Continual Maintenance of Remission Defined by the ACR/EULAR Criteria in Daily Practice Leads to Better Functional Outcomes in Patients with Rheumatoid Arthritis

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ABSTRACT. ***Objective.*** To evaluate longterm functional outcomes in rheumatoid arthritis (RA) based on the number of times that the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) or the 28-joint Disease Activity Score (DAS28) remission criteria were fulfilled.

Methods. Patients with RA who participated in all 6 data collections in an observational cohort from 2008 to 2010 and who fulfilled the DAS28 remission criteria at baseline were studied. Patients were classified by the number of times they fulfilled the ACR/EULAR [Boolean trial, Boolean practice, Simplified Disease Activity Index (SDAI), or Clinical Disease Activity Index (CDAI)] or DAS28 remission criteria at each collection. The OR for the Japanese version of the Health Assessment Questionnaire (J-HAQ) progression, based on the number of times each set of remission criteria was fulfilled, were calculated by logistic regression.

Results. A total of 915 patients were studied. The OR (95% CI) for J-HAQ progression were 0.54 (0.33–0.87), 0.55 (0.33–0.92), 0.48 (0.28–0.82), 0.29 (0.16–0.51), 0.24 (0.13–0.47), and 0.07 (0.03–0.15) for those fulfilling the Boolean trial remission from 1 to 6 times. This tendency was also observed for the other 4 criteria. The OR (95% CI) for J-HAQ progression in patients who achieved remission at all 6 data collections were 0.07 (0.03–0.14) for the Boolean practice, 0.10 (0.05–0.20) for the SDAI, and 0.07 (0.04–0.15) for the CDAI, whereas 0.15 (0.08-0.29) for the DAS28.

Conclusion. Continual fulfillment of any remission criteria was strongly effective in preventing patients from progression of functional disability; however, the ACR/EULAR criteria appear to be preferable. (J Rheumatol First Release December 1 2016; doi:10.3899/jrheum.160395)

Key Indexing Terms:
RHEUMATOID ARTHRITIS
REMISSION CRITERIA
FUNCTIONAL DISABILITY
DISEASE ACTIVITY

Rheumatoid arthritis (RA) is a chronic inflammatory disease that causes joint damage and leads to functional disability. Suppression of inflammation can prevent joint damage and functional disability throughout the RA disease course[1]. Remission has become a therapeutic target in the management of patients with RA[2]. Further, RA disease activity is strongly associated with functional disability[1,3]. Thus, the primary goals of current therapy in patients with RA should be the achievement of remission and the improvement of functional disability. RA disease activity is measured using several composite scores. The American College of Rheumatology (ACR) remission criteria were created in 1981[4]. The 28-joint Disease Activity Score (DAS28)[5], the Simplified Disease Activity Index (SDAI)[6], and the Clinical Disease Activity Index (CDAI)[7] defined cutoff points for remission in 2004, 2005, and 2006, respectively. Sokka, *et al* reported on different remission criteria, including the ACR definition, DAS28, CDAI, clinical remission assessed using

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H. Yamanaka has received research grants from Astellas Pharma Inc. and Bristol-Myers-Squibb.

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Accepted for publication October 25, 2016.

42 and 28 joints, patient's self-reported Routine Assessment of Patient Index Data 3, and physician's reports of no disease activity in 5845 patients with RA in 24 countries using a large cross-sectional cohort in 2008. The proportions of remissions were 8.6% for the ACR criteria, 13.8% for the SDAI, and 19.6% for the DAS28[8]. These results suggest that the achievement of DAS28 remission criteria is easier than that of other remission criteria.

DAS28 is commonly used to measure disease activity[9,10]; however, power Doppler ultrasonography (US) revealed that RA patients with SDAI remission showed less joint inflammation compared with those with DAS28 remission[11]. Further, patients with RA with CDAI remission have been shown to have a better quality of life, closer to that of the general population, compared with patients with DAS28 remission[12]. These results suggest that achievement of CDAI and SDAI remission criteria are applied to a more suppressed disease activity state than that for the DAS28 remission criteria.

New remission criteria were proposed by the ACR and the European League Against Rheumatism (EULAR) to achieve better patient outcomes in 2011[13]. The committee developed the definition of remission using clinical trial data. Achievement of remission in the short term is an important treatment goal in clinical practice. Hmamouchi, *et al* reported that the Boolean remission criteria were the most stringent and hardest to achieve of all the remission criteria, even in early RA[14]. However, the longterm clinical outcomes of patients with RA in daily practice who fulfill the new remission criteria have not been well elucidated. The new remission criteria should be validated as a meaningful remission definition in clinical practice as well as in clinical trials. If such an evaluation is performed, the new remission criteria can be adopted into clinical practice and further improve the management of RA in daily practice.

The objective of our study was to evaluate the longterm functional outcomes in patients with RA based on the number of times the ACR/EULAR or DAS28 remission criteria were fulfilled in clinical practice using an observational cohort study of patients with RA.

MATERIALS AND METHODS

Cohort database. We have established a large observational cohort of patients with RA who were treated at the Institute of Rheumatology, Tokyo Women's Medical University, beginning in October 2000[15], designated as the Institute Of Rheumatology Rheumatoid Arthritis (IORRA) cohort. All patients with RA diagnosed using the ACR classification criteria[16] were registered, and their clinical information was collected biannually (in April and October) when they visited the outpatient clinic. Clinical information consisted of 3 components: (1) physician evaluation, including the number of tender joints [tender joint count (TJC)], number of swollen joints [swollen joint count (SJC)], and visual analog scale (VAS) score of disease activity (physician-VAS); (2) patient information, including VAS for pain, VAS for general health, and disability level using the Japanese-validated version of the Health Assessment Questionnaire (J-HAQ) score[15]; and (3) patient laboratory data. Data collected from each component were integrated into a single database for analysis. The study was approved by the ethics committee of Tokyo Women's Medical University (2952R), and all patients provided written informed consent.

Design and study population. Among 7419 patients with RA who participated in the IORRA survey from April 2008 to October 2010, 1346 patients participated in all 6 IORRA data collections for this 2.5-year period. Of these, 915 patients who met the DAS28 remission criteria at baseline were selected for our present analysis. Patients were excluded if they lacked data for the DAS28, C-reactive protein (CRP), SJC, TJC, patient's global assessment (PtGA), physician-VAS, or J-HAQ score. The relationship between the fulfillment status of remission criteria and the progression of physical function was assessed during this study period. Physical function was measured by the J-HAQ score. Change in J-HAQ score (ΔJ-HAQ) was defined as the value resulting from subtraction of the October 2010 J-HAQ score from that of April 2008. Progression of J-HAQ score was defined as a ΔJ-HAQ score in 2.5 years > 0.

The 4 ACR/EULAR definitions of remission and the DAS28 remission were applied in our study. The ACR/EULAR remission criteria were defined as follows[13]: Boolean trial criteria (SJC ≤ 1, TJC ≤ 1, PtGA ≤ 1, and CRP ≤ 1), SDAI criteria ≤ 3.3, Boolean practice criteria (SJC ≤ 1, TJC ≤ 1, and PtGA ≤ 1), and CDAI criteria ≤ 2.8. The DAS28 remission criteria were defined as DAS28 < 2.6[5].

Statistical analysis. The numbers of patients, mean [standard error (SE)] ΔJ-HAQ scores, and proportions of patients with J-HAQ score progression according to the number of times each set of remission criteria was fulfilled among the 6 data collections were calculated and reported separately. A probability plot of ΔJ-HAQ score was constructed that showed the individual data for all patients who continuously achieved each set of remission criteria for 2.5 years. The association between progression of J-HAQ score and the number of times each set of remission criteria were fulfilled were analyzed using a logistic regression model by adjusting for sex, age, RA disease duration, body mass index (BMI), DAS28, rheumatoid factor (RF) level, nonsteroidal antiinflammatory drug (NSAID) use, corticosteroid use, disease-modifying antirheumatic drug (DMARD) use, and biologics use at baseline. Adjusted OR are reported with 95% CI. Subanalyses were also conducted by stratifying patients with an RA disease duration of ≤ 5, > 5 to ≤ 10, and > 10 years according to the number of times the remission criteria were fulfilled (0, 1 or 2, 3 or 4, or 5 or 6 times).

Statistical significance was defined by a p value < 0.05, and multiplicity of the test was not considered. All statistical analyses were performed using R-3.0.1 statistical software (www.cran-r.org).

RESULTS

A total of 915 patients with RA who participated in all 6 IORRA data collections for 2.5 years and who met the DAS28 remission criteria at baseline were studied. The following baseline characteristics were observed: female sex (80%), age (median 59.3 yrs, interquartile range 49.7–66.2), and RA disease duration (10.0 yrs, 6.0–16.0). The mean (SD) of DAS28, CDAI, SDAI, and J-HAQ scores were 2.1 (1.7–2.4), 1.8 (0.6–3.4), 1.9 (0.7–3.6), and 0.0 (0.0–0.4), respectively (Table 1).

J-HAQ score progression for each set of remission criteria over 2.5 years. Table 2 shows the mean (SE) ΔJ-HAQ scores of patients who achieved each set of remission criteria according to the number of times data were collected and the proportion of patients with J-HAQ score progression for each set of remission criteria. The mean (SE) ΔJ-HAQ scores for patients who continuously fulfilled the remission criteria at all 6 data collections for each set of remission criteria were

Table 1. Baseline characteristics of 915 patients with rheumatoid arthritis. Values are median (interquartile range) unless otherwise specified.

Characteristics	Values
Female, %	80.0
Age, yrs	59.3 (49.7–66.2)
Duration, yrs	10.0 (6.0–16.0)
DAS28	2.1 (1.7–2.4)
CDAI	1.8 (0.6–3.4)
SDAI	1.9 (0.7–3.6)
Boolean trial remission, %	51.4
CDAI remission, %	70.1
Boolean practice remission, %	53.4
SDAI remission, %	68.2
J-HAQ score	0.0 (0.0–0.4)
No. tender joints, out of 28	0 (0–0)
No. swollen joints, out of 28	0 (0–0)
Patient's pain assessment, mm	7 (1–16)
PtGA, mm	8 (2–18)
PGA, mm	3 (0–8)
CRP, mg/dl	0.07 (0.03–0.21)
ESR, mm/h	12.0 (7.5–18.0)
NSAID use, %	52.9
DMARD use, %	93.3
MTX use, %	63.9
MTX dose, mg/week	7.5 (6.0–10.0)
Corticosteroid use, %	40.2
Corticosteroid dose, mg/day	3.0 (2.0–5.0)
Biologics use, %	4.9

DAS28: 28-joint Disease Activity Score; CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index; J-HAQ: Japanese version of the Health Assessment Questionnaire; PtGA: patient's global assessment; PGA: physician's global assessment; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs; MTX: methotrexate.

–0.02 (0.01) for the Boolean trial criteria, –0.01 (0.01) for the SDAI, –0.01 (0.01) for the Boolean practice criteria, –0.01 (0.01) for the CDAI, and –0.01 (0.01) for DAS28 remission. The proportion of patients whose J-HAQ score progressed was 45.5% among patients who never fulfilled the Boolean trial remission criteria among patients who achieved the DAS28 remission criteria at least once. This proportion was decreased monotonically to 6.2% according to the number of data collections in which patients achieved the Boolean trial remission criteria. This phenomenon was observed for all of the remission criteria. The proportions of patients with J-HAQ score progression among patients who continuously met the remission criteria at all 6 data collections during the 2.5-year period were 6.2% for the Boolean trial criteria, 8.5% for the SDAI, 5.7% for the Boolean practice criteria, and 7.1% for the CDAI, whereas 14.2% of patients achieved DAS28 remission.

A probability plot showed ΔJ-HAQ score in patients who continuously achieved data collection 6 times for each remission criterion. Progression of J-HAQ scores was seen in more patients continuously achieving DAS28 remission criteria than in those continuously achieving the other remission criteria (Figure 1).

OR for J-HAQ score progression over 2.5 years. Table 3 shows the OR for J-HAQ score progression for the number of times remission was achieved, relative to 0 times for the 4 ACR/EULAR remission criteria and 1 time for the DAS28 remission criteria by adjusting for sex, age, RA disease duration, BMI, DAS28, RF level, NSAID use, corticosteroid use, DMARD use, and biologics use at baseline. The OR decreased as the number of times the remission criteria were fulfilled increased for all sets of criteria; for the Boolean trial criteria, the OR (95% CI) were 0.54 (0.33–0.87) for 1 time to 0.07 (0.03–0.15) for all 6 times of fulfillment relative to 0 times for fulfillment.

This phenomenon was observed for all sets of remission criteria. The corresponding OR (95% CI) for J-HAQ score progression in patients who continuously achieved remission at all 6 data collections were 0.10 (0.05–0.20) for the SDAI criteria, 0.07 (0.03–0.14) for the Boolean practice criteria, and 0.07 (0.04–0.15) for the CDAI criteria, whereas the OR (95% CI) was 0.15 (0.08–0.29) for the DAS28 remission criteria. Direct comparison among the 5 different remission criteria could not be applied using the analytical methods in

Table 2. J-HAQ score progression for each set of remission criteria over 2.5 years.

N	Boolean Trial			SDAI			Boolean Practice			CDAI			DAS28		
	All Cases	ΔJ-HAQ, Mean (SE)	J-HAQ Progression, %	All Cases	ΔJ-HAQ, Mean (SE)	J-HAQ Progression, %	All Cases	ΔJ-HAQ, Mean (SE)	J-HAQ Progression, %	All Cases	ΔJ-HAQ, Mean (SE)	J-HAQ Progression, %	All Cases	ΔJ-HAQ, Mean (SE)	J-HAQ Progression, %
0	222	0.11 (0.02)	45.5	87	0.13 (0.04)	47.1	212	0.10 (0.02)	45.3	100	0.12 (0.04)	47.0	–	–	–
1	130	0.05 (0.02)	30.8	97	0.10 (0.03)	47.4	123	0.06 (0.02)	31.7	102	0.12 (0.02)	47.1	63	0.16 (0.04)	57.1
2	112	0.05 (0.04)	29.5	112	0.06 (0.03)	33.9	111	0.04 (0.04)	28.8	107	0.02 (0.03)	29.0	70	0.18 (0.05)	40.0
3	102	0.06 (0.02)	27.5	118	0.04 (0.02)	25.4	99	0.05 (0.02)	27.3	134	0.04 (0.02)	27.6	128	0.07 (0.03)	36.7
4	102	0.01 (0.02)	19.6	125	0.10 (0.03)	32.0	100	0.04 (0.03)	24.0	117	0.10 (0.03)	31.6	161	0.08 (0.02)	34.2
5	86	0.03 (0.02)	17.4	129	0.01 (0.02)	24.0	95	0.03 (0.02)	20.0	128	0.02 (0.02)	24.2	175	0.00 (0.02)	20.6
6	161	–0.02 (0.01)	6.2	247	–0.01 (0.01)	8.5	175	–0.01 (0.01)	5.7	227	–0.01 (0.01)	7.1	318	–0.01 (0.01)	14.2

N: no. data collections in which patients fulfilled remission criteria; ΔJ-HAQ: the value resulting from the subtraction of October 2010 J-HAQ scores from April 2008 J-HAQ scores; J-HAQ: Japanese version of the Health Assessment Questionnaire; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; DAS28: 28-joint Disease Activity Score; SE: standard error.

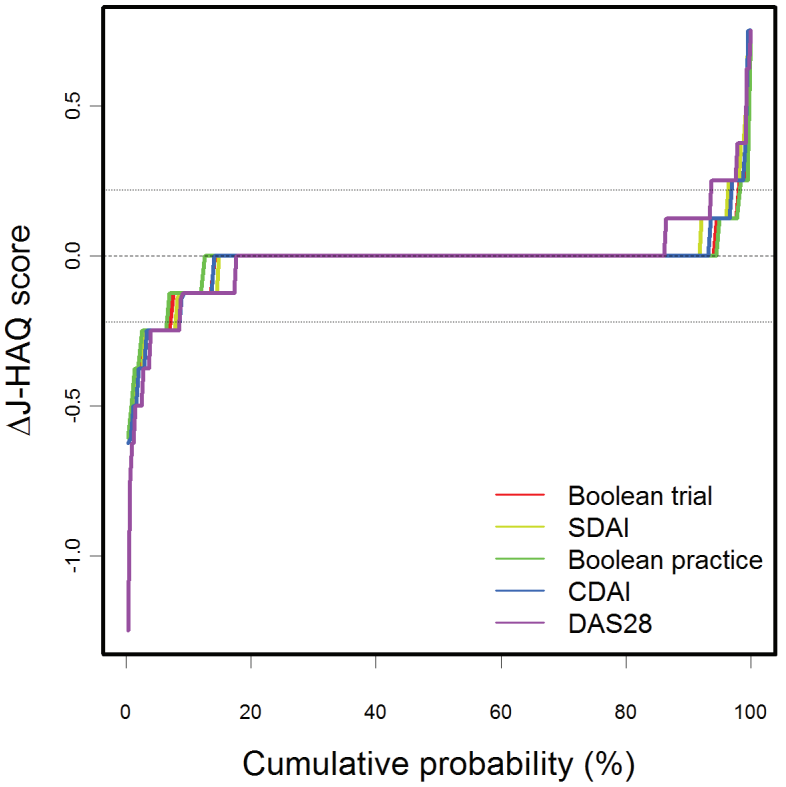

Figure 1. Progression of J-HAQ score was detected in more patients continuously achieving DAS28 remission criteria than in those continuously achieving other remission criteria. J-HAQ: Japanese version of the Health Assessment Questionnaire; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; DAS28: 28-joint Disease Activity .

our study; however, it seems that the frequency of J-HAQ score progression was lower among patients who more frequently fulfilled the ACR/EULAR remission criteria compared with the DAS28 remission criteria.

J-HAQ score progression for each set of remission criteria stratified by baseline disease duration over 2.5 years. Subanalyses were conducted by stratifying patients by baseline disease duration using logistic regression. Table 4 shows that the OR for J-HAQ score progression decreased as the number of data collections in which patients met remission criteria increased. These results were more apparent in patients with a shorter disease duration than in those with a longer disease duration when analyzed using the ACR/EULAR remission criteria. The OR (95% CI) for J-HAQ score progression in patients who fulfilled the Boolean remission criteria at 5 or 6 data collections were 0.04 (95% CI 0.01–0.18) in patients with a disease duration ≤ 5 years, 0.09 (95% CI 0.03–0.24) in patients with a disease

Table 3. The OR of the J-HAQ score progression by logistic regression model in patients fulfilling various remission criteria over 2.5 years. Values are OR (95% CI).

N	Boolean Trial	SDAI	Boolean Practice	CDAI	DAS28
0	—	—	—	—	—
1	0.54 (0.33–0.87)	0.98 (0.54–1.81)	0.59 (0.36–0.97)	0.92 (0.51–1.64)	—
2	0.55 (0.33–0.92)	0.58 (0.32–1.06)	0.51 (0.31–0.86)	0.44 (0.24–0.80)	0.58 (0.28–1.17)
3	0.48 (0.28–0.82)	0.39 (0.21–0.73)	0.50 (0.29–0.86)	0.42 (0.24–0.75)	0.48 (0.26–0.91)
4	0.29 (0.16–0.51)	0.56 (0.31–1.01)	0.40 (0.23–0.70)	0.50 (0.28–0.90)	0.46 (0.25–0.85)
5	0.24 (0.13–0.47)	0.36 (0.20–0.68)	0.29 (0.16–0.54)	0.38 (0.21–0.70)	0.23 (0.12–0.44)
6	0.07 (0.03–0.15)	0.10 (0.05–0.20)	0.07 (0.03–0.14)	0.07 (0.04–0.15)	0.15 (0.08–0.29)

J-HAQ: Japanese version of the Health Assessment Questionnaire; N: no. data collections in which patients achieved remission criteria; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; DAS28: 28-joint Disease Activity Score.

Table 4. The OR of the J-HAQ score progression by a logistic regression model stratified by baseline disease duration. Values are OR (95% CI).

Disease Duration ≤ 5 Yrs, n = 213					
N	Boolean Trial	SDAI	Boolean Practice	CDAI	DAS28
0	—	—	—	—	—
1, 2	0.79 (0.30–2.06)	0.29 (0.05–1.65)	0.90 (0.34–2.40)	0.56 (0.13–2.48)	—
3, 4	0.25 (0.08–0.76)	0.18 (0.03–1.00)	0.32 (0.11–0.97)	0.27 (0.06–1.18)	1.24 (0.41–3.77)
5, 6	0.04 (0.01–0.18)	0.02 (0.00–0.14)	0.05 (0.01–0.22)	0.04 (0.01–0.22)	0.27 (0.09–0.86)
Disease Duration > 5 Yrs to ≤ 10 Yrs, n = 296					
N	Boolean Trial	SDAI	Boolean Practice	CDAI	DAS28
0	—	—	—	—	—
1, 2	0.37 (0.17–0.79)	0.69 (0.26–1.87)	0.36 (0.16–0.77)	0.50 (0.18–1.36)	—
3, 4	0.30 (0.13–0.69)	0.34 (0.13–0.90)	0.29 (0.12–0.67)	0.31 (0.11–0.84)	0.68 (0.29–1.60)
5, 6	0.09 (0.03–0.24)	0.16 (0.06–0.46)	0.11 (0.04–0.29)	0.15 (0.05–0.43)	0.31 (0.13–0.73)
Disease Duration > 10 Yrs, n = 406					
N	Boolean Trial	SDAI	Boolean Practice	CDAI	DAS28
0	—	—	—	—	—
1, 2	0.51 (0.28–0.94)	0.98 (0.48–2.00)	0.49 (0.26–0.92)	0.74 (0.37–1.48)	—
3, 4	0.49 (0.26–0.93)	0.65 (0.31–1.37)	0.64 (0.34–1.22)	0.60 (0.30–1.20)	0.52 (0.28–0.94)
5, 6	0.19 (0.09–0.39)	0.34 (0.16–0.71)	0.18 (0.08–0.36)	0.26 (0.12–0.55)	0.23 (0.12–0.44)

J-HAQ: Japanese version of the Health Assessment Questionnaire; N: no. data collections in which patients achieved remission criteria; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; DAS28: 28-joint Disease Activity Score.

duration > 5 years to ≤ 10 years, and 0.19 (0.09–0.39) in patients with a disease duration > 10 years. This phenomenon was observed for other ACR/EULAR remission criteria, but not for the DAS28 remission criteria. These results indicate that maintenance of ACR/EULAR remission was more preventive of J-HAQ score progression in patients with a disease duration ≤ 5 years than in patients with a longer disease duration. Among patients with a disease duration ≥ 5 years, the remission rate using the ACR/EULAR remission criteria appears preferable for avoiding future physical dysfunction.

DISCUSSION

Remission is the current treatment goal for RA[17]. New remission criteria have been proposed by the ACR and EULAR as good predictors of outcome in clinical trials[13]. Herein we studied the relationship between the ACR/EULAR or DAS28 remission criteria and functional outcomes, as well as the progression over time (2.5 yrs) using an observational cohort of Japanese patients with RA in clinical practice. The results of our current study indicate that to continually fulfill any of the remission criteria is more predictive of better functional outcome. Direct comparison could not be performed given the analytical methods in our study; however, achieving the ACR/EULAR remission criteria appears to be preferable compared with achieving the DAS28 remission criteria for avoiding future progression, particularly among patients with a shorter disease duration.

Relationships between remission criteria, including ACR/EULAR, remission definitions, and outcomes, have been studied in clinical practice[18,19,20]. The ACR/EULAR remission definitions at baseline have been reported to predict better outcomes with respect to radiographic damage, functional disability, and less US-detected synovitis than achievement of DAS28 remission at baseline[18,19]. In addition, the effect of continually achieving remission criteria has been assessed. In the Brigham and Women's Hospital Rheumatoid Arthritis Sequential Study cohort, the prevalence of fulfilled remission for at least 1 year was 7.6% for the Boolean trial, 8.2% for the SDAI, and 7.6% for the CDAI, whereas 25% for the DAS28 remission; almost half of the patients with RA were treated with MTX, and one-third were treated with biologic DMARD[20]. In that cohort, the effect of continual achievement of remission demonstrated that patients who met the ACR/EULAR remission criteria more frequently were better protected from radiographic damage than those who achieved DAS28 remission for 2 years. In our study, the prevalence of fulfilled remission for 2.5 years was 17.6% for the Boolean trial, 26.9% for the SDAI, 19.1% for the Boolean practice, and 24.8% for the CDAI, while it was 34.7% for the DAS28 remission in patients who were continually followed for 2.5 years and who fulfilled the DAS28 remission at baseline. Our study showed that more frequent achievement of ACR/EULAR remission as a treatment target was more likely to prevent progression of functional disability for 2.5 years. Moreover, a similar tendency was more apparent in patients with a shorter disease duration than in those with a long disease duration when analyzed using

the ACR/EULAR remission criteria. These results supported that continual maintenance of ACR/EULAR remission criteria may be harder and may lead to better longterm outcomes.

The HAQ score has a reversible component reflecting disease activity and an irreversible component reflecting structural damage[21]. The reversible component of the HAQ score can be improved by suppression of inflammation. Remission criteria can be used as a measuring tool for RA disease activity. The present study demonstrated that progression of J-HAQ score can be prevented by more frequent achievement of ACR/EULAR remission. This result supports the view that frequent achievement of the ACR/EULAR remission criteria may be applied to more suppressed disease activity. Therefore, patients who more frequently achieved the ACR/EULAR remission criteria experienced better functional outcomes because of a larger reduction of disease activity. A larger effect of the frequency of fulfillment remission criteria was observed in patients with shorter disease durations. Additionally, because the risk of J-HAQ progression appears high even in patients who fulfilled the DAS28 remission criteria 5 or 6 times, rating remission with the ACR/EULAR remission criteria seems to be more appropriate than the DAS28 criteria. Physical dysfunction is influenced by disease activity to a greater degree in patients with a shorter disease duration than in patients with a longer disease duration[1]. Therefore, in patients with shorter disease durations, physical function may be improved by suppression of disease activity to a larger extent than that of patients with established RA. These results suggest that sustaining ACR/EULAR remission as a clinical goal before irreversible damage develops may result in better functional outcomes than the goal of sustaining DAS28 remission.

The minimally important difference (MID) in physical function is a clinically meaningful value that patients themselves notice. The MID in HAQ score in clinical practice was reported to be 0.15 for worsening[22]. In our present study, the ΔJ-HAQ of patients who achieved DAS28 remission only once or twice among the 6 observation points were 0.16 or 0.18, respectively; thus, these patients might have noticed aggravation of functional disability even though they achieved DAS28 remission. Based on the ΔJ-HAQ value, continual fulfillment even of DAS28 remission criteria is meaningful for obtaining good functional ability. Based on our present analysis, continual achievement of ACR/EULAR remission status results in better physical function.

Our study had some limitations. First, our study was conducted only in patients who could consistently visit our institute and had sufficient data over 2.5 years. Second, we did not evaluate the treatments used before and during the study period. Therefore, specific influences on the achievement of remission were not identified. Third, we could not analyze longterm functional outcomes in patients with shorter disease durations in whom HAQ might have shifted dramatically because the number of patients with disease durations < 1 year, < 2 years, and < 3 years were too few to analyze (5, 34, and 57 cases, respectively). However, even though our study has these limitations, the present results suggest that the continual fulfillment of remission criteria leads to better functional ability.

Continual achievement of any remission criteria appears to be indicative of better physical functional outcomes. Fulfillment of the ACR/EULAR remission criteria seems to be preferable for obtaining more stringent functional outcomes compared with fulfillment of the DAS28 remission criteria, particularly in patients with shorter disease durations.

ACKNOWLEDGMENT

We thank all the patients participating in this study. We appreciate all the members of the Institute of Rheumatology of the Tokyo Women's Medical University, Tokyo, Japan, for their successful management of the Institute Of Rheumatology Rheumatoid Arthritis cohort.

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