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Can Remission in Rheumatoid Arthritis Be Assessed Without Laboratory Tests or a Formal Joint Count? Possible Remission Criteria Based on a Self-report RAPID3 Score and Careful Joint Examination in the ESPOIR Cohort

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ABSTRACT. Objective. To explore 5 possible criteria for remission in rheumatoid arthritis (RA) based on a patient self-report index, the Routine Assessment of Patient Index Data (RAPID3), with a careful joint examination and possible physician global estimate (DOCGL), but without a formal joint count or laboratory test.

Methods. The ESPOIR early RA cohort of 813 French patients recruited in 2002–2005 was analyzed to identify patients in remission 6 months after enrollment, according to 2 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria: Boolean ≤ 1 for total tender joint count-28, swollen joint count-28, C-reactive protein, and patient global estimate (PATGL), and Simplified Disease Activity Index (SDAI) ≤ 3.3 . Agreement with 7 other remission criteria was analyzed — Disease Activity Score-28 (DAS28) ≤ 2.6 , Clinical Disease Activity Index (CDAI) ≤ 2.8 , and 5 candidate criteria based on RAPID3, joint examination, and DOCGL: “RAPID3R” (RAPID3 ≤ 3.0); “RAPID3R+SJ1” (RAPID3 ≤ 3.0 , ≤ 1 swollen joint); “RAPID3R+SJ1+D1” (RAPID3 ≤ 3.0 , ≤ 1 swollen joint, DOCGL ≤ 1); “RAPID3R+SJ0” (RAPID3 ≤ 3.0 , 0 swollen joints); and “RAPID3R+SJ0+D1” (RAPID3 ≤ 3.0 , 0 swollen joints, DOCGL ≤ 1), according to kappa statistics, sensitivity, and specificity. Residual global, articular, and questionnaire abnormalities according to each criteria set were analyzed.

Results. Among 813 ESPOIR patients, 720 had complete data to compare all 9 possible criteria. Substantial agreement with the Boolean criteria was seen for SDAI, CDAI, RAPID3R+SJ1, RAPID3R+SJ1+D1, RAPID3R+SJ0, and RAPID3R+SJ0+D1 (92.2%–94.7%, kappa 0.67–0.79), versus only moderate agreement for DAS28 or RAPID3R (79.9%–85.8%, kappa 0.46–0.55).

Conclusion. Remission according to CDAI and RAPID3R+SJ1, but not DAS28 or RAPID3R, is similar to that of the ACR/EULAR criteria. RAPID3 scores require a complementary careful joint examination for clinical decisions, do not preclude formal joint counts or other indices, and may be useful in busy clinical settings. (First Release Feb 1 2013; J Rheumatol 2013;40:386–93; doi:10.3899/jrheum.121059)

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RHEUMATOID ARTHRITIS REMISSION CRITERIA PATIENT QUESTIONNAIRES
PATIENT-REPORTED OUTCOMES REMISSION PHYSICIAN GLOBAL ASSESSMENT

Current criteria for remission in rheumatoid arthritis (RA) all contain a formal joint count, the most specific quanti-

tative measure of RA activity, including Boolean and Simplified Disease Activity Index (SDAI) criteria proposed

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by a committee of the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR)^{1,2}; Disease Activity Score with 28-joint count (DAS28)³; and Clinical Disease Activity Index (CDAI)⁴. However, while most visits to most rheumatologists in usual care include a careful joint examination, a formal joint count often is not performed⁵, unless required for clinical research or reimbursement.

One basis for infrequent performance of a formal joint count may involve pragmatic considerations of 90–95 s required⁶. Formal joint counts are characterized by poor measurement properties^{7,8,9,10,11,12,13}, a phenomenon that generally is ignored. Further, tender joint counts (TJC) and swollen joint counts (SJC) are no more efficient (generally less efficient) compared to patient self-report scores or global estimates to recognize differences between active versus control treatments in clinical trials involving methotrexate^{14,15}, leflunomide^{14,15}, adalimumab¹⁶, abatacept^{17,18,19}, and certolizumab²⁰.

Recognition of whether a patient has, say, 1 versus 11 swollen joints is crucial in clinical decisions in RA. However, it may be of little significance to determine whether the patient has 0 versus 1, or 10 versus 11 swollen joints in a formal joint count. Determination of 0 or 1 versus 10 or 11 swollen joints through a careful joint examination may require considerably less time than the 90–95 s required to record a formal joint count⁶, although this matter has not been studied formally. If 2 swollen joints are found within a few seconds on a careful joint examination, the absence of remission could be established without a complete formal joint count.

Routine Assessment of Patient Index Data (RAPID3) is an index of the 3 patient self-report measures in the RA Core Data Set²¹: physical function, pain, and patient global estimate of status^{6,22}. RAPID3 on a multidimensional health assessment questionnaire (MDHAQ) requires 5 seconds to score, versus > 90 seconds for DAS28 or CDAI^{6,22}. RAPID3 is correlated significantly with DAS28 and CDAI in clinical trials^{17,20,23} and clinical care^{6,22}. Categories for high, moderate, and low activity and remission have been reported to be similar (but not identical) according to RAPID3, DAS28, and CDAI^{6,22}. A recent survey of ACR members indicated that RAPID3 is scored by 29% of respondents, as many as DAS28 or any index²⁴.

It appeared of interest to determine possible criteria for remission in RA based on the RAPID3, which would not require a formal joint count but might require a careful joint examination and/or physician global estimate. We analyzed the Etude et Suivi des Polyarthrites Indifférenciées Récentes (ESPOIR) database of patients with early RA from France²⁵ for the number of patients who met criteria for remission according to Boolean and SDAI criteria. We compared patients in remission according to these 2 criteria with one another, as well as with DAS28, CDAI, and 5 candidate

RAPID3-based criteria, which may include 0 or 1 swollen joint and/or a physician global estimate ≤ 1 , as presented in this report.

MATERIALS AND METHODS

The ESPOIR cohort includes 813 patients recruited between December 2002 and March 2005, as described²⁵. Posthoc analyses were performed using Stata, version 12. The patient global estimate (PATGL) and physician global estimate (DOCGL) were converted from 0–100 mm to 0–10 cm for calculation of SDAI, CDAI, RAPID3, and RAPID3-based criteria that include DOCGL. Health Assessment Questionnaire (HAQ) physical function scores of 0–3 were converted to 0–10 to calculate RAPID3, composed of 0–10 scores for physical function, pain, and PATGL^{6,22}, and to calculate RAPID3-based criteria.

The numbers of patients who were classified as in remission 6 months after enrollment were computed according to 4 criteria requiring a formal joint count (and 3 requiring a laboratory test; Table 1): Boolean ≤ 1 for TJC28, SJC28, C-reactive protein (CRP), and PATGL, and SDAI ≤ 3.3 as proposed by the ACR/EULAR committee^{1,2}; DAS28 ≤ 2.6 ³; and CDAI ≤ 2.8 ⁴. Remission according to proposed “clinical” Boolean practice-based criteria, composed of the Boolean criteria without a laboratory test, was also computed but not presented, as results were virtually identical to those for the Boolean criteria (data not shown).

In addition, 5 possible remission criteria based on RAPID3 (Table 1), requiring neither a formal joint count nor a laboratory test, but including a careful joint examination and possible physician global estimate (DOCGL), were evaluated. Only a standard 28 tender and swollen joint count was available from the ESPOIR database, and “careful joint examination” to identify 0 or 1 swollen joint was calculated from the standard SJC28. The 5 RAPID3-based criteria (Table 1) were “RAPID3R” (RAPID3 ≤ 3.0 , as in published reports^{6,16,17,19,20,22}), and 4 more extensive descriptions: “RAPID3R+SJ1” (RAPID3 ≤ 3.0 and ≤ 1 swollen joint; if > 1 swollen joint, the criterion is not met); “RAPID3R+SJ0” (RAPID3 ≤ 3.0 and no swollen joint); “RAPID3R+SJ1+D1” (RAPID3 ≤ 3.0 and ≤ 1 swollen joint and DOCGL ≤ 1); and “RAPID3R+SJ0+D1” (RAPID3 ≤ 3.0 and no swollen joint and DOCGL ≤ 1).

Baseline values of demographic, articular, global, and self-report questionnaire measures and RA indices were analyzed according to whether patients would be in remission 6 months later. Mean values, t tests, and standard error of the mean (SE) were analyzed for normally distributed variables. Median values, Mann-Whitney tests, and 95% CI were analyzed for variables that were not normally distributed.

The number and percentage of patients classified as being in remission according to each of the 9 possible remission criteria was computed. Agreement of the ACR/EULAR Boolean and SDAI criteria with one another, as well as with each of the other 7 criteria, was assessed using kappa statistics²⁶. The strength of agreement was interpreted as kappa 0.81–1.00 = almost perfect; 0.61–0.80 = substantial; 0.41–0.60 = moderate; 0.21–0.40 = fair; 0.00–0.20 = slight; and < 0.00 = poor^{26,27}. The proportions of patients with residual abnormalities, including TJC28, SJC28, CRP, DOCGL, PATGL, or pain > 1, or HAQ function (FN) > 0.5, and specific swollen joints on the 28-joint count were computed according to each remission criteria set — other than for RAPID3R+SJ0 and RAPID3R+SJ0+D1, for which residual abnormalities were already available from RAPID3R+SJ1 and RAPID3R+SJ1+D1, and there were no residual swollen joints by definition. The sensitivity, specificity, positive predictive value, and negative predictive value (to classify patients as being in remission or not) of each of the other remission criteria, compared to the ACR/EULAR Boolean criteria as the referent, were computed using logistic regression²⁸.

RESULTS

Baseline measures in patients who would or would not be in Boolean remission 6 months later. Among the 813 ESPOIR

Table 1. Possible remission criteria to assess patients with rheumatoid arthritis (RA). In each of 9 possible remission criteria, different measures are included (from among 7 RA Core Data Set measures from physician assessment, laboratory test, and/or patient self-report), and different scoring weights are accorded each included.

Measures	Remission Criteria/Definitions								
	Boolean	SDAI	DAS28	CDAI	RAPID3R	RAPID3R +SJ1	RAPID3R +SJ1+D1	RAPID3R +SJ0	RAPID3R +SJ0+D1
Physician-assessed measures									
No. tender joints (28-joint count)	≤ 1	0–28	0.56 × sq rt (TJC28)	0–28	NI	NI	NI	NI	NI
No. swollen joints (28-joint count)	≤ 1	0–28	0.28 × sq rt (SJC28)	0–28	NI	NI	NI	NI	NI
Careful joint examination (but not a formal joint count)	NA	NA	NA	NA	NI	≤ 1	≤ 1	0	0
Physician global estimate (0–10 scale)	NI	0–10	NI	0–10	NI	NI	≤ 1	NI	≤ 1
Laboratory test									
ESR, mm/h, or CRP, mg/dl	CRP ≤ 1 mg/dl	NI	0.70 × In (ESR)	NI	NI	NI	NI	NI	NI
Patient self-report measures									
Physical function (0–3 or 0–10)	NI	NI	NI	NI	0–10	0–10	0–10	0–10	0–10
Pain (0–10)	NI	NI	NI	NI	0–10	0–10	0–10	0–10	0–10
Patient global estimate (0–100 mm or 0–10 cm)	≤ 1	0–10	0.014 × PTGL (0–100 mm)	0–10	0–10	0–10	0–10	0–10	0–10
Score ranges, remission definitions, cutpoints for disease activity categories									
Total score range	NA	0–86	0–10	0–76	0–30	NA	NA	NA	NA
Remission	All ≤ 1	≤ 3.3	≤ 2.6	≤ 2.8	≤ 3	≤ 3 + SJ ≤ 1	≤ 3 + SJ ≤ 1 + DOCGL ≤ 1	≤ 3 + SJ = 0	≤ 3 + SJ = 0 + DOCGL ≤ 1
Low/moderate/high	NA	3.3/11/26	2.6/3.2/5.1	2.8/10/22	3/6/12	NA	NA	NA	NA

SDAI: Simplified Disease Activity Index; DAS:28: Disease Activity Score-28; RAPID3: Routine Assessment of Patient Index Data; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PTGL: patient global estimate; DOCGL: physician global estimate; NA: not applicable; NI: not included (measure not included in criteria to define remission); CDAI: Clinical Disease Activity Index; SJC: swollen joint count; TJC: tender joint count.

patients, 720 had complete data to calculate the proportion in remission according to all 9 study criteria. Baseline mean or median values for demographic, articular, global, and patient self-report measures, as well as RA indices (Table 2), appear typical for a cohort of patients with early RA. Mean or median values were statistically significantly higher for physician-reported and patient-reported measures, but not for erythrocyte sedimentation rate (ESR) or CRP, in patients who would not versus patients who would be classified as in remission 6 months later (Table 2).

Patients in remission according to different criteria. Analyses of the proportions of patients who were in remission according to various RA indices (Table 3) indicated that the highest proportions were seen for DAS28, 234 (32.5%), and for RAPID3R, 181 (25.1%). Lower proportions of patients were in remission according to RAPID3R+SJ1, 131 (18.2%); CDAI, 129 (17.9%); SDAI, 123 (17.1%); for RAPID3R+SJ1+D1, 112 (15.6%); and for RAPID3R+SJ0, 107 (14.9%). The lowest proportions were seen with the Boolean definition, 93 (12.9%), and with RAPID3R+SJ0+D1, 92 (12.8%; Table 3).

Agreement of different remission criteria. Substantial agreement with the Boolean ACR/EULAR criteria was seen for SDAI, CDAI, RAPID3R+SJ1, RAPID3R+SJ0, RAPID3R+SJ1+D1, and RAPID3R+SJ0+D1 criteria

(92.2%–94.7%, kappa 0.67–0.79), particularly SDAI, CDAI, RAPID3R+SJ1, RAPID3R+SJ0, and RAPID3R+SJ1+D1 (kappa 0.73–0.79; Table 3). Only moderate agreement with the Boolean criteria was seen for DAS28 and RAPID3R criteria (79.9%–85.8%, kappa 0.46–0.55), which are less stringent (Table 3). Results for level of agreement and kappa values compared to other remission criteria were quite similar for the SDAI (Table 3) and for the proposed “clinical” Boolean practice-based criteria (data not shown).

Residual abnormalities according to different remission criteria. Analyses of residual abnormal values of TJC28, SJC28, CRP, DOCGL, PATGL, or pain > 1, and HAQ-physical function > 0.5, were performed according to 7 remission criteria (all except RAPID3R+SJ0 and RAPID3R+SJ0+D1, as noted above; Table 4). More than 1 tender joint was seen in 3% of patients who met SDAI or CDAI remission criteria, 11% for DAS28 criteria, 24% for RAPID3R criteria, and 15%–16% for RAPID3R+SJ1 and RAPID3R+SJ1+D1. By definition, no patient had more than 1 swollen joint who met Boolean, RAPID3R+SJ1, RAPID3R+SJ1+D1, RAPID3R+SJ0, or RAPID3R+SJ0+D1 criteria for remission. However, 2% of patients who met the CDAI and SDAI remission criteria had more than 1 swollen joint, as did 16% for the DAS28 and 27% for the RAPID3R remission criteria. Seventeen patients (17%) who met

Table 2. Mean (median) values of demographic, articular, global, self-report questionnaire, and indices of 720 patients from the ESPOIR cohort at baseline and according to whether patients met ACR/EULAR Boolean criteria for remission 6 months after baseline. Data were analyzed according to mean values and t test for normally distributed variables, and median values and Mann-Whitney test for variables that were not normally distributed.

Variables	Baseline, All Patients	Baseline Status of Patients in Remission/Not in Remission 6 Months Later, According to Boolean Remission Criteria		p
		Remission	Not Remission	
No. patients	720	93	627	NA
Age, yrs, mean (\pm SE)	48.2 (12.4)	44.9 (12.7)	48.7 (12.3)	0.007
Sex, % female	76.2	80.6	75.6	0.29
Disease duration, mo, median (IQR)	4.8 (2.9–7.0)	4.0 (2.5–6.1)	4.9 (3.0–7.1)	0.09
Swollen joint counts (0–28), median (IQR)	6 (3–10)	4 (2–10)	6 (3–10)	0.013
Tender joint counts (0–28), median (IQR)	6 (3–12)	4 (2–8)	7 (3–13)	< 0.001
Physician global (0–100), mean (\pm SE)	50.8 (22.2)	44.0 (22.9)	51.8 (21.9)	0.0015
ESR, mm/h, median (IQR)	22 (12–38)	19 (12–35)	22 (12–39)	0.55
CRP, mg/l, median (IQR)	0.9 (0.5–2.5)	0.9 (0.3–2)	0.9 (0.5–2.5)	0.247
HAQ (0–3 scale), median (IQR)	0.875 (0.375–1.375)	0.625 (0.25–1.25)	0.875 (0.375–1.5)	0.011
VAS pain (0–100), mean (IQR)	46.0 (22.2)	36.9 (21.2)	47.4 (22.1)	< 0.0001
Patient global (0–100), median (IQR)	60 (45–80)	54.5 (31.5–75.5)	65.5 (47–80)	0.016
DAS28 (0–10), mean (\pm SE)	5.1 (1.3)	4.7 (1.2)	5.2 (1.2)	0.0005
SDAI (0–86), mean (\pm SE)	29.2 (14.4)	24.3 (14.6)	29.9 (14.2)	0.0005
CDAI (0–76), mean (\pm SE)	26.9 (13.4)	22.5 (14.0)	27.5 (13.2)	0.0007
RAPID3 (0–30), mean (\pm SE)	13.8 (5.7)	11.7 (5.8)	14.1 (5.6)	0.0002

IQR: interquartile range; SDAI: Simplified Disease Activity Index; DAS28: Disease Activity Score-28; RAPID3: Routine Assessment of Patient Index Data; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; VAS: visual analog scale; ACR: American College of Rheumatology; EULAR: European League Against Rheumatism; HAQ: Health Assessment Questionnaire; CDAI: Clinical Disease Activity Index; NA: not applicable.

Table 3. Comparison of ACR/EULAR Boolean remission criteria with 8 other criteria according to rheumatoid arthritis (RA) indices in 720 RA patients in the ESPOIR cohort (all $p < 0.001$).

Indices	In Remission According to Index*	Boolean Criteria (ACR/EULAR)				Kappa (95% CI)	SDAI Criteria (ACR/EULAR)		
		93 (12.9%)* Remission (R) R**	N**	627 (87.1%)* Non-Remission (N) R**	N**		Agreement, %	Kappa (95% CI)	
SDAI (%)	123 (17.1)	89 (95.7)	4 (4.3)	34 (5.4)	593 (94.6)	94.7	0.79 (0.73–0.86)	NA	NA
DAS28 (%)	234 (32.5)	91 (97.8)	2 (2.2)	143 (22.8)	484 (77.2)	79.9	0.46 (0.39–0.52)	94.7	0.79 (0.73–0.86)
CDAI (%)	129 (17.9)	88 (94.6)	5 (5.4)	41 (6.5)	586 (93.5)	93.6	0.76 (0.69–0.82)	98.6	0.95 (0.92–0.98)
RAPID3R (%)	181 (25.1)	86 (92.5)	7 (7.5)	95 (15.2)	532 (84.8)	85.8	0.55 (0.48–0.62)	85.6	0.57 (0.50–0.64)
RAPID3R+SJ1 (%)	131 (18.2)	86 (92.5)	7 (7.5)	45 (7.2)	582 (92.8)	92.8	0.73 (0.66–0.80)	91.6	0.71 (0.64–0.78)
RAPID3R+SJ1+D1 (%)	112 (15.6)	80 (86.0)	13 (14.0)	32 (5.1)	595 (94.9)	93.7	0.74 (0.67–0.81)	92.1	0.71 (0.64–0.78)
RAPID3R+SJ0 (%)	107 (14.9)	72 (77.4)	21 (22.6)	35 (5.6)	592 (94.4)	92.2	0.67 (0.60–0.75)	91.7	0.69 (0.62–0.76)
RAPID3R+SJ0+D1 (%)	92 (12.8)	68 (73.1)	25 (26.9)	24 (3.8)	603 (96.2)	93.2	0.70 (0.61–0.78)	91.8	0.68 (0.60–0.75)

* Percentage of 720 patients. ** Percentage of 93 patients in remission by Boolean criteria. *** Percentage of 627 patients not in remission by Boolean criteria. SDAI: Simplified Disease Activity index; CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score-28; RAPID3: Routine Assessment of Patient Index Data; ACR: American College of Rheumatology; EULAR: European League Against Rheumatism.

Boolean or RAPID3R+SJ1 remission criteria had 1 (rather than 0) swollen joint. DOGCL scores were > 1 in 7% of patients who met Boolean criteria, 8% for CDAI and SDAI, 14% for RAPID3R+SJ1, 23% for RAPID3R, and 37% for

DAS28, but ≤ 1 for RAPID3R+SJ1+D1 and RAPID3R+SJ0+D1 (by definition). CRP > 1 was seen in < 8% of patients classified as in remission according to all criteria (Table 4).

Table 4. Number (%) of 720 patients in the ESPOIR early arthritis cohort who were in remission according to each of 7 criteria, and number (%) who were in remission and had residual abnormalities of specific measures or joints.

N (% of all pts)	Boolean 93 (12.9)	SDAI \leq 3.3 123 (17.1)	DAS28 \leq 2.6 234 (32.5)	CDAI \leq 2.8 129 (17.9)	RAPID3R \leq 3 181 (25.1)	RAPID3R + SJ1 131 (18.2)	RAPID3 + SJ1+D1 112 (15.6)
Measure: no. (%) patients in remission by each description with residual symptoms							
TJC28 > 1	0 (0)	4 (3)	26 (11)	4 (3)	46 (24)	22 (16)	18 (15)
SJC28 > 1	0 (0)	3 (2)	38 (16)	3 (2)	53 (27)	0 (0)	0 (0)
CRP > 1	0 (0)	4 (3)	14 (6)	10 (7)	14 (8)	8 (6)	7 (6)
DOCGL > 1	7 (7)	10 (8)	90 (37)	11 (8)	44 (23)	20 (14)	0 (0)
PATGL > 1	0 (0)	24 (19)	117 (49)	29 (21)	40 (21)	25 (18)	13 (11)
Pain > 1	15 (16)	29 (23)	100 (46)	29 (21)	33 (17)	19 (13)	14 (12)
HAQ-FN > 0.5	5 (5)	12 (9)	29 (12)	13 (9)	3 (1)	3 (2)	3 (2)
Swollen joint counts: no. (%) patients in remission by each description with residual swollen joints							
Knees \geq 1	0 (0)	0 (0)	7 (3)	1 (1)	9 (4)	2 (1.5)	1 (1)
Shoulders \geq 1	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Elbows \geq 1	0 (0)	0 (0)	5 (2)	0 (0)	2 (1)	0 (0)	0 (0)
Wrists \geq 1	5 (5)	5 (4)	19 (8)	5 (4)	22 (11)	6 (4)	6 (5)
MCP \geq 1	9 (9)	11 (9)	46 (21)	10 (7)	52 (27)	13 (9)	10 (8)
PIP \geq 1	3 (3)	5 (5)	24 (11)	5 (4)	14 (19)	4 (3)	4 (3)

CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity index; DAS28: Disease Activity Score-28; RAPID3: Routine Assessment of Patient Index Data; TJC: tender joint count; SJC: swollen joint count; CRP: C-reactive protein; PATGL: patient global estimate; DOCGL: physician global estimate; HAQ-FN: Health Assessment Questionnaire-Function; MCP: metacarpophalangeal; PIP: proximal interphalangeal.

HAQ physical function scores > 0.5 (on a scale of 0–3) were seen in 1%–3% of patients in remission according to RAPID3-based indices, 5% for Boolean criteria, and 9%–12% for DAS28, CDAI and SDAI. Pain scores > 1 were seen in 12%–23% for all criteria, other than 46% for DAS28. Patient global estimate (PATGL) > 1 was seen in 0% for Boolean (by definition); 11% for RAPID3R+SJ0+D1; 18%–21% for CDAI, SDAI, RAPID3R, RAPID3R+SJ1, and RAPID3R+SJ1+DI; and 49% for DAS28 (Table 4).

Analysis of specific joints involved on a 28-joint count indicated no swollen joints in patients classified as in remission by RAPID3R+SJ0 or RAPID3R+SJ0+D1, by definition. Knees were not involved in any patients classified as in remission by Boolean and SDAI criteria, but were involved in 1% for CDAI, RAPID3R+SJ1, and

RAPID3R+SJ1+D1; 3% for DAS28; and 4% for RAPID3R. Shoulders and elbows were involved in < 2% of patients. Wrists were involved in < 6%, metacarpophalangeal (MCP) joints in < 9%, and proximal interphalangeal (PIP) joints in < 5% for all criteria, except for DAS28 (8%, 21%, and 11%, respectively) and RAPID3R (11%, 27%, 19%). Most residual joint involvement involved MCP or PIP joints (Table 4).

Sensitivity and specificity of different remission criteria versus Boolean criteria. Analyses of the sensitivity and specificity of the various remission criteria compared to Boolean criteria (Table 5) indicated sensitivities of 92.5%–95.7% for CDAI, SDAI, RAPID3R, and RAPID3R+SJ1, lower levels of 86% by adding DOCGL \leq 1, and still lower levels of 73.1%–77.4% by specifying no swollen joints. Specificities compared to Boolean criteria were

Table 5. Sensitivity, specificity, positive predictive value, and negative predictive value of each of 8 possible other criteria for remission compared to ACR/EULAR Boolean criteria as the referent.

Possible Remission Criteria	Sensitivity, %	Specificity, %	Positive Predictive Value, %	Negative Predictive Value, %
SDAI	95.7	94.6	72.4	99.3
DAS28	97.8	77.2	38.9	67.2
CDAI	94.6	93.5	68.2	99.1
RAPID3R	92.5	84.8	47.5	86.8
RAPID3R+SJ1	92.5	92.8	65.6	98.8
RAPID3R+SJ1+D1	86.0	94.9	71.4	97.9
RAPID3R+SJ0	77.4	94.4	67.3	96.6
RAPID3R+SJ0+D1	73.1	96.2	73.9	96.0

CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity index; DAS28: Disease Activity Score-28; RAPID3: Routine Assessment of Patient Index Data; ACR: American College of Rheumatology; EULAR: European League Against Rheumatism.

92.8%–96.2% for all criteria other than DAS28 (77%) and RAPID3R (85%). Positive predictive values ranged from 65.6% to 72%, and negative predictive values were > 96%, for all criteria other than DAS28 and RAPID3R (Table 5).

DISCUSSION

The concept of remission in RA has proven complex, in part as no single gold standard quantitative measure is applicable to all individual patients to indicate clinical status²⁹ or remission^{1,2,30}. Further, many patients with recent-onset disease who meet criteria for RA experience spontaneous remission, as seen in early epidemiologic studies^{31,32} and more recent reports from early arthritis clinics^{30,33,34}. Finally, remission status in established RA requires continuing medications and often is temporary^{35,36}.

No set of criteria for remission in RA will give results identical to those of another criteria set^{1,2,30}. The high kappa values seen in our study between Boolean criteria and SDAI, CDAI, and even DAS28 might be anticipated, because 3 of 4 most-included measures are identical, albeit with complex calculations for DAS28 and simple criteria for Boolean remission. The high kappa values seen between Boolean criteria and RAPID3-based indices might be less expected, because only 1 or 2 measures found in the RAPID3-based criteria — patient estimate of global status and 1 or zero swollen joints — are found in the Boolean criteria, whereas scores for physical function and pain (also included in RAPID3) are not found in the Boolean criteria.

The ACR/EULAR committee that developed the Boolean and SDAI remission criteria did not consider criteria that did not include a formal tender joint count, swollen joint count, and CRP³⁷. Rheumatologists have been taught traditionally that a formal joint count should be included at all visits of patients with RA. However, most visits to most rheumatologists for usual care have not included a formal joint count^{5,24}, unless required for clinical research or reimbursement. A recent survey of ACR members indicated that RAPID3 is scored by 29% of respondents, as many as DAS28 or any index²⁴.

The joint count remains the most specific measure of clinical activity in patients with RA. However, the most specific measure is not necessarily the most sensitive or informative measure. Pragmatic limitations are seen to a joint count, including time consumption, with 90–95 s required⁶ for even a 28-joint count, time that often might preferably be spent in doctor-patient communication about concerns of either. This limitation may be overcome by a metrologist who performs the joint count before the patient sees the doctor. However, a metrologist is unavailable in many (if not most) rheumatology settings, and is unlikely to become more widely available, particularly in the current economic climate.

Even if all pragmatic limitations could be eliminated, several observations suggest that MDHAQ/RAPID3

presents a number of measurement advantages. Considerable measurement error and variation have been reported for joint counts^{7,8,9,10,11,12,13}, and the same observer is required in clinical trials and other clinical research at all timepoints. In contrast, the same observer (the patient) completes self-report questionnaires, by definition. Formal TJC and SJC or DAS28 or CDAI are no more likely to distinguish active from control treatment in clinical trials than a patient questionnaire or RAPID3 or global measures^{14,15,16,17,18,19,20}. RAPID3 levels for high, moderate, and low disease severity and remission are similar to those for DAS28 and CDAI¹⁹, suggesting that RAPID3 can be used effectively for treat-to-target in RA³⁸. Severe outcomes of RA such as work disability^{39,40,41,42,43}, costs⁴⁴, and premature death^{45,46,47,48,49,50} are predicted at far more significant levels by patient self-report scores for physical function than by joint counts, laboratory tests, or radiographs. Further, MDHAQ/ RAPID3 is informative in all rheumatic diseases⁵¹.

Limitations to patient self-report also are seen, including the need to translate questionnaires into many languages, and cultural differences in interpretation of pain, fatigue, and other symptoms in different ethnic groups⁵². The capacity of HAQ physical function scores to document clinical improvement is limited in part by irreversible joint damage⁵³, although joint counts and global scores also are less likely to document clinical improvement in the presence of joint damage (Pincus, unpublished data). Evidence that HAQ physical function scores are as reversible as other RA Core Data Set measures is seen in similar relative efficiencies compared to joint counts and global estimates in clinical trials, even in patients with longstanding RA^{14,15,16,17,18,19,20}.

This study has a number of limitations. First, only a single cohort was analyzed, and different results might be seen in other cohorts, as in the deliberations of the ACR/EULAR committee that established the Boolean definition^{1,2}. Second, the estimates of 0 or 1 swollen joint were based on a formal joint count, and prospective studies are needed to determine whether a “careful joint examination” would give similar results without a formal 28-joint count, and with possible inclusion of joints currently excluded from the 28-joint count. Third, these analyses were posthoc, and prospective use of different criteria would be required to estimate their value in clinical care. Fourth, joint counts and DOGGL were performed by many different investigators. Fifth, other possible definitions that include RAPID3 might be considered. Sixth, limitations of self-report are noted above.

Nonetheless, RAPID3 may present a number of additional advantages for rheumatologists in usual care, particularly when the receptionist presents a questionnaire to the patient to complete before seeing the doctor as part of the infrastructure of care^{54,55}. The patient does almost all the work and there is no interference with patient flow.

MDHAQ/RAPID3 helps prepare the patient for the visit to improve doctor communication through an “agenda” or “road map” available before the encounter⁵⁶. Availability of an MDHAQ — with scores for physical function, pain, patient global estimate, fatigue, self-report RADAI joint count, review of systems, and recent medical history — prior to seeing the patient provides an overview in 10–15 s of doctor time while asking no more than 10–15 min from the patient⁵⁶. Scoring the MDHAQ/RAPID3 involves about 5 s compared to more than 90 s for a joint count and almost 2 min for CDAI or SDAI⁶.

The RAPID3-based criteria set most similar to the Boolean and SDAI criteria for remission is RAPID3R+SJ1, which also appears to be the simplest to perform in clinical settings. Proposed RAPID3-based criteria that include DOGGL and/or no swollen joint appear in some ways to be more stringent than the Boolean criteria — addition of DOGGL excludes 7% of patients who meet Boolean criteria, and addition of “no swollen joint” excludes 17% of patients in remission according to Boolean criteria. However, RAPID3R+SJ1+D1 criteria also include 18 patients (15%) with TJC > 1 who would not be in remission by the Boolean criteria. Further research is needed to determine prospectively whether remission in RA might be identified through RAPID3-based criteria with a careful joint examination but not a formal joint count, and optimal measures for such criteria.

A PATGL is required for Boolean, SDAI, CDAI, and DAS28 criteria, so the patient must be given either a sheet of paper or an electronic format — MDHAQ/RAPID3 provides far more information on only 2 sides of 1 sheet of paper. Completion of an MDHAQ by the patient, and scoring of RAPID3 by the doctor, does not prevent a rheumatologist from performing a formal joint count or scoring an additional index — ironically, having all the data from MDHAQ available can provide the rheumatologist with more time for a formal joint count. Rheumatologists might consider use of MDHAQ/RAPID3 in the infrastructure of usual clinical care, for an easily assessed estimate of remission in all patients with RA.

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