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Original article

Prospective observational study to evaluate the use of musculoskeletal ultrasonography in rheumatoid arthritis management: the ECHO study

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Abstract

Objectives. Since the creation of the Canadian Rheumatology Ultrasonography Society, an increasing number of rheumatologists has been trained in the use of musculoskeletal US (MSUS). We compared the effectiveness of MSUS to routine care (RC) as a disease management tool in patients with moderate-to-severe RA requiring a treatment change due to lack of efficacy. The predictive value of MSUS was also assessed.

Methods. This was a prospective, two-cohort, quasi-experimental study. Patients were managed either with MSUS (within the Canadian Rheumatology Ultrasonography Society) or as per RC for up to 1 year. Main outcomes included Clinical Disease Activity Index low disease activity/remission, DAS28 low disease activity/remission, MSUS scores, patient satisfaction and perception of participation in disease management.

Results. A total of 383 patients were enrolled (MSUS: $n = 171$; RC: $n = 212$). At baseline, a greater proportion of MSUS patients were treated with a biologic DMARD (50.3 *vs* 36.8%; P = 0.008) while more patients treated per RC received a non-biologic DMARD (84.2 *vs* 91.5%; P = 0.027). During follow-up, a greater number of RA treatment modifications was applied in the MSUS group compared with RC [adjusted incidence rate ratio (95% CI): 1.4 (1.1, 1.8)], including steroids, non-biologic DMARDs and biologic DMARDs. Regarding clinical and patient-reported outcomes, no remarkable differences were observed between groups. However, throughout the study, 50–80% of MSUS patients in clinical remission has a MSUS synovitis score of ≥ 1, and 37–73% an erosion score of ≥ 1. Significant associations were observed between baseline synovitis and joint erosion during follow-up.

Conclusion. MSUS assessments can be useful in detecting subclinical levels of inflammation and predicting future joint deterioration, thus allowing optimization of RA treatment and patient care.

Key words: rheumatoid arthritis, ultrasonography, diagnostic imaging, foot, hand

Rheumatology key messages

- Musculoskeletal US use did not have a significant impact on clinical outcomes compared with clinically managed patients.
- Composite disease activity measures may not fully reflect the true disease activity state.
- Musculoskeletal US can be useful in detecting subclinical inflammation levels and preventing future joint deterioration.

Introduction

Musculoskeletal US (MSUS) has emerged as a valuable tool in the assessment of patients with inflammatory joint disease including RA. It can be used to assess synovium, joint effusions, erosions, tendons, cartilage, nerves, blood vessels, muscle, skin and ligaments. Particularly attractive to rheumatologists involved in the care of patients with inflammatory arthritides is the detection of synovial thickening and fluid, cartilage thinning and increased blood flow in small vessels, as these

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elements may be used to guide therapeutic decisions, disease activity assessments, prognosis and remission.

MSUS has been compared with clinical assessment in several studies. Szkudlarek *et al*. [1] found US to be superior to clinical examination in the detection of synovitis of the MCP and PIP joints of the hands. More recently, similar superiority in the detection of subclinical synovitis by US compared with clinical examination has been demonstrated in children with JIA [2]. In a case series of 94 patients with established RA, swollen joint count, but not tender joint count, correlated well with US evidence of effusion, synovitis and power Doppler signal [3]. However, in another study, neither joint tenderness nor swelling was found to be predictive of synovial disease, shown by greyscale (GS) and power Doppler US [4].

The use of MSUS could improve diagnostic certainty and alter management decisions. In an early arthritis clinic setting, Karim *et al*. [5] observed that US assessment led to changes in the diagnosis in 53% of patients and in the management plan in 56% of patients, including alterations to steroid (43%) and DMARD (13%) management plans. Similarly, Matsos *et al*. [6] showed that US increased the rheumatologists' diagnostic confidence by increasing the certainty for synovitis (from 9.7 to 38.7%), tenosynovitis (9.7 *vs* 46.8%), erosions (1.6 *vs* 58.1%) and enthesitis (50 *vs* 83.9%).

The MSUS imaging modality is safe and portable, making it ideal for outpatient and inpatient settings, and can be used to assess many joints in multiple planes, and to demonstrate changes in disease activity and structural damage over time. MSUS is gaining popularity among rheumatologists, as increasing evidence supports the added value of a physician-performed US assessment above traditional clinical, laboratory and radiographic measures, enabling greater confidence in diagnostic and management decisions [7]. Although additional longitudinal data are required and further applications are likely to arise, MSUS may well possess the necessary attributes to facilitate best practice in inflammatory arthritis management.

With the creation of the Canadian Rheumatology Ultrasonography Society (CRUS) in 2010, MSUS was introduced into Canadian rheumatology practice and many rheumatologists were trained to use US in the diagnosis and assessment of patients with arthritis. Taking advantage of the introduction and implementation of MSUS in Canada, the current study aimed at assessing the impact of MSUS on the management of patients with RA and comparing its effectiveness with routine care (RC) as a disease management tool.

Methods

Study design

This was a prospective, two-cohort, quasi-experimental study of patients diagnosed with active moderate-to-severe RA managed either with MSUS (within CRUS) or as per RC. In order to be eligible for the study patients had to be 18 years of age or older, with active moderate-to-severe RA as per the Clinical Disease Activity Index (CDAI) definition (>10), and requiring a change in treatment due to lack of efficacy as per the judgment of the treating physician, including initiation of non-biologic or biologic DMARDs (nbDMARD or bDMARD) as well as change in nbDMARD/bDMARD type or dose. Change of treatment due to lack of tolerability, adverse events or poor compliance, as well as initiation or change in steroid dose alone, did not qualify the patient for inclusion in the study.

Patients were enrolled between December 2014 and April 2017 and were followed for 1 year with recommended assessments at baseline, and 3, 6, 9 and 12 months. In accordance with the observational nature of the study, there was no protocol-defined intervention affecting the patient management and all clinical decisions including treatment plans were according to the treating physician's judgment, the Canadian Rheumatology Association's recommendations for RA management, and in adherence to the product monographs, regulatory requirements and provincial reimbursement criteria.

The ECHO study was conducted according to the tenets of the Declaration of Helsinki. All patients provided written informed consent, and ethical approvals for participation in the study were obtained from the Research Ethics Boards of the Jewish General Hospital (REB #: #12-111), the Mount Sinai Hospital (12-0348-E), the University Health Network (13-6435-AE), the Health Research Ethics Board in St John's (#13.111), the Hamilton Integrated Research Ethics Board (#13-186), the Centre hospitalier universitaire de Sherbrooke (CHUS; #13-015), the University of Calgary (#13-0039) and a central Institutional Review Board (IRB Services, Aurora, Ontario, Canada) for non-academic sites.

Data collection

At each visit, all patients were evaluated clinically by their treating rheumatologist. Clinical assessments included the 28-joint tender and swollen counts and the physician's global assessment of patient disease activity using a visual analogue scale ranging from 0 (no arthritis activity) to 100 mm (extremely active arthritis). Serum concentrations of CRP and ESR were also measured and RA treatments were recorded. In addition to clinical data, patients from both treatment groups were asked to assess the severity of their morning stiffness, pain and global disease activity (patient global assessment) using a visual analogue scale (0–100 mm), and to complete the following questionnaires: the HAQ – Disability Index, Patient Participation in Disease Management (PAM-13), and Treatment Satisfaction Questionnaire for Medication.

All MSUS physicians were trained on the standardized administration of a 7-joint US assessment and were provided with an US interpretation template. US assessment was standardized and comprised the following 7-

joint scan in the more affected limb: wrist, MCP joints [2, 3], PIP joints [2, 3] and MTP joints [2, 5].

The following scoring conventions were used:

- A maximum total erosion score of 14 as calculated based on the presence or absence (1 or 0, respectively) of erosion [8] at dorsal, palmar and radial MCP2; at dorsal and palmer MCP3, PIP2 and PIP3; at dorsal and plantar MTP2; and at dorsal, plantar and lateral MTP5.
- A maximum GS synovitis score of 27 as calculated with B mode synovitis (scale 0–3) at dorsal, ulnar and palmar wrist; at palmar MCP2 and MCP3, and PIP2 and PIP3; and at dorsal MTP2, MTP5.
- A maximum power Doppler synovitis score of 39 as calculated with doppler signal (scale 0–3) at dorsal, ulnar and palmar wrist; at dorsal and palmar MCP2 and MCP3, and PIP2 and PIP3; and at dorsal MTP2 and MTP 5.
- A maximum overall synovitis score of 66 calculated as the sum of GS synovitis and power Doppler synovitis scores.

Outcome measures

Disease activity was assessed with the CDAI and DAS28-ESR scores. Clinical outcomes included achievement of CDAI low disease activity (LDA; CDAI $\leq$10), CDAI remission (CDAI $\leq$2.8), DAS28-ESR LDA (DAS28-ESR $\leq$3.2) and DAS28-ESR remission (DAS28-ESR $\leq$2.6).

RA treatment modifications were assessed with the overall number of changes in RA treatments as well as, more specifically, the number of changes in steroids, nbDMARDs, bDMARDs and NSAIDs used for the management of RA. Modifications in treatment included any reported changes in regard with the medications used including the initiation, switch and discontinuation of medications, and changes in doses and frequencies.

MSUS outcomes included the proportion of patients with a MSUS erosion score $\geq$1, as well as the proportions of patients with synovitis (based on GS, power Doppler or either) scores $\geq$1.

Patient satisfaction with regards to treatment effectiveness was measured with the effectiveness subscale of the Treatment Satisfaction Questionnaire for Medication. The score ranges from 0 to 100, with a higher score denoting greater satisfaction with treatment.

The patient perception of participation in disease management was assessed with the Patient Participation in Disease Management (PAM-13) questionnaire. The score ranges from 0 to 100, with a higher score indicating greater level of activation.

Statistical analysis

All analyses were performed on all enrolled patients meeting the inclusion criteria and none of the exclusion criteria.

Descriptive statistics, including the mean and S.D. for continuous variables, and frequency distributions for categorical variables, were produced. Between-group differences in patient demographics, baseline disease characteristics and baseline RA treatments were assessed for statistical significance using the χ^2 statistic or Fisher's exact test, as appropriate, for categorical parameters, and the independent Student's *t*-test for continuous parameters.

The incidence rate ratios for modifications in RA treatments per patient follow-up time during the course of the study were estimated with negative binomial regression models adjusting for age, gender, baseline disease duration, baseline DAS28-ESR, prior use of bDMARD(s) (naïve *vs* non-naïve), evidence of structural joint damage (yes *vs* no) at baseline and follow-up duration. Stratified analyses by patient's erosion status at baseline in the MSUS group were also conducted.

Achievement of clinical endpoints was compared between treatment groups using repeated measures generalized estimating equations models adjusted for the same variables as above. All MSUS parameters, including GS synovitis, power Doppler synovitis, overall synovitis and erosion scores, were assessed descriptively. Scores at each visit were compared with baseline with the paired Student's *t*-test. The association between baseline MSUS parameters and clinical endpoints over time as well as joint damage (increase in total erosion score of $\geq$1) was assessed with logistic regression adjusted for age, gender, baseline disease duration, baseline CDAI or DAS28-ESR, prior use of bDMARD (naïve *vs* non-naïve) and evidence of structural joint damage (yes *vs* no) at baseline. Finally, for each specific MSUS parameter assessed, the proportion of patients with a score $\geq$1 was compared between patients who achieved *vs* did not achieve clinical (CDAI or DAS28-ESR) remission at each time point using the χ^2 or Fisher's exact test, as appropriate.

SAS statistical software version 9.4 (SAS Institute Inc., Cary, NC, USA) was used to perform all analyses.

Results

Patient demographics, characteristics and RA treatment at baseline

A total of 383 RA patients were included in the analysis, 171 in the MSUS group and 212 in the RC group. The majority of patients (71.5%) were female and the mean (S.D.) age and disease duration was 58.7 (11.7) and 7.0 (10.0) years, respectively. The MSUS and RC groups had comparable demographics and baseline disease parameters, with the exception of a higher proportion of patients presenting evidence of structural joint damage (55.0 *vs* 38.7%), higher level of physical disability [mean (S.D.) HAQ – Disability Index score: 1.4 (0.7) *vs* 1.2 (0.7)] and lower perceived level of participation in treatment management [mean (S.D.) PAM-13 score: 61.0 (14.8) *vs* 66.9 (14.0)] in the MSUS group compared with RC (Table 1).

In terms of RA treatment history, no remarkable differences were observed between the MSUS and RC

Table 1 Patient demographics and baseline characteristics

	Group		
	MSUS ($N = 171$)	RC ($N = 212$)	*P*-value[a]
Female gender, *n* (%)	122 (71.3%)	152 (71.7%)	0.939
Age, mean (S.D.), years	58.4 (10.8)	58.9 (12.4)	0.708
Disease duration, mean (S.D.), years	6.4 (9.2)	7.5 (10.6)	0.279
Family history of RA, *n* (%)	64 (37.4%)	73 (34.4%)	0.525
Prior RA-related surgery, *n* (%)	18 (10.5%)	19 (9.0%)	0.604
Evidence of structural joint damage, *n* (%)	94 (55.0%)	82 (38.7%)	**0.002**
DAS28-ESR, mean (S.D.)	5.0 (1.2)	5.2 (1.2)	0.222
CDAI, mean (S.D.)	26.9 (12.5)	28.3 (12.0)	0.284
SDAI, mean (S.D.)	27.2 (11.7)	29.1 (12.5)	0.152
SJC28, mean (S.D.)	7.9 (5.8)	7.9 (5.1)	0.968
SJC66, mean (S.D.)	10.2 (7.5)	9.6 (6.5)	0.402
TJC28, mean (S.D.)	8.6 (6.8)	9.6 (6.4)	0.166
TJC68, mean (S.D.)	11.6 (9.4)	12.8 (9.5)	0.241
ESR, mean (S.D.), mm/h	26.4 (20.8)	25.5 (20.6)	0.710
CRP, mean (S.D.), mg/l	15.1 (23.7)	13.9 (17.5)	0.603
MDGA, mean (S.D.), $VAS_{0–100mm}$	49.2 (20.6)	51.2 (20.7)	0.334
Morning stiffness, mean (S.D.), $VAS_{0–100mm}$	55.0 (25.5)	52.5 (27.2)	0.373
Pain, mean (S.D.), $VAS_{0–100mm}$	61.3 (25.9)	57.5 (26.1)	0.174
PtGA, mean (S.D.), $VAS_{0–100mm}$	61.1 (23.8)	56.2 (25.4)	0.058
HAQ-DI, mean (S.D.)	1.4 (0.7)	1.2 (0.7)	**0.015**
PAM-13, mean (S.D.)	61.0 (14.8)	66.9 (14.0)	**<0.001**
TSQM Global Satisfaction Score, mean (S.D.)	57.9 (20.2)	61.7 (17.5)	0.065

[a]Statistically significant results are highlighted in bold. CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index; SJC: swollen joint count; TJC: tender joint count; MSUS: musculoskeletal US; RC: routine care; MDGA: physician global assessment of disease activity; VAS: visual analogue scale; PtGA: patient global assessment of disease activity; HAQ-DI: HAQ – Disability Index; PAM-13: Patient Participation in Disease Management; TSQM: Treatment Satisfaction Questionnaire for Medication.

groups, with the majority of patients having been treated with at least one nbDMARD (61.4 *vs* 57.6%) and ~15% (16.4 *vs* 14.6%) with at least one bDMARD (Table 2). At baseline, significantly more patients managed by RC had nbDMARD treatment modifications compared with the MSUS group (52.1 *vs* 79.3%; $P < 0.001$), while significantly more patients in the MSUS group experienced changes in regards with bDMARDs (MSUS *vs* RC: 45.0 *vs* 17.9%; $P < 0.001$). Including baseline treatment modifications, a higher number of patients in the MSUS group were treated at baseline with a bDMARD (50.3 *vs* 36.8%; $P = 0.008$) while patients in the RC group were more likely to be treated with an nbDMARD(s) (84.2 *vs* 91.5%; $P = 0.027$).

RA treatment modifications over time

The majority of patients had at least one modification to their RA treatment regimen during the course of the study, excluding baseline adjustments, without significant differences between groups (MSUS *vs* RC: 71.9 *vs* 75.5%; $P = 0.433$) (Table 2). However, the overall number of RA treatment modifications over time was significantly greater in the MSUS group compared with RC, with an adjusted incidence rate ratio (95% CI) over time of 1.41 (1.12, 1.79) (Table 3). This difference in the number of modifications was observed in steroids [1.73 (1.08, 2.77)], nbDMARDs [1.37 (1.06, 1.77)] and bDMARDs [1.75 (1.13, 2.71)]. In subgroup analysis, MSUS patients without erosion at baseline had a significantly higher number of overall RA treatment modifications over time compared with RC patients [1.48 (1.09, 2.02)], which involved mainly changes in steroids [2.13 (1.15, 3.95)] and bDMARDs [1.95 (1.12, 3.40)] (supplementary Table S1, available at *Rheumatology* online). Among MSUS patients with erosion at baseline, the higher number of modifications in treatment mainly involved nbDMARD modifications [1.61 (2.00, 2.17)].

Clinical outcomes

Although numerically higher in the MSUS group, no significant differences were observed in the odds of achieving CDAI remission, CDAI LDA, DAS28-ESR remission and DAS28-ESR LDA over time upon adjusting for potential confounders (Table 4).

TSQM and PAM-13

In terms of patient-reported outcomes, after adjusting for age, gender, baseline evidence of structural joint

Table 2 Description of RA treatments

	Group		
	MSUS (*N* = 171)	RC (*N* = 212)	*P*-value[a]
RA treatment history[b]			
nbDMARD, *n* (%)	105 (61.4)	122 (57.6)	0.445
bDMARD, *n* (%)	28 (16.4)	31 (14.6)	0.637
Steroid, *n* (%)	47 (27.5)	62 (29.3)	0.704
NSAID, *n* (%)	44 (25.7)	36 (17.0)	**0.036**
Narcotics, *n* (%)	3 (1.8)	4 (1.9)	0.923
Modifications to RA treatment at baseline[c]			
Any change in regards with nbDMARD, *n* (%)	89 (52.1)	168 (79.3)	**<0.001**
Switch nbDMARD, *n* (%)	15 (8.8)	11 (5.2)	0.166
Dose change, *n* (%)	17 (9.9)	31 (14.6)	0.169
Addition of another nbDMARD, *n* (%)	37 (21.6)	117 (55.2)	**<0.001**
Initiate treatment with nbDMARD, *n* (%)	26 (15.2)	17 (8.0)	**0.027**
Any change in regards with bDMARD, *n* (%)	77 (45.0)	38 (17.9)	**<0.001**
Switch bDMARD, *n* (%)	34 (19.9)	16 (7.6)	**<0.001**
Addition of bDMARD, *n* (%)	19 (11.1)	20 (9.4)	0.590
Initiate treatment with bDMARD, *n* (%)	24 (14.0)	2 (0.9)	**<0.001**
RA treatment at baseline			
nbDMARD, *n* (%)	144 (84.2)	194 (91.5)	**0.027**
bDMARD, *n* (%)	86 (50.3)	78 (36.8)	**0.008**
Steroid, *n* (%)	64 (37.4)	76 (35.9)	0.750
NSAID, *n* (%)	52 (30.4)	89 (42.0)	**0.020**
Narcotics, *n* (%)	4 (2.3)	14 (6.6)	0.050
Folic acid and others, *n* (%)	163 (95.3)	170 (80.2)	**<0.001**
Patients with ≥1 RA treatment modification over time[c] (excluding baseline)			
Any change in RA treatment, *n* (%)	123 (71.9)	160 (75.5)	0.433
Any change in steroids, *n* (%)	55 (32.2)	74 (34.9)	0.572
Any change in nbDMARDs, *n* (%)	89 (52.1)	114 (53.8)	0.736
Any change in bDMARDs, *n* (%)	54 (31.6)	50 (23.6)	0.080
Any change in NSAIDs, *n* (%)	11 (6.4)	23 (10.9)	0.131
Any change in narcotics, *n* (%)	0 (0.0)	1 (0.5)	0.999
Any change in folic acid and other treatments, *n* (%)	3 (1.8)	16 (7.6)	**0.009**

[a]Statistically significant results are highlighted in bold. [b]nbDMARDs and bDMARds at any point prior to baseline; all other treatments within 6 months prior to baseline. [c]More then one type of RA treatment medication may have been reported for a patient. MSUS: musculoskeletal US; RC: routine care; bDMARD: biologic DMARD; nbDMARD: non-biologic DMARD.

Table 3 Number of changes in RA treatment per patient over time by group

	MSUS *vs* RC	
Changes in RA treatments	IRR (95% CI)[a]	*P*-value
Any change in RA treatment	1.41 (1.12; 1.79)	**0.004**
Any change in steroids	1.73 (1.08; 2.77)	**0.023**
Any change in nbDMARDs	1.37 (1.06; 1.77)	**0.015**
Any change in bDMARDs	1.75 (1.13; 2.71)	**0.012**
Any change in NSAIDs	0.49 (0.21; 1.14)	0.097
Any change in narcotics	NC	NC
Any change in folic acid and other treatments	0.17 (0.04; 0.64)	**0.009**

[a]Based on negative binomial regression models adjusted for age, gender, baseline disease duration, baseline DAS28-ESR, baseline bDMARD use (yes *vs* no), evidence of structural joint damage (yes *vs* no) at baseline and duration of follow-up. Statistically significant results are highlighted in bold. IRR: incidence rate ratio; MSUS: musculoskeletal US; RC: routine care; NC: not calculable due to the low number of changes; nbDMARD: non-biologic DMARD; bDMARD: biologic DMARD.

Table 4 Clinical outcome achievement over time by group

	MSUS *vs* RC	
Changes in RA treatments	OR (95% CI)[a]	*P*-value
CDAI remission	1.29 (0.78, 2.11)	0.317
CDAI LDA	1.20 (0.86, 1.68)	0.281
DAS28-ESR remission	1.09 (0.75, 1.58)	0.656
DAS28-ESR LDA	1.12 (0.77, 1.65)	0.548

[a]Based on generalized estimating equations models adjusted for age, gender, baseline disease duration, baseline CDAI or DAS28-ESR, baseline bDMARD use (yes *vs* no), evidence of structural joint damage (yes *vs* no) at baseline and duration of follow-up. OR: odds ratio; CDAI: Clinical Disease Activity Index; LDA: low disease activity; MSUS: musculoskeletal US; RC: routine care.

damage, baseline disease duration, DAS28-ESR and PAM-13 scores, and bDMARD use, no statistical differences were observed over time between treatment groups in either perception of participation in disease management or satisfaction with treatment effectiveness (supplementary Fig. S1a and b, available at *Rheumatology* online).

MSUS parameters over time

The levels of MSUS parameters over time are presented in supplementary Fig. S2, available at *Rheumatology* online, showing significant improvements from baseline over time in GS synovitis, power Doppler synovitis, overall synovitis and erosion. More specifically, the mean (S.D.) GS synovitis score decreased from 5.9 (4.8) at baseline to 2.1 (2.2) at month 12 ($P < 0.001$), the power Doppler synovitis score from 6.3 (4.9) to 2.3 (2.7) ($P < 0.001$), and the overall synovitis score from 12.2 (8.6) to 4.4 (4.4). A decrease in the erosion score from baseline to 9 and 12 months was also observed, which was likely due to low reliability. When evaluating the MSUS scores by presence of clinical remission, 50 and 76.9% of MSUS patients, respectively, who achieved CDAI and DAS28-ESR remission at 3 months had a MSUS synovitis score of $\geq$1 (Fig. 1c and supplementary Fig. S3c, available at *Rheumatology* online), while 37.5 and 50% had an erosion of $\geq$1 (Fig. 1d and supplementary Fig. S3d, available at *Rheumatology* online). These detection rates among patients in remission remained stable or increased over time and were statistically comparable to those of patients not in remission at 6, 9 and 12 months.

Predictive value of MSUS

MSUS parameters at baseline were not found to be associated with achievement of CDAI remission or LDA during follow-up, although a higher score of power Doppler synovitis at baseline was associated with increased odds of DAS28-ESR remission at 9 and 12 months [odds ratio (OR) (95% CI): 1.17 (1.02, 1.33) and 1.21 (1.05, 1.39), respectively], as well as of DAS-ESR LDA at 9 months [OR (95% CI): 1.16 (1.01, 1.34)] (Table 5). Furthermore, significant associations were observed between increased power Doppler synovitis [OR (95% CI): 1.10 (1.01, 1.19)] and overall synovitis [OR (95% CI): 1.05 (1.00, 1.10)] at baseline, with increased odds for joint deterioration during follow-up.

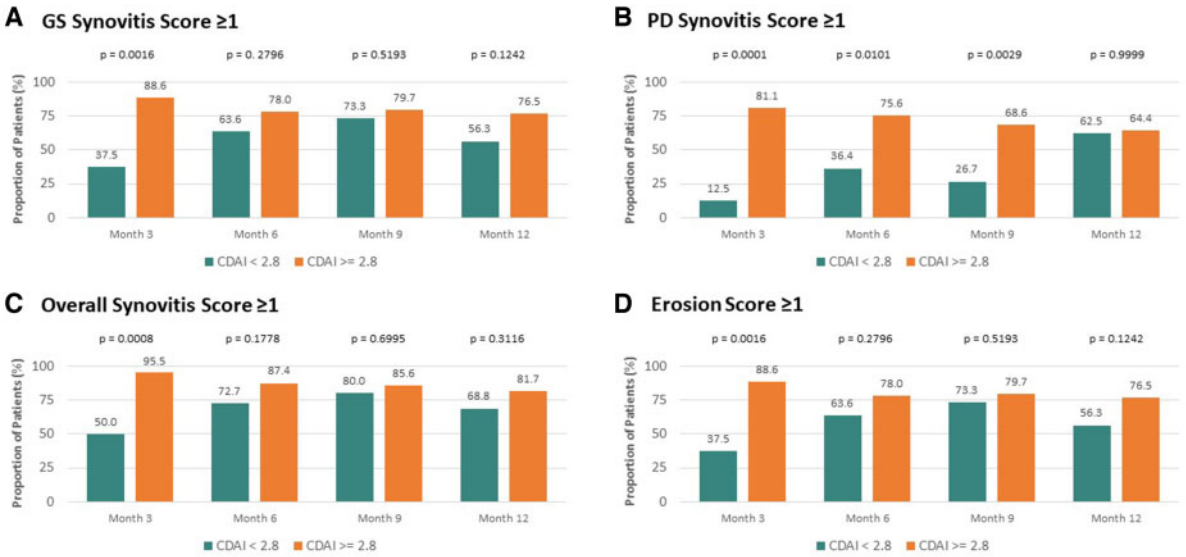
Discussion

This was an observational, prospective, two-cohort, quasi-experimental study of patients diagnosed with moderate-to-severe RA managed either with MSUS or as per RC and who were requiring a change in their RA treatment as per the judgment of the treating physician. This study aimed to assess the impact of MSUS on the management of patients with RA in Canada and to compare the effectiveness of MSUS with that of RC as a disease management tool. During the course of the study, patients in the MSUS group experienced higher rates of RA treatment modifications compared with patients treated as per RC, more specifically with regards to steroids, nbDMARDs and bDMARDs.

Overall, there were no remarkable differences between the two treatment groups with respect to achieving standard clinical outcomes, including CDAI/DAS28-ESR remission and LDA. This is in agreement with the ARCTIC and TaSER studies, which also showed that use of MSUS was not associated with better clinical outcomes but also not with radiographic outcomes [9, 10]. However, interestingly, throughout the study, 50–80% of MSUS patients in clinical remission had a MSUS synovitis score of $\geq$1 and 37–73% had an erosion score of $\geq$1. Brown *et al.* [11, 12] similarly observed structural progression occurring in RA patients despite the presence of clinical remission, and reported a significant association between the synovitis detected by MSUS at baseline and progression of joint structural deterioration over 12 months. Low agreement between clinical and imaging outcomes were also reported by Horton *et al.* [13], although using a US imaging protocol diverging from the 7-joint US assessment used in the current study. Our study results may be explained by the fact that clinical criteria of remission are not sufficiently sensitive to accurately detect clinically relevant levels of inflammation [14], indicating, as suggested by Brown *et al.* [12], that imaging assessment is necessary for the accurate evaluation of disease status and definition of 'true' remission representing patients in clinical remission with absence of synovitis. Karim *et al.* [15] also suggested that the information obtained on the presence of synovitis by US assessments is superior to clinical examination, while Nakagomi *et al.* [16] demonstrated the potential of imaging in improving RA assessment accuracy.

MSUS is a valuable point-of-care non-invasive imaging tool that can accurately evaluate IA and periarticular structures involved in rheumatic diseases [17]. GS and power Doppler have been found to be more sensitive in

FIG. 1 MSUS scores by presence of CDAI remission over time



(A) GS synovitis score ≥1; (B) PD synovitis score ≥1; (C) Overall synovitis score ≥1; (D) Erosion score ≥1. MSUS: musculoskeletal US; GS: greyscale; PD: power Doppler. Statistical significance was assessed with Chi-square statistic or Fisher's exact test, as appropriate.

TABLE 5 Association of baseline MSUS parameters with future clinical and MSUS outcomes

	Baseline MSUS parameters [OR (95% CI)]			
	GS synovitis	Power Doppler synovitis	Overall synovitis	Erosion
CDAI remission				
Month 3	0.88 (0.71, 1.09)	0.76 (0.57, 1.01)	0.88 (0.77, 1.02)	0.64 (0.33, 1.24)
Month 6	0.92 (0.78, 1.10)	0.94 (0.78, 1.13)	0.95 (0.86, 1.05)	0.99 (0.66, 1.47)
Month 9	0.97 (0.84, 1.11)	0.93 (0.80, 1.09)	0.97 (0.89, 1.05)	0.90 (0.62, 1.31)
Month 12	1.01 (0.86, 1.17)	1.01 (0.88, 1.16)	1.01 (0.92, 1.09)	1.10 (0.79, 1.53)
CDAI LDA				
Month 3	0.93 (0.85, 1.02)	0.95 (0.86, 1.04)	0.96 (0.91, 1.01)	0.87 (0.69, 1.08)
Month 6	0.95 (0.87, 1.03)	0.91 (0.83, 1.00)	0.95 (0.91, 1.00)	0.96 (0.80, 1.16)
Month 9	1.04 (0.96, 1.13)	1.10 (0.99, 1.21)	1.04 (0.99, 1.10)	1.01 (0.83, 1.22)
Month 12	1.01 (0.92, 1.10)	1.04 (0.94, 1.15)	1.02 (0.96, 1.07)	0.92 (0.75, 1.12)
DAS28-ESR remission				
Month 3	0.94 (0.83, 1.07)	1.08 (0.97, 1.22)	1.01 (0.95, 1.07)	1.21 (0.91, 1.60)
Month 6	0.93 (0.84, 1.03)	0.96 (0.85, 1.08)	0.96 (0.90, 1.03)	0.99 (0.78, 1.25)
Month 9	1.05 (0.94, 1.16)	1.17 (1.02, 1.33)*	1.06 (0.99, 1.13)	0.95 (0.74, 1.22)
Month 12	1.02 (0.9, 1.13)	1.21 (1.05, 1.39)*	1.06 (0.99, 1.13)	1.08 (0.84, 1.37)
DAS28-ESR LDA				
Month 3	0.99 (0.90, 1.10)	1.08 (0.97, 1.21)	1.02 (0.96, 1.08)	1.13 (0.87, 1.47)
Month 6	0.93 (0.85, 1.02)	0.99 (0.89, 1.10)	0.97 (0.92, 1.03)	0.98 (0.78, 1.23)
Month 9	1.05 (0.95, 1.17)	1.16 (1.01, 1.34)*	1.06 (0.99, 1.13)	0.97 (0.76, 1.25)
Month 12	0.97 (0.87, 1.08)	1.13 (0.98, 1.31)	1.02 (0.95, 1.09)	1.03 (0.80, 1.33)
Joint damage (ΔErosion ≥1)				
Any time during follow-up	1.06 (0.98, 1.14)	1.10 (1.01, 1.19)*	1.05 (1.00, 1.10)*	0.90 (0.75, 1.08)

Logistic regressions adjusted for age, gender, disease duration, CDAI or DAS28, biologic naïve (yes *vs* no) and evidence of structural joint damage (yes *vs* no) at baseline. *Indicates statistical significance ($P < 0.05$). MSUS: musculoskeletal US; OR: odds ratio; GS: greyscale CDAI: Clinical Disease Activity Index; LDA: low disease activity.

detecting synovitis than clinical examination and to be predictive of joint deterioration [18], which has been confirmed in our study.

A strength of this study is that patients were assessed as per routine clinical practice and the judgment of the treating physician, which increases the external validity of the findings. As the experience of the sonographer and the quality of the equipment used may affect the accuracy and reliability of the MSUS imaging results, prior to the study, all participating physicians completed a certification training provided by CRUS and were trained on the standardized administration of the 7-joint US assessment and interpretation. In addition, all sites used equivalent MSUS equipment. Finally, in order to minimize possible confounding by site parameters, RC sites were matched to MSUS sites with respect to geographical location and type of practice (i.e. community *vs* academic/university centre).

In conclusion, the results of the current study suggest that MSUS can be useful in the real-world setting for detecting subclinical levels of inflammation and predicting future joint deterioration, thus enabling tailoring of RA treatment and patient care. Future studies should focus on identifying patient subgroups that would benefit the most from a routine use of MSUS.

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Supplementary data

Supplementary data are available at *Rheumatology* online.

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