Subclinical inflammation and joint damage progression in patients with early RA fulfilling 2011 vs 2022 ACR/EULAR Boolean remission criteria: data from the ARCTIC study

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Remission has become an achievable goal for a large proportion of patients with rheumatoid arthritis (RA).[1] In 2022, ACR and EULAR proposed a new version of their Boolean remission criteria, allowing patients to achieve remission with a higher level of patient global assessment (PGA). In the updated version, the threshold for PGA (0–10 cm) is 2 (Boolean 2.0), compared with the original threshold of 1 (Boolean 1.0).[2 3] We aimed to investigate subclinical inflammation according to ultrasound and MRI, as well as radiographic progression, in patients with early RA fulfilling ACR/EULAR Boolean 2011 and 2022 remission criteria.

The ARCTIC trial was a multicentre, open-label, randomised controlled strategy trial conducted in Norway. Patients were 18–75 years, fulfilled the 2010 ACR/EULAR classification criteria for RA, disease-modifying anti-rheumatic drug (DMARD) naïve and had an indication for DMARD therapy when included in the trial.[4]

A structured ultrasound grey scale and power Doppler assessment of 32 joints, and evaluation of MRI synovitis, tenosynovitis, bone marrow oedema and MRI total inflammation score of dominant wrist and hand were performed at baseline, 12 and 24 months. At 12 and 24 months, patients were categorised as being in Boolean 1.0 remission or remission according to only Boolean 2.0 (ie, in Boolean 2.0 but not 1.0 remission). Linear mixed effect regression models were fit to ultrasound and MRI inflammation data, treating time as a categorical effect and with an indicator for whether a patient was in Boolean 1.0 or only 2.0 remission at the visit. Sensitivity analyses were done with log transformation of the MRI and ultrasound variables. In addition, clinical disease activity was assessed by Simplified Disease Activity Index and Disease Activity Score for comparison. We analysed joint damage progression (defined as total van der Heijde Sharp score (vdHSS) ≥1 unit per year) between 12 and 24 months according to radiographs of hands and feet, and RAMRIS MRI erosions in patients in remission at 12 months according to the two criteria.[5 6]

Of 230 patients, 105 (46%) patients fulfilled Boolean 1.0 remission criteria at 12 months, and 113 (49%) patients at 24 months. Only Boolean 2.0 remission criteria were fulfilled by 26 (11%) patients at 12 months and 15 (7%) patients at 24 months.

Low levels of ultrasound and MRI inflammation were present in patients of both groups at 12 months, and remained low at 24 months of the study, with no statistically significant differences observed between the groups (table 1).

Radiographic data have been obtained for 127 of 131 patients fulfilling either remission criteria at 12 months. Radiographic progression between 12 and 24 months developed in 42 of 103 (41%) of patients fulfilling Boolean 1.0 criteria at 12 months, in 9 of 24 (38%) fulfilling Boolean 2.0 and in 33 of 68 (49%) patients with available radiographic data not fulfilling any Boolean remission criteria. No statistically significant difference was observed among patients fulfilling Boolean 1.0 vs only 2.0 criteria (p value 0.82, Fisher's exact test). The median (IQR) change in vdHSS between 12 and 24 months was 0.5 (0.0–1.0) units/year in Boolean 1.0 group and 0.5 (0.0–1.0) in Boolean 2.0 group (p value 0.27, Wilcoxon test). The median (IQR) change in vdHSS for patients not fulfilling either of Boolean criteria was 1.0 (0.0–2.0) units/year. The median (IQR) change in MRI erosions between 12 and 24 months was 0 (0.0–0.0) units/year in both the Boolean 1.0 and 2.0 groups (p value 0.26, Wilcoxon test). Twelve patients (11%) in Boolean 1.0 remission, and two patients (13%) in only Boolean 2.0 remission had MRI erosion change >0.

Remission is a key concept in modern RA care and research. When assessing patients fulfilling ACR/EULAR Boolean 1.0 or the less stringent Boolean 2.0 remission criteria, we found no significant difference in ultrasound or MRI inflammation. Radiographic joint damage and MRI progression were low in both groups in 12–24 months period. The data support the use of the updated version of the ACR/EULAR Boolean remission criteria.

Table 1 Mean (SD) ultrasound and MRI inflammation in patients fulfilling ACR/EULAR Boolean 1.0 remission, and in patients fulfilling only ACR/EULAR Boolean 2.0 remission. Linear mixed model results (12-month and 24-month visits). SDAI and DAS values, as well as the number of patients receiving biological treatment, for comparison

	12 months		24 months			
	Boolean 1.0 remission (n=105)	Only Boolean 2.0 remission (n=26)	Boolean 1.0 remission (n=113)	Only Boolean 2.0 remission (n=15)	Adjusted difference* (95% CI)	P value
Power Doppler (ultrasound)	0.41 (1.26)	0.62 (1.75)	0.53 (1.95)	0.47 (0.74)	−0.33 (−0.85 to 0.19)	0.22
Grey scale (ultrasound)	4.17 (5.10)	6.04 (5.62)	3.74 (3.94)	4.27 (4.85)	−1.40 (−2.93 to 0.13)	0.07
MRI synovitis	3.66 (2.61)	3.92 (3.12)	4.03 (2.75)	3.33 (1.91)	0.17 (−0.66 to 1.00)	0.69
MRI tenosynovitis	1.47 (2.25)	2.08 (2.48)	1.55 (2.41)	1.27 (1.28)	−0.12 (−0.92 to 0.68)	0.77
MRI bone marrow oedema	2.34 (3.00)	2.28 (2.56)	2.08 (2.83)	2.20 (3.12)	−0.20 (−0.96 to 0.57)	0.61
MRI total inflammation score	7.47 (5.42)	8.28 (6.17)	7.66 (5.92)	6.80 (4.65)	0.16 (−1.57 to 1.89)	0.86
MRI erosions	3.11 (3.71)	3.56 (4.21)	3.22 (4.12)	3.33 (2.79)	0.17 (−0.11 to 0.45)	0.24
DAS	0.82 (0.37)	1.11 (0.55)	0.75 (0.36)	1.16 (0.42)	−0.33 (−0.45 to −0.20)	<0.001
SDAI	1.20 (0.86)	3.02 (1.02)	1.18 (0.92)	2.81 (0.61)	−1.67 (−1.97 to −1.38)	<0.001
Patients on a bDMARD†, n (%)	15 (14)	3 (12)	15 (13)	3 (20)	NA	NA

*Mean difference based on the linear mixed model with both 12-month and 24-month data.
†All bDMARDs were TNF-alfa inhibitors.
bDMARDs, biological disease-modifying antirheumatic drugs; DAS, Disease Activity Score; SDAI, Simplified Disease Activity Index.

TRANSPARENCY STATEMENT

The lead author (VM) affirms that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

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Data availability statement A de-identified patient data set can be made available to researchers upon on reasonable request. The data will only be made available after submission of a project plan outlining the reason for the request and any proposed analyses, and will have to be approved by the ARCTIC project group. Project proposals can be submitted to the corresponding author. Data sharing will have to follow appropriate regulations. The study protocol and statistical analysis plan are made available together with the paper.

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