# Prediction of Remission in a French Early Arthritis Cohort by RAPID3 and other Core Data Set Measures, but Not by the Absence of Rheumatoid Factor, Anticitrullinated Protein Antibodies, or Radiographic Erosions

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***ABSTRACT.*** ***Objective.*** To identify baseline variables that predict remission according to different criteria in rheumatoid arthritis (RA) in a comprehensive French ESPOIR early arthritis database.

***Methods.*** Individual variables and indices at baseline were analyzed in 664 patients for capacity to predict remission either 6 or 12 months later according to 4 criteria that require a formal joint count: the American College of Rheumatology/European League Against Rheumatism Boolean criteria, the Simplified Disease Activity Index, the Clinical Disease Activity Index, and the 28-joint Disease Activity Score; and 2 remission criteria that do not require a formal joint count: the Routine Assessment of Patient Index Data 3 (RAPID3) and the RAPID3 ≤ 3 + swollen joint, using univariate and multivariate logistic regressions.

***Results.*** Remission was predicted significantly 6 and/or 12 months later in 26.8%–51.4% of patients, according to all 6 criteria by younger age, low index scores, and better status for the 6/7 clinical RA core dataset measures: tender joint count, swollen joint count (SJC), physician's global estimate, patient self-report Health Assessment Questionnaire (HAQ) physical function, pain, and patient's global estimate. Remission was not predicted by the absence of "poor prognosis RA" indicators, rheumatoid factor (RF), anticitrullinated protein antibodies (ACPA), or radiographic erosions. In multivariate regressions that included only 3 variables, low HAQ function predicted remission by all criteria as effectively as SJC, erythrocyte sedimentation rate, or C-reactive protein.

***Conclusion.*** Younger age and 6 core dataset clinical measures, but not the absence of traditional "poor prognosis RA" indicators, RF, ACPA, or radiographic erosions, predicted remission according to 6 criteria, including 2 without a formal joint count. (J Rheumatol First Release April 15 2016; doi:10.3899/jrheum.141586)

*Key Indexing Terms:*
RHEUMATOID ARTHRITIS REMISSION CRITERIA RAPID3 ESPOIR

An American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) expert committee designated 2 criterion sets for remission in rheumatoid arthritis (RA): the Boolean and the Simplified Disease Activity Index (SDAI) < 3.3, based on a decision that remission criteria should include a formal tender joint count (TJC), swollen joint count (SJC), and a laboratory test[1]. Therefore, it was relatively unexpected that similar results for remission in the ACR/EULAR criteria, as well as the 28-joint Disease Activity Score (DAS28) and the Clinical Disease Activity Index (CDAI), were seen according to an index that did not include formal joint counts or a laboratory

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*Supported by Health Report Services Inc. An unrestricted grant from Merck Sharp and Dohme was allocated for the first 5 years of the ESPOIR cohort. Two additional grants from INSERM were obtained to support part of the biological database. The French Society of Rheumatology, AbbVie, Pfizer, and Roche also supported the ESPOIR cohort. Dr. Pincus is president of Health Report Services Inc., which owns a copyright and a trademark for MDHAQ and RAPID3.*

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*Accepted for publication March 1, 2016.*

test: RAPID3 ≤ 3 + SJ ≤ 1 (Routine Assessment of Patient Index Data 3 + 1 or 0 swollen joints), in patients in the French ESPOIR early arthritis database[2]. RAPID3 is composed of the 3 patient self-report measures among the 7 RA core dataset measures[3], physical function, pain, and patient's global assessment (PtGA)[4].

RAPID3 is correlated significantly with DAS28 and CDAI in clinical trials and clinical care, and distinguishes active from control treatment in RA clinical trials as efficiently as these indices[5]. RAPID3 is feasible in busy clinical rheumatology settings because it requires only 5 s to score, in contrast with 114 s for the DAS28 and 110 s for the CDAI[6]. The Multi-Dimensional HAQ (MDHAQ)/RAPID3 completed by a patient in the waiting area[7] provides a quantitative measure to enhance clinical decisions in busy clinical settings, particularly because most rheumatologists do not perform a formal joint count in most patients[8,9]. RAPID3 has been found to be valuable in all rheumatic diseases in which it has been studied[10,11,12,13,14,15,16].

The observation that RAPID3-based remission criteria identified patients who were in remission similarly to criteria that included formal joint counts and laboratory tests suggested that patient questionnaire measures might also predict remission as effectively as laboratory and radiographic measures. We formulated a hypothesis that RAPID3, an index of patient self-report measures only, would predict remission as effectively as the absence of variables that are regarded as indicators of "poor prognosis RA," such as rheumatoid factor (RF), anticitrullinated protein antibodies (ACPA), and radiographic erosions[17,18].

Most reported studies concerning the prediction of remission in RA are primarily based on data from clinical trials[19], which include a minority of selected patients[20,21] and only a limited number of variables[19]. The ESPOIR database includes a comprehensive set of baseline variables from actual clinical care. In our report, we analyzed individual measures and indices at baseline to predict remission either 6 or 12 months later (or at both timepoints) according to 6 different criteria.

## MATERIALS AND METHODS

*The ESPOIR cohort*. The ESPOIR is a prospective observational cohort of patients with early arthritis sponsored by the French Society for Rheumatology. Patients had early arthritis (disease duration < 6 mos), a certain/probable clinical diagnosis of RA or undifferentiated arthritis potentially becoming RA, and were naive to disease-modifying antirheumatic drugs (DMARD). Corticosteroids were permitted only if prescribed for < 2 weeks and with a maximum mean dose of 20 mg/day[22]. A total of 813 patients were enrolled between December 2002 and March 2005 at 14 academic regional centers, with the participation of a network of private rheumatologists. Patients were treated by their rheumatologists according to standard of care and evaluated per protocol every 6 months over the first 2 years and every year thereafter. Further details are described in a previous report[22].

The ESPOIR database includes demographic, clinical, and radiographic variables, and is used by multiple investigators who apply to perform specific studies. The database available through application for the study reported here included only the first year of observation. Analyses were restricted to 664 individuals with complete data at baseline, 6 months, and 12 months for each variable studied. Baseline characteristics were similar in the study patients to non-included ESPOIR patients (data not shown).

*Remission criteria*. Remission was defined retrospectively using prospectively collected data at 6 months, 12 months, or both timepoints according to 6 different criteria including the Boolean [TJC28, SJC28, C-reactive protein (CRP), and PtGA ≤ 1[1,23]], SDAI < 3.3[24], CDAI < 2.8[25], DAS28 ≤ 2.6[26], RAPID3 ≤ 3, and RAPID3 ≤ 3 + SJ ≤ 1[2]. The rationale for studying the 6 criteria were the following: Boolean and SDAI were recommended by the ACR/EULAR committee, DAS28 is the criterion for remission in 90% of published reports, CDAI is widely used instead of SDAI and DAS28, and RAPID3-SJ1 is the focus of our study and should be analyzed to recognize how it differs from RAPID3 because it requires an extra step by the assessor.

*Clinical variables as possible predictors of remission*. Available baseline variables were analyzed for capacity to predict remission, including demographic variables (age, sex, and family history of RA), disease duration, traditional variables regarded as indicating "poor prognosis RA"[18,27] (RF, ACPA positivity, and presence of erosions at baseline using the score for erosions from a baseline Sharp/van der Heijde score as a dichotomous variable), RA core dataset variables [3 from a physician: TJC28, SJC28, and physician's global assessment (PGA)], 1 laboratory test [erythrocyte sedimentation rate (ESR) or CRP], 3 from patient self-report [Health Assessment Questionnaire (HAQ) physical function scores (0–3 converted to 0–10 to calculate RAPID3)[28], 0–10 visual analog scale for pain, and for PtGA], and 4 RA indices (DAS28[26], SDAI[25], CDAI[29], and RAPID3[4].

*Statistical analysis*. Data were analyzed using Stata, version 12 (StataCorp). Individual variables were assessed descriptively at baseline as mean and SD for normally distributed variables, and median and interquartile range for non-normally–distributed variables. Baseline variables were compared for patients in remission versus not in remission according to each of the 6 remission criteria. Student t tests were performed for variables with normal distributions, and Mann-Whitney U tests for variables with non-normal distributions.

Univariate regressions were performed to identify baseline individual variables and indices as potential predictors of remission. Those variables with p values < 0.10 were carried forward into multivariate logistic regressions. Results are presented as multivariate OR with 95% CI.

A separate multivariate regression was performed in view of the unexpected finding that patient questionnaire data were more likely to predict remission than a laboratory test or joint counts. These analyses included only 3 measures, 1 from each category of the core dataset, SJC, ESR, or CRP because they are regarded by most rheumatologists as optimal indicators of inflammation[1], and HAQ physical function, regarded as most likely to be affected by joint damage and is irreversible[30,31,32] and therefore a poor indicator of inflammation. The other 4 RA core dataset measures (TJC, PGA, pain, and PtGA) and demographic measures were not included in these regressions.

## RESULTS

Among the 664 patients studied, 507 (76.4%) were women. The mean age was 48.4 years, and the median duration of disease was 4.8 months (Table 1). The number and proportion of patients who were in remission at 6 and/or 12 months according to the Boolean criteria was 165 (24.8%), compared with 339 (51.4%) by DAS28, 204 (30.8%) by SDAI, 205 (30.9%) by CDAI, 273 (41.1%) by RAPID3, and 209 (31.5%) by RAPID3 ≤ 3 + SJ ≤ 1 (Table 2, Table 3).

Possible predictors of remission showed a similar pattern for each of the 6 remission criteria (Table 2). In univariate analyses, 5 of 7 core dataset measures (TJC, PGA, HAQ function, pain, and PtGA) were significant to predict

*Table 1*. Characteristics of the 664 patients from the ESPOIR cohort at baseline and comparison of the remission group versus nonremission at 6 or 12 months according to the Boolean criteria. Student t test was performed for variables with a normal distribution and Mann-Whitney U test for variables with a non-normal distribution. Values are median (interquartile range) unless otherwise specified.

| Variables | Baseline, All Patients, n = 664 | Remission According to Boolean Criteria at 6 and/or 12 Mos | | |
|---|---|---|---|---|
| | | Remission, n = 165 | No Remission, n = 499 | p |
| Age, yrs, mean (SD) | 48.4 (12.3) | 44.9 (12.2) | 49.5 (12.1) | < 0.001 |
| Female, n (%) | 507 (76.4) | 158 (31.2) | 349 (68.9) | 0.09 |
| Erosive at baseline, n (%) | 220 (35) | 55 (35) | 165 (34.7) | 0.946 |
| Family history of RA, n (%) | 107 (16.1) | 21 (12.7) | 86 (17.2) | 0.172 |
| Disease duration, mos | 4.8 (2.9–7.1) | 4.2 (2.8–6.0) | 4.9 (2.9–7.3) | 0.06 |
| SJC, 0–28 | 6 (3–10) | 5 (2–9) | 6 (3–10) | 0.001 |
| TJC, 0–28 | 6 (3–13) | 5 (2–10) | 7 (4–14) | < 0.001 |
| PGA, 0–100, mean (SD) | 50.7 (22.1) | 43.6 (22.9) | 53.0 (21.4) | < 0.001 |
| PtGA, 0–100 | 64 (44–79) | 55.0 (31.0–75.0) | 66.0 (47–80) | < 0.001 |
| Function, 0–10 | 2.9 (1.2–4.6) | 2.5 (0.8–4.2) | 3.3 (1.7–5) | 0.005 |
| Pain, 0–10 | 4.5 (2.2) | 3.9 (2.2) | 4.8 (2.2) | < 0.001 |
| ESR, mm/h | 22 (12–38) | 19 (12–35) | 22 (12–39) | 0.55 |
| CRP, mg/l | 0.9 (0.5–2.5) | 0.9 (0.3–2) | 0.9 (0.5–2.5) | 0.247 |
| ACPA, n (%) | 266 (40) | 61 (37) | 205 (41) | 0.35 |
| RF+, n (%) | 290 (43.7) | 70 (42.4) | 220 (44.1) | 0.71 |

RA: rheumatoid arthritis; SJC: swollen joint count; TJC: tender joint count; PGA: physician's global assessment; PtGA: patient's global assessment; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ACPA: anticitrullinated protein antibodies; RF: rheumatoid factor.

*Table 2*. Univariate logistic regression models to estimate the associations among baseline variables that are potential predictors of remission by the Boolean criteria, DAS28, SDAI, CDAI, RAPID3, and RAPID3-SJ1 at 6 and/or 12 months.

| Baseline Variables | Boolean Criteria, n = 165 (24.8%) | | SDAI ≤ 3.3, n = 204 (30.8%) | | CDAI ≤ 2.8, n = 205 (30.9%) | | DAS28 ≤ 2.6, n = 339 (51.4%) | | RAPID3 ≤ 3, n = 273 (41.1%) | | RAPID3 ≤ 3 + SJ ≤ 1, n = 209 (31.5%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) | p | OR (95% CI) | p | OR (95% CI) | p | OR (95% CI) | p | OR (95% CI) | p | OR (95% CI) | p |
| Age, yrs | 0.97 (0.96–0.98) | < 0.001 | 0.97 (0.95–0.98) | < 0.001 | 0.97 (0.95–0.98) | < 0.001 | 0.98 (0.97–0.99) | 0.02 | 0.98 (0.97–1.00) | 0.011 | 0.97 (0.96–0.99) | < 0.001 |
| Disease duration, mos | 0.99 (0.96–1.01) | 0.26 | 0.99 (0.97–1.01) | 0.255 | 0.99 (0.97–1.01) | 0.300 | 0.99 (0.98–1.01) | 0.76 | 1.00 (0.98–1.02) | 0.953 | 0.99 (0.98–1.01) | 0.91 |
| Female | 1.05 (0.69–1.59) | 0.83 | 1.05 (0.71–1.56) | 0.796 | 1.02 (0.69–1.51) | 0.914 | 0.59 (0.41–0.85) | 0.05 | 0.83 (0.58–1.19) | 0.312 | 0.94 (0.64–1.38) | 0.76 |
| Erosive at baseline, yes = 1 | 1.01 (0.69–1.48) | 0.95 | 1.07 (0.75–1.52) | 0.716 | 1.01 (0.71–1.44) | 0.955 | 1.16 (0.83–1.61) | 0.38 | 0.91 (0.65–1.27) | 0.587 | 0.85 (0.60–1.21) | 0.37 |
| Family history of RA, yes = 1 | 0.70 (0.42–1.17) | 0.17 | 0.65 (0.40–1.06) | 0.082 | 0.65 (0.40–1.05) | 0.076 | 0.55 (0.36–0.85) | 0.006 | 0.72 (0.47–1.11) | 0.135 | 0.62 (0.38–1.00) | 0.05 |
| TJC, 0–28 | 0.94 (0.91–0.97) | < 0.001 | 0.92 (0.89–0.95) | < 0.001 | 0.92 (0.89–0.94) | < 0.001 | 0.93 (0.91–0.95) | < 0.001 | 0.97 (0.94–0.99) | 0.003 | 0.95 (0.92–0.97) | < 0.001 |
| SJC, 0–28 | 0.96 (0.92–0.99) | 0.01 | 0.94 (0.90–0.97) | < 0.001 | 0.93 (0.90–0.97) | < 0.001 | 0.98 (0.95–1.01) | 0.15 | 1.00 (0.97–1.03) | 0.923 | 0.96 (0.93–0.99) | 0.01 |
| PGA, 0–100 | 0.98 (0.97–0.99) | < 0.001 | 0.98 (0.97–0.99) | < 0.001 | 0.98 (0.97–0.99) | < 0.001 | 0.98 (0.97–0.99) | < 0.001 | 0.98 (0.98–0.99) | < 0.001 | 0.98 (0.97–0.99) | < 0.001 |
| ESR | 0.99 (0.99–1.01) | 0.83 | 1.00 (0.99–1.01) | 0.893 | 1.00 (1.00–1.01) | 0.615 | 0.99 (0.98–0.99) | 0.03 | 1.00 (0.99–1.01) | 0.809 | 1.00 (0.99–1.00) | 0.50 |
| CRP | 0.99 (0.94–1.04) | 0.76 | 0.99 (0.94–1.04) | 0.649 | 1.00 (0.96–1.05) | 0.897 | 1.00 (0.96–1.05) | 0.89 | 1.00 (0.96–1.05) | 0.908 | 1.01 (0.96–1.06) | 0.66 |
| ACPA+, yes = 1 | 0.84 (0.58–1.21) | 0.35 | 0.84 (0.60–1.18) | 0.316 | 0.88 (0.63–1.24) | 0.467 | 0.82 (0.60–1.12) | 0.21 | 0.94 (0.69–1.29) | 0.704 | 0.87 (0.62–1.22) | 0.42 |
| RF+, yes = 1 | 1.07 (0.75–1.53) | 0.71 | 1.16 (0.83–1.62) | 0.375 | 1.14 (0.82–1.60) | 0.429 | 1.35 (0.99–1.84) | 0.06 | 1.09 (0.79–1.48) | 0.607 | 1.13 (0.81–1.57) | 0.47 |
| Function, 0–10 | 0.89 (0.82–0.97) | 0.006 | 0.87 (0.81–0.94) | < 0.001 | 0.89 (0.82–0.96) | 0.002 | 0.85 (0.80–0.91) | < 0.001 | 0.82 (0.77–0.89) | < 0.001 | 0.85 (0.79–0.92) | < 0.001 |
| Pain, 0–100 | 0.98 (0.97–0.99) | < 0.001 | 0.98 (0.97–0.98) | < 0.001 | 0.98 (0.97–0.98) | < 0.001 | 0.98 (0.97–0.99) | < 0.001 | 0.97 (0.97–0.98) | < 0.001 | 0.98 (0.97–0.99) | < 0.001 |
| PtGA, 0–100 | 0.99 (0.98–0.99) | < 0.001 | 0.99 (0.98–0.99) | < 0.001 | 0.99 (0.98–0.99) | < 0.001 | 0.98 (0.97–0.99) | < 0.001 | 0.98 (0.98–0.99) | < 0.001 | 0.99 (0.98–0.99) | < 0.001 |

DAS28: Disease Activity Score at 28 joints; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; RAPID3: Routine Assessment of Patient Index Data 3; SJ: swollen joint; RA: rheumatoid arthritis; SJC: swollen joint count; TJC: tender joint count; PGA: physician's global assessment; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ACPA: anticitrullinated protein antibodies; RF: rheumatoid factor; PtGA: patient's global assessment.

remission according to all 6 criteria. SJC was significant for 4 criteria (Boolean, SDAI, CDAI, and RAPID3 ≤ 3 + SJ ≤ 1), and ESR for 1 criteria set (DAS28). Among other measures, younger age was significant to predict remission according to all 6 criteria, no family history of RA for 2 criteria (DAS28 and RAPID3 ≤ 3 + SJ ≤ 1), and female sex only for DAS28. RF, ACPA, radiographic erosions, CRP, or disease duration were not significant to predict remission according to any of the 6 criteria (Table 2).

Multivariate logistic regressions that included individual variables with p values < 0.10 in univariate analyses (Table 3) indicated significant prediction of remission for the Boolean criteria ($p < 0.05$) by low age, low TJC28, and pain (Table 3); for DAS28 by low age, male sex, no family history

*Table 3*. Multivariate logistic regression models to estimate the associations among baseline variables that are potential predictors of remission by the Boolean criteria, DAS28, SDAI, CDAI, RAPID3, and RAPID3-SJ1 at 6 and/or 12 months. Disease duration, erosive at baseline, CRP, ACPA, and RF were not significant in univariate analysis for any of the criteria and were not included in the multivariate analysis.

| Baseline Variables | Boolean Criteria, n = 165 (24.8%) | | DAS28 ≤ 2.6, n = 339 (51.4%) | | SDAI ≤ 3.3, n = 204 (30.8%) | | CDAI ≤ 2.8, n = 205 (30.9%) | | RAPID3 ≤ 3, n = 273 (41.1%) | | RAPID3 ≤ 3 + SJ ≤ 1, n = 209 (31.5%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) | p | OR (95% CI) | p | OR (95% CI) | p | OR (95% CI) | p | OR (95% CI) | p | OR (95% CI) | p |
| Age, yrs | 0.97 (0.95–0.98) | < 0.001 | 0.98 (0.97–0.99) | 0.01 | 0.96 (0.95–0.98) | < 0.001 | 0.97 (0.95–0.98) | < 0.001 | 0.98 (0.97–0.99) | 0.004 | 0.97 (0.96–0.98) | < 0.001 |
| Female | NS | NS | 0.59 (0.39–0.87) | 0.009 | NS | NS | NS | NS | NS | NS | NS | NS |
| Family history of RA, yes = 1 | NS | NS | 0.58 (0.37–0.92) | 0.02 | NS | NS | NS | NS | NS | NS | 0.65 (0.39–1.08) | 0.09 |
| TJC, 0–28 | 0.96 (0.93–0.99) | 0.03 | 0.95 (0.92–0.97) | < 0.001 | 0.94 (0.91–0.98) | 0.001 | 0.93 (0.90–0.96) | < 0.001 | 1.00 (0.98–1.03) | 0.69 | 0.98 (0.94–1.00) | 0.14 |
| SJC, 0–28 | 1.02 (0.97–1.07) | 0.39 | NS | NS | 1.00 (0.96–1.05) | 0.69 | 1.01 (0.97–1.05) | 0.54 | NS | NS | 1.01 (0.97–1.06) | 0.55 |
| PGA, 0–100 | 0.99 (0.98–1.00) | 0.06 | 0.99 (0.99–1.00) | 0.55 | 0.99 (0.97–0.99) | 0.03 | 0.98 (0.97–0.99) | 0.01 | 1.00 (0.99–1.01) | 0.63 | 0.99 (0.98–1.00) | 0.38 |
| ESR | NS | NS | 0.99 (0.99–1.00) | 0.28 | NS | NS | NS | NS | NS | NS | NS | NS |
| Function, 0–10 | 1.02 (0.92–1.13) | 0.66 | 0.98 (0.90–1.08) | 0.77 | 1.02 (0.93–1.13) | 0.61 | 1.04 (0.94–1.14) | 0.76 | 0.89 (0.81–0.98) | 0.01 | 0.93 (0.84–1.02) | 0.11 |
| Pain, 0–100 | 0.99 (0.98–0.99) | 0.03 | 0.99 (0.98–0.99) | 0.04 | 0.98 (0.97–0.99) | 0.002 | 0.98 (0.97–0.99) | 0.002 | 0.98 (0.97–0.98) | < 0.001 | 0.98 (0.97–0.99) | 0.004 |
| PtGA, 0–100 | 0.99 (0.98–1.00) | 0.75 | 0.99 (0.99–1.00) | 0.48 | 1.00 (0.99–1.01) | 0.66 | 0.99 (0.98–1.00) | 0.36 | 0.99 (0.99–1.00) | 0.62 | 0.99 (0.99–1.00) | 0.99 |

DAS28: Disease Activity Score at 28 joints; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; RAPID3: Routine Assessment of Patient Index Data 3; SJ: swollen joint; CRP: C-reactive protein; ACPA: anticitrullinated protein antibodies; RF: rheumatoid factor; RA: rheumatoid arthritis; TJC: tender joint count; SJC: swollen joint count; PGA: physician's global assessment; ESR: erythrocyte sedimentation rate; PtGA: patient's global assessment; NS: variables not significant in univariate analysis and therefore not included in multivariate analysis for each specific criteria set.

of RA, low TJC28, and low pain; for SDAI and CDAI by low age, TJC28, PGA , and pain; for RAPID3 by low age, pain, and HAQ physical function; and for RAPID3 ≤ 3 + SJ ≤ 1 by low age and pain (Table 3). Only low age and low pain were associated independently with each of the 6 remission criteria, and TJC with 4 of 6 (Table 3). Again, RF, ACPA, radiographic erosions, CRP, and disease duration were not significant to predict remission by any of the 6 criteria.

Analyses according to the 4 RA clinical indices, CDAI, DAS28, RAPID3, and SDAI (Table 4), indicated that all were significant to predict remission status at both 6 and 12 months according to all 6 remission criteria in univariate logistic regressions. The lowest OR (indicating greatest capacity) to predict remission according to all remission criteria were seen for the DAS28, followed by RAPID3. In multivariate regressions, only RAPID3 predicted remission significantly according to the Boolean criteria, RAPID3, and RAPID3 ≤ 3 + SJ ≤ 1. No index was significant to predict remission criteria according to the SDAI criteria, only CDAI predicted CDAI remission significantly, and DAS28 remission was predicted by DAS28, CDAI, and RAPID3.

Two separate logistic regressions were performed that included only 3 measures (SJC, either ESR or CRP, and HAQ physical function) as independent variables to predict each of the 6 remission criteria as dependent variables (Table 5). As noted, these analyses were based on a rationale that SJC,

*Table 4*. Univariate and multivariate logistic regressions to estimate associations among 4 indices (SDAI, CDAI, RAPID3, and DAS28) to predict remission status at both 6- and 12-month timepoints. All univariate logistic regression results to predict SDAI or CDAI remission are p < 0.001 except for RAPID3, which is p < 0.01. All multivariate logistic regression results are p < 0.001 except the Boolean criteria to predict SDAI, CDAI, DAS28, and RAPID3, which are p = 0.18, p = 0.52, p = 0.75, and p = 0.02, respectively.

| Baseline Variables | Boolean Criteria, n = 165 (24.8%) OR (95% CI) | SDAI ≤ 3.3, n = 204 (30.8%) OR (95% CI) | CDAI ≤ 2.8, n = 205 (30.9%) OR (95% CI) | DAS28 ≤ 2.6, n = 339 (51.4%) OR (95% CI) | RAPID3 ≤ 3, n = 273 (41.1%) OR (95% CI) | RAPID3 ≤ 3 + SJ ≤ 1, n = 209 (31.5%) OR (95% CI) |
|---|---|---|---|---|---|---|
| Univariate logistic regression | | | | | | |
| SDAI | 0.81 (0.77–0.84) | 0.96 (0.95–0.97) | 0.96 (0.95–0.97) | 0.97 (0.96–0.98) | 0.98 (0.97–1.00) | 0.97 (0.96–0.99) |
| CDAI | 0.80 (0.77–0.84) | 0.95 (0.94–0.97) | 0.95 (0.94–0.97) | 0.97 (0.95–0.98) | 0.98 (0.97–0.99) | 0.97 (0.96–0.98) |
| DAS28 | 0.32 (0.26–0.40) | 0.68 (0.59–0.78) | 0.69 (0.60–0.79) | 0.64 (0.56–0.73) | 0.81 (0.71–0.92) | 0.75 (0.65–0.85) |
| RAPID3 | 0.76 (0.72–0.80) | 0.92 (0.89–0.95) | 0.92 (0.89–0.95) | 0.91 (0.89–0.94) | 0.90 (0.87–0.93) | 0.92 (0.89–0.95) |
| Multivariate logistic regression | | | | | | |
| SDAI | 0.91 (0.69–1.20) | 1.01 (0.96–1.07) | 1.03 (0.97–1.09) | 1.09 (1.03–1.16) | 1.05 (0.99–1.11) | 1.05 (1.00–1.11) |
| CDAI | 0.96 (0.72–1.26) | 0.95 (0.90–1.00) | 0.93 (0.88–0.98) | 0.93 (0.88–0.99) | 0.97 (0.92–1.02) | 0.94 (0.90–1.00) |
| DAS28 | 0.78 (0.55–1.12) | 1.05 (0.78–1.41) | 1.07 (0.79–1.44) | 0.55 (0.41–0.73) | 1.00 (0.76–1.33) | 0.89 (0.66–1.20) |
| RAPID3 | 0.91 (0.85–0.99) | 0.97 (0.93–1.01) | 0.97 (0.93–1.01) | 0.96 (0.92–0.99) | 0.87 (0.84–0.91) | 0.94 (0.90–0.98) |

SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; RAPID3: Routine Assessment of Patient Index Data 3; DAS28: Disease Activity Score at 28 joints; SJ: swollen joint.

ESR, and CRP are regarded as optimal indicators of inflammation[1], while HAQ physical function is regarded as least reversible because of joint damage[30,31,32]. However, HAQ physical function was significant independently to predict remission for all 6 criteria sets, including for the 4 criteria sets that do not include HAQ physical function: the Boolean, SDAI, CDAI, and DAS28 (Table 5). SJC (as well as HAQ physical function) was significant to predict remission according to the SDAI and CDAI. ESR was significant in these analyses to predict remission by CDAI, RAPID3, and RAPID3 ≤ 3 + SJ ≤ 1. CRP was significant to predict remission by RAPID3 and RAPID3 ≤ 3 + SJ ≤ 1.

## DISCUSSION

In our study, younger age and the 6 clinical core dataset measures, but not traditional indicators of "poor prognosis RA," including absence of baseline RF, ACPA, or radiographic damage[17,18], were significant predictors of remission according to 6 remission criteria in univariate analyses. Traditional variables for poor prognosis would likely be significant with a larger number of patients. However, younger age and low TJC, SJC, PGA, HAQ function, pain, and PtGA would appear to be more robust predictors of remission 6 and/or 12 months later than laboratory tests and radiographs in the ESPOIR database.

An excellent systematic review of 18 studies of baseline variables that might predict RA remission indicated that these were prognostic in some studies but not all: younger age, male sex, short disease duration, low baseline DAS28, low radiographic damage, absence of RF, absence of ACPA, and low levels of acute-phase reactants[19,33,34,35,36,37]. Most of these reports analyzed only selected variables from selected patients from clinical trials, for which most patients with RA have not been eligible[20,21], and other clinical research studies in which patients may be selected for many variables thought to connote "poor prognosis RA"[17,18] rather than a comprehensive set of demographic, clinical, patient questionnaire, and laboratory variables[19]. Results with a limited number of variables in selected populations may differ from those seen in patients in routine care. Further, most of these studies assessed remission according to the DAS28[19,33,34,35,36,37], which is regarded as insufficiently stringent[1].

The observation that HAQ physical function was as likely as SJC, ESR, or CRP to predict remission (or more likely) may appear inconsistent with reports that HAQ function score is more likely than other core dataset measures to be unresponsive to therapies because scores reflect damage more than other variables[30,31,32]. Favorable HAQ function score could be more prognostic for remission without necessarily being responsive to treatment, simply serving as a marker for low severity. However, HAQ function was as responsive as SJC, ESR, or CRP to distinguish between active and control treatments in the 9 reported comparisons in clinical trials of DMARD and biological agents[38]. Differences from other reports[30,31,32] may be explained in part by different methods, different populations, and other features of different studies.

RAPID3 and RAPID3 ≤ 3 + SJ ≤ 1, which includes only patient self-report scores and observation of 1 swollen joint or none, have been developed to overcome the workflow complexities in busy clinical settings to collect more elaborate remission criteria[7]. It is far simpler in busy settings to ask patients to complete the same questionnaire at each visit than to collect different patient questionnaires for patients with different diagnoses. The MDHAQ/RAPID3 has been shown to document improvement in many rheumatic diseases[11,12,13,14,15,16,39], and can be of value in new (or return) patients with an unknown diagnosis.

Several limitations are seen in our study. Only a single cohort of patients (664) with early arthritis from France was analyzed. Analyses were conducted only at baseline, 6 months, or 12 months after baseline, to identify remission status. It might be more desirable to analyze potential predictors of sustained remission, which is uncommon in clinical cohorts[40,41], although associated with better outcomes[42]. However, only the first year of observation was

*Table 5*. Multivariate models to predict remission at 6 and/or 12 months according to 6 criteria using only SJC, ESR or CRP, and HAQ function.

| Models | Boolean Criteria, n = 165 (24.8%) | | SDAI ≤ 3.3, n = 204 (30.8%) | | CDAI ≤ 2.8, n = 205 (30.9%) | | DAS28 ≤ 2.6, n = 339 (51.4%) | | RAPID3 ≤ 3, n = 273 (41.1%) | | RAPID3 ≤ 3 + SJ ≤ 1, n = 209 (31.5%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) | p | OR (95% CI) | p | OR (95% CI) | p | OR (95% CI) | p | OR (95% CI) | p | OR (95% CI) | p |
| Model 1 | | | | | | | | | | | | |
| SJC | 0.97 (0.93–1.00) | 0.086 | 0.95 (0.91–0.98) | 0.004 | 0.94 (0.91–0.98) | 0.002 | 1.00 (0.97–1.03) | 0.907 | 1.04 (1.00–1.07) | 0.029 | 0.98 (0.94–1.01) | 0.206 |
| ESR | 1.00 (1.00–1.01) | 0.281 | 1.01 (1.00–1.01) | 0.068 | 1.01 (1.00–1.02) | 0.045 | 1.00 (0.99–1.01) | 0.644 | 1.01 (1.00–1.01) | 0.007 | 1.01 (1.00–1.01) | 0.008 |
| HAQ | 0.70 (0.51–0.95) | 0.025 | 0.66 (0.49–0.88) | 0.005 | 0.70 (0.52–0.94) | 0.019 | 0.61 (0.46–0.79) | < 0.001 | 0.40 (0.30–0.54) | < 0.001 | 0.54 (0.40–0.73) | < 0.001 |
| Model 2 | | | | | | | | | | | | |
| SJC | 0.97 (0.93–1.01) | 0.094 | 0.95 (0.91–0.98) | 0.005 | 0.94 (0.91–0.98) | 0.002 | 1.00 (0.97–1.04) | 0.828 | 1.04 (1.01–1.07) | 0.022 | 0.98 (0.94–1.01) | 0.238 |
| CRP | 1.02 (0.97–1.08) | 0.476 | 1.02 (0.97–1.08) | 0.395 | 1.03 (0.98–1.09) | 0.196 | 1.05 (1.00–1.10) | 0.053 | 1.06 (1.01–1.11) | 0.022 | 1.06 (1.00–1.11) | 0.040 |
| HAQ | 0.72 (0.53–0.98) | 0.039 | 0.70 (0.52–0.93) | 0.015 | 0.74 (0.55–0.98) | 0.038 | 0.53 (0.41–0.70) | < 0.001 | 0.42 (0.32–0.56) | < 0.001 | 0.57 (0.42–0.76) | < 0.001 |

SJC: swollen joint count; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; HAQ: Health Assessment Questionnaire; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score at 28 joints; RAPID3: Routine Assessment of Patient Index Data 3; SJ: swollen joint.

available for the reported study. No adjustment was made for treatment, recognizing that early aggressive treatment improved RA outcomes, regardless of other variables[43,44]. Finally, the 7 RA core dataset measures are correlated significantly with one another, which may distort statistical significance of individual variables and indices because of multicollinearity.

Nonetheless, RAPID3 appears to be a robust index for feasible prediction and identification of remission compared with other indices, particularly because formal joint counts are not performed in usual care[8,9], and most rheumatology settings in the United States do not include assessment of any index[9]. Remission is excluded by recognizing more than 1 swollen joint, which is far more feasible than performing a formal joint count. Laboratory tests are frequently the only quantitative clinical measures available in the medical records of most patients with RA to support clinical decisions in patient care, despite being regarded as inadequate by regulatory agencies, for which an RA index is required.

Variables regarded as indicators of "poor prognosis RA," such as laboratory tests and radiographic erosions, were not statistically significant to predict remission according to 6 criteria. Predictors of remission according to all 6 criteria appear more similar than different. RAPID3 and RAPID3 ≤ 3 + SJ ≤ 1 criteria, based primarily on patient variables, predict remission similarly to criteria that require a formal joint count, including 4 criteria that do not include pain or HAQ physical function. In an earlier report, we found that remission criteria based only on RAPID3 and a careful joint examination instead of a formal joint count yielded similar results compared with the Boolean and other remission criteria[2]. Collection of RAPID3 does not exclude a formal joint count as well as formal scoring of DAS28, SDAI, and CDAI. However, RAPID3 does assure that some quantitative data beyond laboratory tests will be recorded at each patient visit. RAPID3 ≤ 3 + SJ ≤ 1 may provide a feasible approach to predict and document remission in usual patient care.

## ACKNOWLEDGMENT

The authors thank Nathalie Rincheval for expert monitoring and data management, and all the investigators who recruited and followed the patients: F. Berenbaum, Paris-Saint Antoine; M.C. Boissier, Paris-Bobigny; A. Cantagrel, Toulouse; P. Fardelonne and P. Boumier, Amiens; P. Bourgeois, Paris-La Pitie; R.M. Flipo, Lille; P. Goupille, Tours; F. Liote, Paris-Lariboisiere; X. Le Loet and O. Vittecoq, Rouen; X. Mariette, Paris Bicetre; O. Meyer, Paris Bichat; A. Saraux, Brest; T. Schaeverbeke, Bordeaux; and J. Sibilia, Strasbourg.

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