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Construct Validity of the Routine Assessment of Patient Index Data 3 (RAPID3) in the Evaluation of Axial Spondyloarthritis

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ABSTRACT. ***Objective.*** Although there are different tools to evaluate axial spondyloarthritis (axSpA), they are hardly used in routine clinical practice due to time constraints. The Routine Assessment of Patient Index Data 3 (RAPID3) is a composite measure feasible for use as a sole metric in busy clinics. We aimed to test its measurement properties in patients with axial SpA in a real-world clinical setting.

Methods. This cross-sectional study included 131 consecutive patients with axial SpA. The convergent (Spearman ρ) and discriminant (receiver-operating characteristic [ROC] curve analysis) validity of RAPID3 were tested against several axSpA-specific measures (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI], Ankylosing Spondylitis Disease Activity Score [ASDAS], Bath Ankylosing Spondylitis Functional Index [BASFI], and modified Stoke Ankylosing Spondylitis Spinal Score [mSASSS]). A multivariate model was built to detect disease factors associated with RAPID3 remission (values ≤ 3).

Results. The study included 82 men and 49 women, with a median age of 55 (IQR 46–61) years, and a median disease duration of 11 (IQR 6–24) years. Mean RAPID3 was 9.45 ± 6.7. The BASDAI showed moderate correlation with ASDAS (ρ 0.66, $P < 0.0001$), but higher correlations with BASFI (ρ 0.78, $P < 0.0001$) and RAPID3 (ρ 0.75, $P < 0.0001$). The ASDAS had moderate correlations with BASFI, BASDAI, and RAPID3 (ranges 0.66–0.68, $P < 0.0001$). Higher correlations were found between BASFI and BASDAI (ρ 0.78, $P < 0.0001$), and BASFI and RAPID3 (ρ 0.73, $P < 0.0001$). The mSASSS did not show any correlation with any of the above composite measures. κ agreement between RAPID3 remission and other SpA remission criteria was moderate (κ 0.46–0.56). The RAPID3 thresholds to define remission ranged from values ≤ 2 to ≤ 6 with areas under the ROC curve between 0.86–0.91. Female sex (OR 0.34, 95% CI 0.12–0.90, $P = 0.03$) and nonsteroidal antiinflammatory drug intake (OR 0.26, 95% CI 0.10–0.66, $P = 0.005$) were independently associated with lower odds of achieving RAPID3 remission.

Conclusion. RAPID3 demonstrated construct validity in this cross-sectional study. This index can be useful for a more comprehensive assessment of axSpA in busy clinical settings.

Key Indexing Terms: axial spondyloarthritis, disease assessment, quality of life, RAPID3

The spectrum of spondyloarthritis (SpA) encompasses diseases with common clinical and imaging features, along with a shared genetic base through HLA-B27. As a group, these diseases affect more than 1.5% of the general population, and as they affect mainly a young population, the direct and indirect costs associated with them are enormous.[1,2,3] SpA may include diseases where the symptoms of joint pain and stiffness mainly affect the axial skeleton, as in ankylosing spondylitis (AS) and nonradiographic axial spondyloarthritis (nr-axSpA), as well as other diseases where these symptoms predominate in the peripheral joints, as is the case in psoriatic arthritis (PsA).[1] Be that as it may, these processes seriously compromise the physical function and quality of life (QOL) of patients.[3]

Over the past few decades, many instruments have been used to assess the disease activity, physical function, movement metrics, or structural damage that accompanies SpA.[4] More recently, there has also been a notable boost in the investigation of instruments that can capture the effect of these disease outcomes on the day-to-day lives of patients.[5,6] Although all these tools provide information of undoubted value in clinical or therapeutic decision making, their use has become widespread mainly in the field of clinical trials or in the follow-up of large cohorts of patients with SpA.[4] However, its penetration into clinical routine has been very uneven, and rather testimonial.[4] The latter is surely due to the difficulty of using tools that are time-consuming, and that must be added to the metrics typical of other diseases treated in rheumatology clinics. For this reason, the search for an instrument that is reliable, simple, and easy to

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apply and interpret continues to be a need not yet fully covered in the field of rheumatic disease metrology.[4]

The Routine Assessment of Patient Index Data 3 (RAPID3) is an index composed of 3 patient self-reported measures: physical function, pain, and disease global assessment.[7] RAPID3 shows sufficient reliability, simplicity, responsiveness, and applicability to cover a good part of the metrological needs in high-demand consultations.[4,7] As it is a measure that includes relevant outcomes and is not time-consuming, it meets the ideal conditions for its use as the sole metric in routine practice.[4,7] Its good psychometric properties have been tested in different rheumatic diseases such as osteoarthritis, rheumatoid arthritis (RA), PsA, or axSpA, among others.[4,7] Despite this, it is a measurement that, outside the field of RA, has hardly been used in real-world clinical practice. Therefore, more information is still needed on the added value of RAPID3 in rheumatic diseases other than RA. RAPID3 has shown good construct validity in both cross-sectional and longitudinal SpA studies.[8,9,10,11,12] This way, it can be used as a comprehensive assessment measure in SpA. However, there is little information on its discriminant validity and on factors associated with poor health according to the thresholds of this instrument. In the present study, we have analyzed both the convergent and discriminant validity of RAPID3 in patients with axSpA. We also aimed to investigate which disease factors are more likely to be associated with a state of remission according to RAPID3 cut-offs.

METHODS

This cross-sectional study included 131 consecutive patients with axSpA classified according to the 2009 Assessment of Spondyloarthritis international Society (ASAS) criteria.[13] The patients included were adults of both sexes who attended the rheumatology service of a regional hospital in northern Spain. The patients were informed of the objectives of the study and their informed consent was requested for their inclusion in it. Study period extended from June to December 2019. The study was approved by the clinical research ethics committee of the Palencia University Healthcare Complex (no. 2020/035).

The study subjects were evaluated according to a study protocol in which sociodemographic, clinical, analytical, radiographic, and treatment variables were collected. All patients were adults of both sexes. Data were collected on educational level, disease duration, family history of SpA and other rheumatic diseases, as well as the presence of comorbidities, especially of the cardiovascular type. Within the analytical variables, erythrocyte sedimentation rate (ESR; mm/h), C-reactive protein (CRP; mg/L), rheumatoid factor, antinuclear antibodies, and HLA-B27 were included, among others. The presence of enthesitis, dactylitis, uveitis, and inflammatory bowel disease (IBD) was also included among study variables. All patients underwent a radiographic examination that included an anteroposterior (AP) projection of the pelvis, as well as AP and lateral views of the cervical and lumbar spine. The radiographic evaluation of structural damage was performed using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS), which includes evaluation from C2 to the upper part of T1, and from the lower part of T12 to the upper plateau of S1. The score range is 0–72, and the existence in vertebral corners of squaring, erosions, sclerosis, and/or syndesmophytes are scored on lateral cervical and lumbar spine views.[14] Structural damage in sacroiliac joints was evaluated by New York criteria.[15]

Disease activity was evaluated with the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[16] and the Ankylosing Spondylitis Disease Activity Score (ASDAS)-CRP.[17] Physical function was assessed with the Bath Ankylosing Spondylitis Functional Index (BASFI).[18] A 44-joint count was used to evaluate peripheral arthritis. Although some metrics of axial skeleton movement were collected, a specific spinal metrology index was not determined in this study.

The clinimetric ability of RAPID3 to assess axSpA was the main objective of this study. RAPID3 is an index composed of 3 patient self-reported measures from the RA core data set: physical function on the Health Assessment Questionnaire (HAQ) or its multidimensional version (MDHAQ), along with pain and the patient overall disease assessment on 2 visual analog scales (range 0–10).[7] In this study, physical function was assessed by the HAQ. The RAPID3 is calculated as the sum of its 3 domains, each domain reaching a maximum of 10 points, so that the range is from 0 to 30. Severity categories have been defined for RA as follows: ≤ 3 for remission, 3.1–6.0 for low, 6.1–12.0 for moderate, and > 12 for high severity.[19] The same categories were used in this study.

Statistical methodology. A descriptive statistical analysis of all the variables was performed, including central tendency and dispersion measures for continuous variables, and absolute and relative frequencies for categorical variables. For continuous variables, the goodness of fit for the normal distribution was verified by applying the Shapiro-Wilk test. In those variables with normal distribution, the mean with its 95% CI and SD were used. The median and IQR were used in the case of variables that did not adjust to a normal distribution. Mann-Whitney *U* test, *t* test, or Kruskal-Wallis test was used to compare quantitative variables, and Pearson chi-square or Fisher exact tests for qualitative variables. We examined construct convergent validity by correlating the scores of the RAPID3 against ASDAS-CRP, BASDAI, BASFI, and mSASSS. Spearman ρ correlation coefficients were obtained to quantify these relationships. Correlations were interpreted as follows: very high (> 0.90), high (0.70–0.89), moderate (0.50–0.69), low (0.26–0.49), and poor or almost nil (≤ 0.25). To distinguish between patients with active and inactive disease (discriminant validity) and to assess the RAPID3 respective cut-off values for these states, the receiver-operating characteristic (ROC) curve analysis was used. Cohen κ statistic was used to assess the degree of agreement between the definitions of remission according to the ASDAS, BASDAI, and RAPID3. A weighted κ statistic was calculated between the 4 ASDAS activity categories and the 4 RAPID3 severity levels. Cohen κ concordance was considered as follows: < 0.20 = poor, 0.21–0.40 = fair, 0.41–0.60 = moderate, 0.61–0.80 = good, and 0.81–1.00 = very good. Multivariate analyses were performed to assess predictors of BASDAI remission (BASDAI sum score ≤ 2 plus acute-phase reactants within the normal range), ASDAS inactive disease (ASDAS < 1.3), and RAPID3 remission. Statistical significance was set at $P < 0.05$. Data were analyzed using SPSS V19.0 statistical software (IBM Corp.).

RESULTS

This study included 131 patients, 82 men and 49 women, with a median age of 55 (IQR 46–61) years, and a median disease duration of 11 (IQR 6–24) years. Of the study population, 111 (84.7%) patients had radiographic axial disease, whereas the remaining 20 (15.3%) had nr-axSpA. One-third of patients presented peripheral involvement (mostly asymmetric arthritis of the lower limbs). Only 3 and 6 patients had dactylitis and enthesitis, respectively. Anterior uveitis was diagnosed in 21 (16%) patients, while 19 (14.5%) patients had concomitant IBD. HLA-B27 was determined in 122 patients; of these, 60.7% were positive. Upon study entry, 72 (55%) patients were taking nonsteroidal antiinflammatory drugs (NSAIDs), 40 (30.5%) were taking conventional synthetic disease-modifying antirheumatic drugs (DMARDs; mostly sulfasalazine), and 91 (69.5%) were receiving biological therapies (mostly tumor necrosis factor blockers). Table 1 shows the main characteristics of the study among men and women.

Table 1. Disease characteristics among men and women in this study.

	Men, n = 82	Women, n = 49	*P*
Age, yrs, mean (SD)	54.7 (11.9)	53.6 (12.3)	NS
Disease duration, yrs, mean (SD)	16.3 (11.2)	11.0 (8.3)	0.002
Education level, %			
Primary	14.6	8.1	NS
Secondary	73.2	63.3	NS
University	12.2	28.6	0.02
CV comorbidity, %			
Tobacco	25.6	32.7	NS
Obesity	7.3	8.2	NS
Diabetes	3.7	8.2	NS
Dyslipidemia	18.3	20.4	NS
Hypertension	19.5	16.3	NS
Hyperuricemia	11.0	2.0	0.09
Disease pattern, %			
Axial	70.7	61.2	NS
Peripheral	29.3	38.8	NS
Other SpA features, %			
Dactylitis	1.2	4.1	NS
Enthesitis	2.4	8.2	NS
Uveitis	19.5	10.2	NS
IBD	9.8	22.4	0.05
Radiographic structural disease[a], %			
Yes	92.7	71.4	0.001
Syndesmophytes	52.4	20.4	< 0.0005
Treatment, %			
NSAIDs	53.7	57.1	NS
csDMARDs	26.8	36.7	NS
Biologics	63.4	79.6	0.05
Laboratory variables			
HLA-B27–positive, n (%)	50/76 (65.8)	24/46 (52.2)	NS
CRP, mg/L, mean (SD)	2.8 (4.6)	2.9 (5.1)	NS
ESR, mm/h, mean (SD)	5.8 (8.2)	9.0 (7.3)	0.03
Outcome measures, mean (SD)			
BASDAI	3.1 (2.3)	4.8 (2.5)	0.0001
ASDAS-CRP	1.9 (0.9)	2.2 (0.7)	0.07
BASFI	3.4 (2.5)	4.0 (2.3)	NS
RAPID3	8.2 (6.7)	11.5 (6.3)	0.005

[a] Presence of sacroiliitis according to New York criteria with or without spinal involvement. ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; CRP: C-reactive protein; csDMARD: conventional synthetic disease-modifying antirheumatic drug; CV: cardiovascular; ESR: erythrocyte sedimentation rate; IBD: inflammatory bowel disease; NS: not significant; NSAID: nonsteroidal antiinflammatory drug; RAPID3: Routine Assessment of Patient Index Data 3; SpA: spondyloarthritis.

Of the 103 patients with radiographic axial disease with HLA-B27 status, HLA-B27 was positive in 72 (70%), $P < 0.001$. On the other hand, 16 of the 19 patients (84.2%) with anterior uveitis were B27-positive ($P = 0.02$). However, we did not find a statistically significant association between this antigen and syndesmophyte formation.

Patients with radiographic structural disease were older (55.5 [SD 11.9] vs 47.6 [SD 11.1] yrs, $P = 0.006$), with longer disease duration (15.3 [SD 10.7] vs 8.9 [SD 6.8] yrs, $P = 0.001$), and logically showed higher mean mSASSS values (15 [SD 19.8] vs 2.4 [SD 4.0], $P < 0.001$), compared to subjects with nr-axSpA. However, patients with nr-axSpA showed higher mean values, both for BASDAI (5.3 [SD 2.9] vs 3.5 [SD 2.3], $P = 0.002$) and RAPID3 (12.3 [SD 6.4] vs 9 [SD 6.6], $P = 0.04$). We did not find significant differences between both groups in terms of ASDAS or BASFI.

Mean BASDAI was 3.7 (SD 2.5), ASDAS was 2.06 (SD 0.82), BASFI was 3.61 (SD 2.5), and RAPID3 was 9.45 (SD 6.7). Convergent validity was moderate to high for RAPID3 in relation to other specific measures of axSpA (Table 2, Figure 1A–C). The BASDAI showed moderate correlation with ASDAS (ρ 0.66, $P < 0.0001$), but higher correlations with BASFI (ρ 0.78, $P < 0.0001$) and RAPID3 (ρ 0.75, $P < 0.0001$). The ASDAS had moderate correlations with BASFI, BASDAI, and RAPID3 (range 0.66–0.68, $P < 0.0001$). Higher correlations were found between BASFI and BASDAI (ρ 0.78,

Table 2. Spearman ρ correlation coefficients between the different outcome measures of this study.

	mSASSS	BASDAI	ASDAS-CRP	BASFI	RAPID3
mSASSS		ρ −0.17 *P* 0.054	ρ −0.11 *P* 0.19	ρ 0.07 *P* 0.42	ρ −0.10 *P* 0.23
BASDAI	ρ −0.17 *P* 0.054		ρ 0.66 *P* < 0.0001	ρ 0.78 *P* < 0.0001	ρ 0.75 *P* < 0.0001
ASDAS-CRP	ρ −0.11 *P* 0.19	ρ 0.66 *P* < 0.0001		ρ 0.68 *P* < 0.0001	ρ 0.66 *P* < 0.0001
BASFI	ρ 0.07 *P* 0.42	ρ 0.78 *P* < 0.0001	ρ 0.68 *P* < 0.0001		ρ 0.73 *P* < 0.0001
RAPID3	ρ −0.10 *P* 0.23	ρ 0.75 *P* < 0.0001	ρ 0.66 *P* < 0.0001	ρ 0.73 *P* < 0.0001	

The correlations are significant at the 0.01 level (bilateral). ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score based on C-reactive protein; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; mSASSS: modified Stoke Ankylosing Spondylitis Spine Score; RAPID3: Routine Assessment of Patient Index Data 3.

P < 0.0001), and BASFI and RAPID3 (ρ 0.73, *P* < 0.0001). The mSASSS did not show any correlation with any of the above composite measures.

Of the 131 patients, 41 (31.3%) achieved BASDAI remission, whereas 24 (18.3%) were in the ASDAS category of inactive disease (κ 0.46, 95% CI 0.29–0.63). κ agreement (0.53, 95% CI 0.37–0.69) was better between BASDAI remission and RAPID3 remission (28.2%). Finally, the best agreement was found between ASDAS inactive disease and RAPID3 remission (κ 0.56, 95% CI 0.39-0.72). However, when the 4 ASDAS activity categories were compared with the 4 RAPID3 severity levels, only a fair agreement was obtained with a weighted κ of 0.34 (95% CI 0.25–0.44).

Regarding the discriminant validity (Figure 2), the best cut-off on the RAPID3 to identify the inactive disease ASDAS category was ≤ 2, with area under the ROC curve (AUC) 0.91, sensitivity 83.3%, specificity 88.8%, and *P* < 0.0001. With respect to BASDAI remission, these values were as follows: optimal criterion ≤ 6, AUC 0.86, sensitivity 78%, specificity 86.7%, *P* < 0.0001. Table 3 shows the optimal RAPID3 criteria to identify the other categories of disease according to BASDAI and ASDAS.

Finally, a multivariate logistic regression was carried out to identify disease traits associated with remission states according to BASDAI, ASDAS, and RAPID3. For BASDAI remission, the only factor associated with this outcome was NSAID intake (OR 0.18, 95% CI 0.07–0.49, *P* = 0.001). With respect to ASDAS inactive disease, both NSAID (OR 0.08, 95% CI 0.02–0.28, *P* < 0.0001) and DMARD (OR 0.19, 95% CI 0.05–0.79, *P* = 0.02) exposure were negatively associated with this category. Regarding RAPID3 remission, women with axSpA were less likely to achieve this goal (OR 0.34, 95% CI 0.12–0.90, *P* = 0.03). Also, NSAID intake was negatively associated with RAPID3 remission (OR 0.26, 95% CI 0.10–0.66, *P* = 0.005).

DISCUSSION

In this study of patients with long-standing axSpA, the RAPID3, an instrument belonging to RA metrology, showed both good convergent and discriminant validity. Interestingly, the RAPID3 cut-off thresholds to discriminate remission by BASDAI and ASDAS were different; however, these cut-offs were similar for the high activity categories of both instruments. Another relevant finding of this study is that NSAID intake was significantly and independently associated with the failure to achieve a state of remission according to the thresholds of the 3 instruments. Women were less likely to achieve RAPID3 remission. Of all the SpA-specific tools, the only one that did not correlate with the others was the mSASSS. According to our results, it may be necessary to establish specific cut-off points for RAPID3 in subjects with axSpA, different from those set for RA, although this would require more studies. Therefore, as the analysis of construct validity demonstrated a good correlation between the RAPID3 sum score and both disease activity and functional disability indices, the RAPID3 may be measuring a broader concept than just disease activity or functional disability.

Multiple SpA-related questionnaires have been developed to assess disease status accurately, but feasibility remains a problem in clinical practice.[4] The BASDAI remains the gold standard for assessing disease activity in a routine practice, despite poor correlation with CRP levels and magnetic resonance imaging (MRI) inflammation. On the other hand, ASDAS performs better than BASDAI in assessing disease activity, and correlates with MRI inflammation.[4] However, it lacks feasibility as ESR and CRP values are often not available during a clinic visit, and these inflammatory markers are elevated in only 30–50% of patients.[4] In addition, the BASFI may not be sufficiently sensitive to detect subtle changes in functioning in patients without severe impairments.[4] Other less-used instruments such as the ASAS Health Index or the Bath AS Metrology Index are time-consuming, require training, and may not be feasible in busy clinics.[4] Therefore, although ASAS, in collaboration with Outcomes Measures in Rheumatology (OMERACT), developed a composite core set of variables to be measured for clinical and functional assessment, and for monitoring of axSpA in different clinical scenarios, most of these tools are difficult to implement in daily practice due to time constraints.[4] Therefore, there is a continuous search for new instruments to measure health in patients with axSpA that could be attractive and

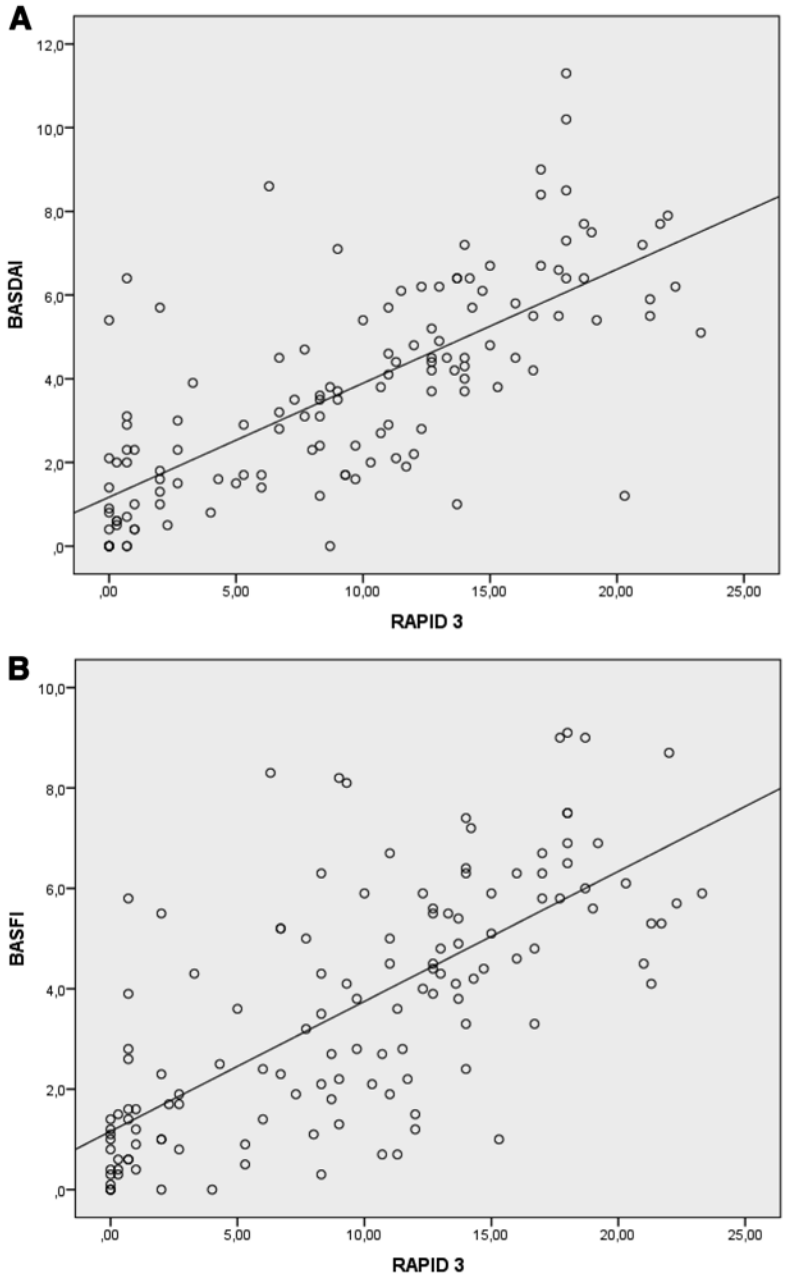

Figure 1. Graphs of correlations between RAPID3 and other axial SpA measures. The correlations were somewhat better between (A) RAPID3 and BASDAI and (B) RAPID3 and BASFI, compared to (C) ASDAS-CRP. ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score based on C-reactive protein; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; RAPID3: Routine Assessment of Patient Index Data 3; SpA: spondyloarthritis.

reliable in real-world clinical practice settings. RAPID3 could meet part of these expectations; however, as we will see below, in the last decade only 5 studies (indexed in PubMed) have been published on its usefulness in axSpA.

In a study by Michelsen, *et al* that compared the disease burden between RA, PsA, and axSpA, RAPID3 showed moderate to high correlations with the Disease Activity Score in 28 joints (ρ 0.52) and Clinical Disease Activity Index (ρ 0.77) in RA and PsA, and with BASDAI (ρ 0.90) and BASFI (ρ 0.87) in axSpA.[8] Cinar, *et al* found that RAPID3 was strongly correlated with BASDAI and ASDAS-ESR (r = 0.842 and r = 0.815, respectively). Among 209 patients with BASDAI high activity, 83.3% had high or moderate severity according to RAPID3 (κ 0.69).[9] In a Korean AS population, Park, *et al* showed that RAPID3 scores were correlated significantly with BASDAI (ρ 0.82) and ASDAS-ESR (ρ 0.76). All 21 patients with BASDAI ≥ 4, were among 39 patients who had RAPID3 > 12, whereas 79% of 33 patients with ASDAS > 1.3, had RAPID3 high severity.[10] Danve,

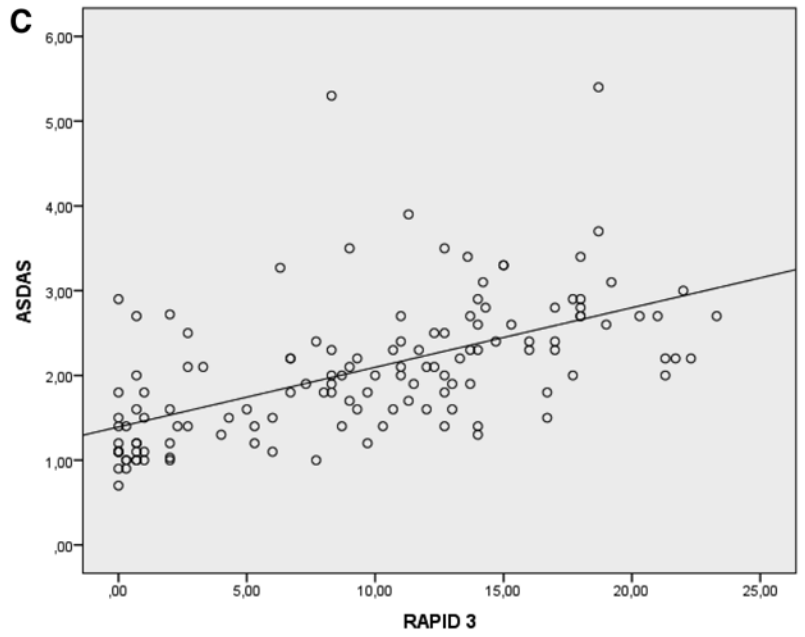

Figure 1. Continued.

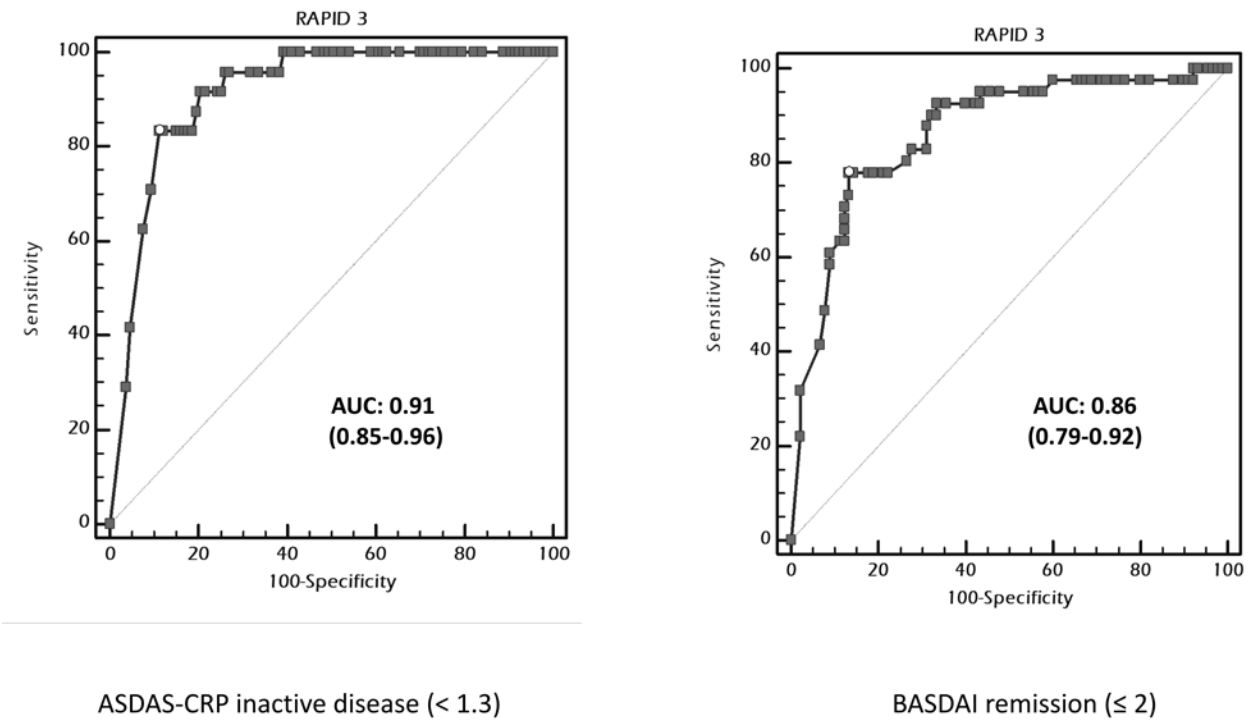

Figure 2. The AUC of the RAPID3 thresholds to identify the categories of inactive disease of ASDAS-CRP and BASDAI remission. ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score based on C-reactive protein; AUC: area under receiver-operating characteristic curve; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; RAPID3: Routine Assessment of Patient Index Data 3.

et al demonstrated high discriminant ability for RAPID3 with respect to BASDAI activity categories.[11] However, Castrejón, *et al* found that the strength of agreement of RAPID3 with ASDAS-CRP was moderate (κ 0.44) and was lower with BASDAI (κ 0.37). Responsiveness over 6 months was slightly higher for ASDAS-CRP and RAPID3-like index than that for BASDAI.[12] Our results (Spearman ρ range 0.66–0.78, and κ agreements range 0.34–0.56) are in line with the data presented above, reinforcing its reliability. In the cited studies, no information was provided on the possible association between structural

Table 3. Optimal cut-off thresholds of RAPID3 to identify activity categories other than remission according to ASDAS and BASDAI.

	RAPID3 Optimal Criterion	AUC (95% CI)	Sensitivity, %	Specificity, %	*P*
BASDAI LDA	≤ 10.7	0.86 (0.77–0.92)	75	86.2	< 0.0001
ASDAS LDA	≤ 10.7	0.75 (0.66–0.83)	65.2	73.8	< 0.0001
BASDAI HDA	> 10.7	0.89 (0.83–0.94)	86.2	84.9	< 0.0001
ASDAS H/vHDA	> 10.7	0.82 (0.75–0.88)	73.8	77.1	< 0.0001

BASDAI LDA: > 2 to < 4, ASDAS LDA: > 1.3 to < 2.1, BASDAI HDA: ≥ 4, ASDAS H/vHDA: ≥ 2.1. ASDAS: Ankylosing Spondylitis Disease Activity Score; AUC: area under receiver-operating characteristic curve; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; H: high; HDA: high disease activity, LDA: low disease activity; RAPID3: Routine Assessment of Patient Index Data 3; vHDA: very high disease activity.

damage and RAPID3. We evaluated this point but found no correlation between mSASSS and RAPID3. This was in some way an unexpected finding. However, we know from some reports that patients with structural damage and long-lasting disease who may be in clinical remission or low disease activity may have low disease impact. Therefore, it seems that structural damage is more closely related to disease impact and poor QOL in the short term but not so in the long term.[20]

Of all the factors analyzed, the one most consistently associated with failure to achieve remission as defined by BASDAI, ASDAS, and RAPID3, was the regular intake of NSAIDs. This aspect has already been pointed out in the literature and forces us to rethink the place that these drugs should occupy in the treatment of these conditions.[21] Regarding RAPID3 remission, the likelihood for the women in our study with axSpA to achieve this goal was reduced by 66%. It is known that women with axSpA tend to score higher for both pain and disease activity.[22] However, our finding is especially interesting if we consider very recent data showing that women with AS had an increased risk of delivering infants requiring intensive care and that a high RAPID3 score was associated with a higher risk of cesarean delivery.[23]

Our study has limitations. This was a cross-sectional observation and thus, RAPID3 responsiveness has not been determined. Further, results have not been presented on internal consistency or reproducibility, although both aspects have been contrasted in other RAPID3 publications.[7–12] We have also not contrasted the correlation between RAPID3 against enthesitis or axial metrology indices. Nevertheless, our results were consistent with those of previous studies, thus reinforcing its robustness and validity.

In summary, RAPID3 offers a comprehensive estimate for an optimal evaluation of axSpA in routine clinical practice. However, more studies are needed to endorse its role in this context.

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