 and 12 months for combined dichotomized baseline DAS28 and DSI in the total population and in the labelled-dosage group are shown in Table 4. Neither B-mode variables nor the remaining clinical and laboratory variables reached statistical significance in the multiple regression analysis at 6 or 12 months.

Discussion

In our study population, 45.5% of patients presented BT tapering failure at 12 months, 65.7% of them in the first 6 months of follow-up. Overall, our results seem relatively similar to (or little poorer than) those from some other studies on BT tapering [16–18]. In accordance with previously published data, we did not find radiographic structural progression at 12 months, despite clinical failure [19]. Nevertheless, longer time assessment of radiographic progression should confirm this finding.

Of particular note was that in our study, most importantly the presence of Doppler synovitis in any studied joint but also the baseline DAS28 were strongly associated with BT tapering failure at both 6 and 12 months. Recently, Iwamoto *et al*. [20] reported a significant association between disease relapse at 6 months (42.5% of patients) and the baseline power Doppler synovitis score in 42 patients with established RA in DAS28-determined remission who discontinued BT. Conversely, we did not find other predictors among demographics, RA or treatment characteristics. Our results suggested that before considering BT tapering in RA patients in sustained clinical remission, preferably with a low DAS28, a DUS assessment may be highly useful in confirming the absence of Doppler synovitis to indicate the appropriateness of patient selection for this therapeutic decision. Our results also suggested that a reduced DUS assessment might be a feasible valid option for this strategy.

Table 2 Baseline clinical, laboratory and Doppler US parameters in patients with successful and failed biologic therapy tapering at 6 and 12 months

Baseline variables	Successful BT tapering at 6 months ($n = 54$)	Failed BT tapering at 6 months ($n = 23$)	*P*-values	Successful BT tapering at 12 months ($n = 42$)	Failed BT tapering at 12 months ($n = 35$)	*P*-values
Age, mean (S.D.), years	58 (13.8)	58.6 (11.6)	0.853	56.6 (13.9)	60.1 (12)	0.247
Sex (women), *n* (%)	35 (67.3)	17 (32.7)	0.596	26 (50)	26 (50)	0.330
Disease duration, mean (S.D.), years	11.9 (6.6)	15.8 (6.8)	0.020	11.2 (6.7)	15.3 (6.4)	0.009
Duration of clinical remission, mean (S.D.), months	38.7 (31.6)	28.6 (17.4)	0.156	39.5 (34.7)	31 (17.5)	0.170
Time from symptom onset to synthetic DMARDs, mean (S.D.), months	12.8 (23.6)	23.6 (34.2)	0.114	10.5 (23.5)	22.6 (30.7)	0.060
Duration of synthetic DMARD treatment, mean (S.D.), years	11.3 (18.2)	11.3 (5.2)	0.994	9.3 (11.3)	13.7 (19.3)	0.222
Number of synthetic DMARDs, mean (S.D.)	1.8 (0.9)	2.3 (1)	0.049	1.6 (0.8)	2.3 (1)	0.003
Time from symptom onset to biologic DMARDs, mean (S.D.), months	78.2 (72.5)	95.4 (64.6)	0.331	76.6 (77.3)	91.5 (60.9)	0.357
Number of biologic DMARDs, mean (S.D.)	1.4 (0.9)	1.7 (0.9)	0.371	1.4 (0.8)	1.7 (1)	0.233
Concomitant synthetic DMARD, *n* (%)	31 (66)	16 (34)	0.445	26 (55.3)	21 (44.7)	1.000
Concomitant CS, *n* (%)	4 (44.4)	5 (55.6)	0.117	2 (22.2)	7 (77.8)	0.071
Smokers, *n* (%)	9 (75)	3 (25)	1.000	5 (41.7)	7 (58.3)	0.362
DAS28 (0–9.4), mean (S.D.)	1.68 (0.57)	2.14 (0.58)	0.002	1.66 (0.60)	2.01 (0.56)	0.011
SDAI (0–86), mean (S.D.)	2.05 (2.06)	3.74 (2.54)	0.003	1.85 (2.08)	3.4 (2.37)	0.003
Positive RF, *n* (%)	24 (63.2)	14 (36.8)	0.220	17 (44.7)	21 (55.3)	0.111
Positive ACPA, *n* (%)	38 (67.9)	18 (32.1)	0.582	28 (50)	28 (50)	0.211
SHI (0–108), mean (S.D.)	6.4 (5.4)	6.2 (4.3)	0.831	5.7 (4.7)	7.2 (5.4)	0.187
DSI (0–108), mean (S.D.)	0.4 (1.2)	1.2 (1)	0.002	0.1 (0.5)	2.3 (2.5)	<0.0005
12-joint SHI (0–36), mean (S.D.)	3.3 (2.8)	4 (3)	0.370	2.9 (2.3)	4.3 (3.3)	0.028
12-joint DSI (0–36), mean (S.D.)	0.5 (1.5)	1.8 (1.8)	0.001	0.1 (0.2)	1.9 (2.1)	<0.0005
WMAM SHI (0–60), mean (S.D.)	4.2 (4.3)	4 (3)	0.837	4 (3.9)	4.4 (4)	0.646
WMAM DSI (0–60), mean (S.D.)	0.4 (1.6)	1.9 (1.5)	<0.0005	0.1 (0.5)	1.7 (2.2)	<0.0005

DUS: Doppler US; BT: biologic therapy; SHI: global index for synovial hypertrophy; DSI: global index for Doppler synovitis; WMAM: wrist–MCP–ankle–MTP.

Table 3 Multivariate logistic models for the total population and the labelled-dosage population

BT tapering failure	Model	Included variable	All patients		Baseline labelled-dosage patients	
			OR (95% CI)	*P*-values	OR (95% CI)	*P*-values
6 months	A	DSI > 0	13.91 (3.44, 56.29)	<0.0005	21.11 (3.81, 117.10)	<0.0005
		DAS28 ⩾ 2.2	11.27 (2.79, 45.54)	0.001	11.70 (2.13, 64.30)	0.005
	B	12-joint DSI > 0	13.33 (3.28, 54.19)	<0.0005	18.11 (3.40, 96.35)	0.001
		DAS28 ⩾ 2.2	11.43 (2.85, 45.88)	0.001	11.38 (2.12, 61.10)	0.005
	C	WMAM DSI > 0	18.32 (4.39, 76.41)	<0.0005	27.08 (4.92, 149.10)	<0.0005
		DAS28 ⩾ 2.2	9.83 (2.40, 40.31)	0.002	9.17 (1.66, 50.76)	0.011
12 months	A	DSI > 0	29.92 (6.81, 131.40)	<0.0005	23.07 (5.03, 105.83)	<0.0005
		DAS28 ⩾ 2.2	5.81 (1.62, 20.93)	0.007	3.79 (0.95, 15.13)	0.059
	B	12-joint DSI > 0	42.86 (7.91, 232.34)	<0.0005	31.82 (5.67, 178.46)	<0.0005
		DAS28 ⩾ 2.2	6.25 (1.72, 22.69)	0.005	4.02 (0.99, 16.29)	0.051
	C	WMAM DSI > 0	29.32 (5.79, 148.47)	<0.0005	21.79 (4.22, 112.47)	<0.0005
		DAS28 ⩾ 2.2	4.19 (1.25, 14.04)	0.020	2.54 (0.69, 9.31)	0.159

BT: biologic therapy; DSI: global index for Doppler synovitis; WMAM: wrist–MCP–ankle–MTP; OR: odds ratios.

TABLE 4 Odds and probability of failure at 12 and 6 months for combined dichotomized baseline DAS28 and DSI

Baseline variables in all patients	Odds of BT tapering failure at 6 months	Odds of BT tapering failure at 12 months	Probability of BT tapering failure at 6 months	Probability of BT tapering failure at 12 months
DAS 28 $< 2.2 +$ DSI $= 0$	0.05	0.15	0.04	0.13
DAS 28 $< 2.2 +$ DSI > 0	0.64	4.52	0.39	0.82
DAS 28 $\geqslant 2.2 +$ DSI $= 0$	0.52	0.88	0.34	0.47
DAS 28 $\geqslant 2.2 +$ DSI > 0	7.21	26.02	0.88	0.96
Baseline variables in baseline labelled-dosage patients	**Odds of BT tapering failure at 6 months**	**Odds of BT tapering failure at 12 months**	**Probability of BT tapering failure at 6 months**	**Probability of BT tapering failure at 12 months**
DAS 28 $< 2.2 +$ DSI $= 0$	0.03	0.18	0.03	0.15
DAS 28 $< 2.2 +$ DSI > 0	0.58	4.13	0.37	0.81
DAS 28 $\geqslant 2.2 +$ DSI $= 0$	0.32	0.68	0.24	0.40
DAS 28 $\geqslant 2.2 +$ DSI > 0	6.80	15.66	0.87	0.94

BT: biologic therapy; DSI: global index for Doppler synovitis.

Some limitations in our study should be mentioned. The RA population was relatively small and very heterogeneous regarding RA characteristics and biologic agent and dosage. However, this was an observational study based on real clinical practice at our centre, where a non-evidence-based one-step tapering strategy had been previously implemented. In conclusion, we propose that DUS may contribute to improving appropriate selection for BT tapering among RA patients in sustained clinical remission. Further studies on other RA populations are warranted to confirm these results.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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