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BRIEF REPORT

Correlation between rapid-3, DAS28, CDAI and SDAI as a measure of disease activity in a cohort of Colombian patients with rheumatoid arthritis

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Abstract The objective of this study is to correlate the patient-driven tool Routine Assessment of Patient Index Data 3 (RAPID-3) with other common tools used in daily practice to measure disease activity in rheumatoid arthritis (RA).One hundred nineteen RA patients according to 1987 American College of Rheumatology criteria who consecutively attended a RA outpatient clinic between August and December 2015 were evaluated. Data was stored in an electronic form that included demographic information, comorbidities, concomitant medication, and laboratory results. The disease activity was determined by tender and swollen joint count, pain and disease activity visual analog scales (VAS), disease activity score 28 (DAS28), Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), and multidimensional health assessment questionnaire (MDHAQ). Correlations between RAPID-3 and other disease activity tools were assessed. Mean age was 61 ± 13.8 years with a median disease duration of 14 years (IQR 5–21), 77% were females. Median scores were MDHAQ 0.5 (IQR 0.1–1.2), DAS 28 3.8 (IQR 2.7–5.1), and RAPID-3 12.3 (IQR 6–19). A strong correlation was obtained between RAPID-3 and DAS 28 (r 0.719, $p < 0.001$), CDAI (r 0.752, $p < 0.001$), and SDAI (r 0.758, $p < 0.001$). RAPID-3 had a high correlation with tools regularly used for disease activity assessment of RA patients in daily practice. The ease of its application favors routine use as it does not require laboratory results and joint counts.

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Introduction

In the last 20 years, we have witnessed remarkable progress in rheumatoid arthritis (RA) treatment. Clinical remission is a goal that is desired in all patients [1, 2]. Disease activity indices or clinimetrics facilitates decision-making to achieve goals of remission or low activity. Currently, there is enough evidence to support the advantages of treat to target objectives [3–5].

The concept of clinimetrics started at the end of the 1930s with Dr. Taylor, who suggested a chart to describe the degree of damage in chronic arthritis or rheumatism, based on clinical and radiological findings [6]. Later in the 1940s, Dr. Keele started working on a pain measurement, a work complemented in the 1970s by Dr. Huskisson, who published a visual analog scale (VAS), a tool currently used in rheumatology [7]. In 1949, the published therapeutic criteria by The New York Rheumatism Association established for the first time a classification for disease progression, functional capability, and response to treatment. In the 1950s, Dr. Landsbury published several articles on the quantification of RA activity and lab parameters including the degree of inflammatory involvement of affected joints [8–13]. In 1990, the disease activity score (DAS) was published, which included 44 joint count at first, and later was reduced to 28 tender and swollen joint count, as well as patient global assessment (PtGA) and erythrocyte sedimentation rate (ESR) as an acute phase reactant [14, 15].

Since the 1970s, the impact of RA in the patient's functionality began to be important, which subsequently led to the

development of tools like the Health Assessment Questionnaire (HAQ) and the Arthritis Impact Measurement Scales (AIMS) [16, 17]. Later on in the 1990s, the American College of Rheumatology (ACR) disease activity measures emerged, widely used in clinical trials, but complex for the use in daily clinical practice [18].

Currently, there are more than 60 indices to measure disease activity; however, only 6 are recommended by the ACR for use in clinical practice. These can be divided according to the information used by the tool: indices self-reported by the patient like PtGA and RAPID-3; indices with patient and provider information like CDAI; and indices with patient, provider, and lab tests (ESR, C-reactive protein or CRP) like DAS 28 or SDAI [1, 4, 19].

The European League Against Rheumatism (EULAR) only refers to composite indices that include joint count (DAS 28, CDAI, SDAI) and emphasizes that the ACR/EULAR remission definition includes SDAI as a clinimetric index [2, 5].

RAPID-3 is a composite index with information exclusively from the patient, collected through a self-reported questionnaire which includes three measurements: functionality (MDHAQ), pain VAS, and PtGA [20].

In daily practice, to obtain ESR or CRP results close to the time of clinical evaluation can be difficult, which can alter the results in composite indices like DAS 28 or SDAI. On the other hand, it has been discussed the contribution of acute phase reactants in the clinimetry result, especially considering that 40% of RA patients have normal values at the beginning of the disease [21]. Therefore, indices that do not require laboratory data have been proposed [22–24]. That is why we decided to evaluate the correlation between RAPID-3 and commonly clinimetric tools in a cohort of Colombian patients with RA, and consequently, determine RAPID-3 as a valid measure of disease activity.

Methods

Study population

Patients with RA according to 1987 American College of Rheumatology (ACR) criteria who consecutively attended the Hospital Militar Central rheumatology outpatient RA clinic in Bogotá, Colombia, between August and December 2015 were evaluated. Data was recollected and stored in a previously approved and validated structured electronic questionnaire (eHealth), which included demographic information, characteristics of the disease, comorbidities, previous and current treatment, laboratory test results, MDHAQ, pain VAS, and PtGA [25]. Physical examination was made by expert rheumatologists previously trained in joint assessment. It included 28 tender and swollen joints. Blood samples for ESR and CRP determination were obtained the day of clinical evaluation.

Table 1 Demographic characteristics

Age (mean; SD)	61 ± 14
Sex (*n*, %)	
Male	27 (22.7)
Female	92 (77.3)
Years of disease (median, IQR)	14 (5–21)
Cardiovascular comorbidities (*n*, %)	
Hypertension	55 (46.2)
Metabolic comorbidities (*n*, %)	
Hypothyroidism	25 (21.0)
Osteoporosis	30 (25.2)
Autoimmune comorbidities (*n*, %)	
SLE	1 (0.8)
Sjögren Syndrome	14 (11.8)
Treatment (*n*, %)	
Glucocorticoids	64 (53.8)
Methotrexate	79 (66.4)
Leflunomide	49 (41.2)
Sulfasalazine	15 (12.6)
Antimalarials	29 (24.4)
Etanercept	4 (3.4)
Rituximab	7 (5.9)
Tocilizumab	1 (0.8)
Abatacept	3 (2.5)
Certolizumab	2 (1.7)
Infliximab	2 (1.7)
Adalimumab	10 (8.4)

SD standard deviation, *SLE* systemic lupus erythematosus

DAS 28 by ESR, CDAI, SDAI, and RAPID-3 was calculated for each patient.

Statistical analysis

All stored data were reviewed and refined before analysis in the statistical package SSPS version 19.0 (SPSS Inc., USA). For data presentation, central tendency measurements, percentages, and frequency tables according to normal distribution of the variables were used. For group comparison, Student's *t* test, chi-squared, and Mann-Whitney *U* were used according to the variable characteristics. Spearman or Pearson correlation coefficient was used according to the data distribution. A value of statistical significance at $p < 0.05$ and 95% confidence intervals were established.

Results

Study population

In total, 119 patients were evaluated, 77% were females. The median disease duration was 14 (IQR 5–21) years. The most frequent comorbidity was arterial hypertension (*n* 55, 46.2%). The demographic characteristics are depicted in Table 1.

Disease activity

Median scores were MDHAQ 0.5 (IQR 0.1–1.2), DAS 28 3.8 (IQR 2.7–5.1), and RAPID-3 12.3 (IQR 6–19). The studied population was classified according to the degree of disease activity. Remission is as follows: 12.6% RAPID-3, 23.5% DAS 28, 10.9% CDAI, and 11.8% SDAI. Results in detail are presented in Table 2.

Correlations

In general, the correlation of RAPID-3 was good with DAS 28 (r 0.71, $p < 0.001$), and better with SDAI (r 0.75, $p < 0.001$) and CDAI (r 0.75, $p < 0.001$). The results of the different tools are presented in Fig. 1.

Kappa weighted results of the agreement between RAPID-3 and DAS 28 by ESR, MDHAQ, CDAI, and SDAI are 0.61, 0.46, 0.38, and 0.27, respectively.

Discussion

The present study determined the degree of disease activity using common methods used in daily practice in an unselected group of Colombian patients with RA in different stages, comorbidities, and treatment, reflecting the real life of patients seen in an outpatient clinic specialized in the care of patients with RA.

Our study found a high correlation between RAPID-3 compared with ESR-DAS 28, CDAI, and SDAI in patients with RA. We demonstrated that RAPID-3 was a reliable and valid tool compared to other well-established disease activity indices. Although we did not measure the time spent performing any of the assessment tools, it is clear that the RAPID-3 is completed in a much shorter time and does not require staff training.

Although there is few information on the use or validation of RAPID-3 in Latin American populations, a study in Colombia made by Amaya-Amaya et al. found similar results. While the main objective of the study was not a direct correlation between RAPID-3 and different disease indices, they describe a correlation of RAPID-3 with CDAI of 0.73, SDAI of 0.70, and DAS 28 of 0.52 [26]. It is important to note that these results were obtained during rheumatoid arthritis focus groups, while our results were obtained during the actual rheumatology consultation.

In a study from India by Dr. Singh and colleagues, 200 patients sought to compare different categories of severity of the RAPID-3 with those of DAS 28 and CDAI [27]. The study

Table 2 RAPID-3 comparison with other disease activity scores

RAPID-3					
	I (NR)	II (LS)	III (MS)	IV (HS)	Total
	15 (12.6)	15 (13.4)	26 (21.8)	62 (52.1)	119 (100)
DAS 28 ESR (*n*, %)					
I (remission 0–2.6)	13 (86.6)	8 (50.0)	7 (26.9)	0 (0.0)	28 (23.5)
II (low activity 2.61–3.2)	1 (6.7)	2 (12.5)	5 (19.2)	6 (9.7)	14 (11.8)
III (moderate activity 3.21–5.1)	1 (6.7)	5 (31.3)	11 (42.3)	35 (56.5)	52 (43.7)
IV (high activity >5.1))	0 (0.0)	1 (6.3)	3 (11.5)	21 (33.9)	25 (21.0)
CDAI (*n*, %)					
I (remission 0–2.8)	11 (73.3)	2 (12.5)	0 (0.0)	0 (0.0)	13 (10.9)
II (low activity 2.81–10.0)	3 (20.0)	12 (75.0)	18 (69.2)	5 (8.1)	38 (31.9)
III (moderate activity 10.1–22.0)	1 (6.7)	1 (6.3)	7 (26.9)	30 (48.4)	39 (32.8)
IV (high activity >22)	0 (0.0)	1 (6.3)	1 (3.8)	27 (43.5)	29 (24.4)
SDAI (*n*, %)					
I (remission 0–3.3)	12 (80.0)	1 (6.3)	1 (3.8)	0 (0.0)	14 (11.8)
II (low activity 3.31–11.0)	3 (20.0)	14 (87.3)	23 (88.5)	22 (35.5)	62 (52.1)
III (moderate activity 11.1–26.0)	0 (0.0)	1 (6.3)	1 (3.8)	19 (30.6)	21 (17.6)
IV (high activity >26)	0 (0.0)	0 (0.0)	1 (3.8)	21 (33.9)	22 (18.5)
MDHAQ (*n*, %)					
I (no disability 0–0.3)	14 (93.3)	13 (81.3)	10 (38.5)	5 (8.1)	42 (35.3)
II (low disability 0.31–1.3)	1 (6.7)	3 (18.7)	12 (46.2)	17 (27.4)	33 (27.7)
III (moderate disability 1.31–1.8)	0 (0.0)	0 (0.0)	3 (11.5)	27 (43.5)	30 (25.2)
IV (high disability >1.8)	0 (0.0)	0 (0.0)	1 (3.8)	13 (21.0)	14 (11.8)

NR near remission (0–3.0), *LS* low severity (3.1–6.0), *MS* moderate severity (6.1–12.0), *HS* high severity (>12), *DAS 28 ESR* disease activity score 28 erythrocyte sedimentation rate, *CDAI* clinical disease activity index, *SDAI* simplified disease activity index, *MDHAQ* multidimensional health assessment questionnaire

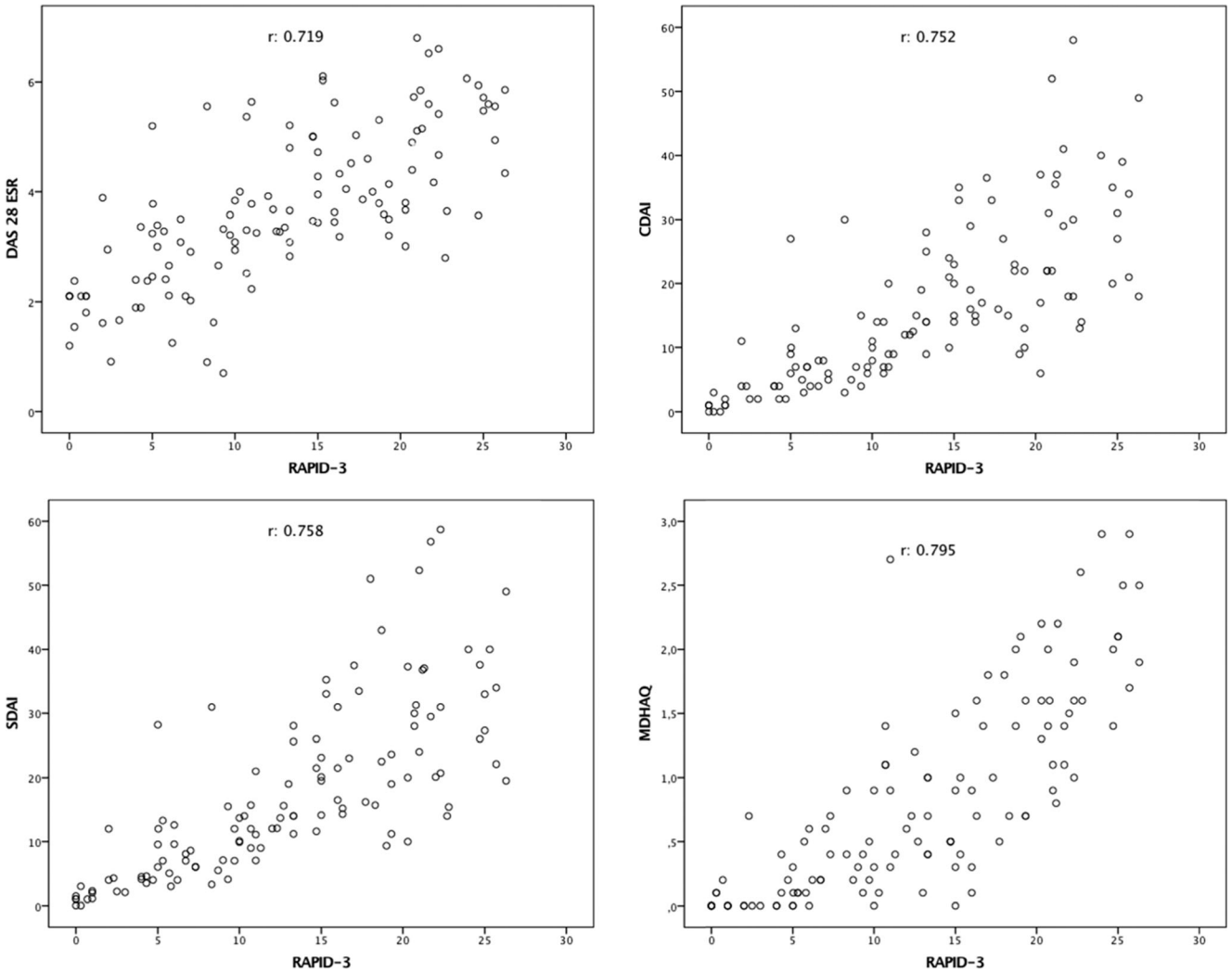

Fig. 1 Correlation between RAPID-3 and other disease activity scores

population was younger than ours, with a mean age of 42.2 years, a lower disease duration (4.9 vs 15.2 years) and a similar male to female ratio. The PtGA was very similar (4.7 vs 4.9) as well as Practitioner Global Assessment (PrGA) (4.0 vs 3.8). As for the results of clinimetry, there were differences between the mean value for the DAS 28 (5.2 vs 3.8) and CDAI (24 vs 15.8), and very similar for RAPID-3 (12.7 vs 12.2).

We do not intend to ignore the importance of physical examination in monitoring patients with RA, but there is no doubt that in clinical settings in which you have little time and where resources are limited or not available reliable laboratory results, the RAPID-3 becomes a valid and attractive option.

RA like many other rheumatic diseases, due to its complexities, lack of a gold standard for measuring and monitoring [28]. Of the numerous indices available for measuring disease activity, only six are recommended for routine use by the ACR [1]. Of those, DAS 28 arguably is the most popular, frequently mentioned in the literature, included in most clinical trials and for some authors, the most specific measurement for monitoring RA especially in the short term, mainly because it includes a formal tender and swollen joint count [29, 30].

On the other hand, the definition of ACR/EULAR remission includes SDAI above other indices but not RAPID-3; this is confirmed in the latest update of the EULAR guidelines for the management of RA [2, 5].

In daily clinical practice, not all rheumatologists perform a routinely complete joint count, or sometimes, the patient's complaint is in the feet, which are not evaluated by the DAS 28, CDAI, or SDAI. Along with this, it should be noted that in countries like Colombia, the small number of rheumatologists (152 per 48 million inhabitants) and the demands of the health system sometimes forces to evaluate a large number of patients in a short period of time, making it increasingly difficult to perform mixed clinimetric indices, and instead offering advantages to those that are self-reported like RAPID-3.

Another limitation that may have tools such as DAS 28 and SDAI is the need for laboratory tests (acute phase reactants), not always available for different reasons. Also, it contributes to increasing the costs of the disease without providing much

to the end result [24]. For example, in the case of DAS 28, ESR seems to contribute more in the scenario of low disease activity [31]. For this reason, the use of questionnaires, which can be self-reported in the waiting room, is quite more attractive.

Several studies have evaluated the time required to complete these scores, finding that the RAPID-3 can be finished in seconds with more than acceptable correlation regarding scores and classification according to activity degrees [27, 32–34]. This was also observed using data from two clinical studies that evaluated the efficacy of abatacept in patients with inadequate response to methotrexate and anti TNF, where RAPID-3 showed a similar performance DAS 28 [35].

It must be taken into account that when disease activity is evaluated by RAPID-3, a tendency of higher disease activity rather than remission will appear, meaning that most of the patients will concentrate on higher disease activity categories. This could be explained by the fact that the RAPID-3 is based exclusively on answers by the patient, while the other indices combine measures of patient, physician, and laboratory results, which could modulate the importance that the patient gives to their symptoms independently of the objective improvement in laboratory results and physician evaluation. Clinicians should be aware of this situation in the regular use of these indices in clinical practice.

Our study has limitations. First, although we included patients with early arthritis, most of the patients had an established rheumatoid arthritis (mean disease duration of 15 years), which does not allow to determine if the correlation between RAPID-3 and other disease activity indices is the same in different stages of the disease. Second, although CRP was measured, not all the patients had the same CRP laboratory technique. This issue avoided us to calculate DAS 28 with CRP.

The results obtained in this study support the fact that RAPID-3 should be considered for routine evaluation of patients with RA taking into account its very good correlation with DAS 28, CDAI and SDAI.

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Compliance with ethical standards The study was approved by the ethical committees of the Hospital Militar Central (2013-17897). All patients signed informed consent. Data confidentiality was guaranteed. The protocol fulfilled the Colombian Ministry of Health policies according to the resolution 8430 of 1993 (https://www.invima.gov.co/resoluciones-medicamentos/2977-resolucion-no-8430-del-4-de-octubre-de-1993.html).

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