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Is There a Correlation Between DAS28/RADAI in a Cohort of Rheumatoid Arthritis Patients Treated with Biological Therapy

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Abstract

Aim: To describe the degree of activity of RA patients receiving biological agents co-monitored by rheumatologist and nurses. To assess RA activity using validated methods: DAS28, RADAI, visual analog scales (VAS), and to evaluate the correlation between them and the applicability in routine clinical practice.

Methods: 114 patients with RA treated with biological agents, according to the American College of Rheumatology (ACR) 2010 criteria in shared nursing consultations from 12 Catalan hospitals were included. We analyzed whether there was good correlation between RADAI index and DAS28.

Results: The mean value in the VAS scale was 2.85 (SD = 2.15), the mean RADAI self-assessment questionnaire level was 2.74 and the mean DAS28 index was 2.89. The majority of patients (63.1%) had a low disease activity (DAS28 < 3.2). 49/114 patients (44.1%) had a DAS < 2.6 (remission). Most patients treated with biologic agents have a good control of the disease, as measured by DAS28 objectively and subjectively by RADAI.

Conclusions: The involvement of a multidisciplinary team (rheumatologist/ nursing) can coordinate patient care and establish consensus on the management of RA patients. Even though there are different tools of establishing the status of our patients, metrological evaluation with DAS28 is to date the most reliable, flexible and reproducible outcome measure.

Keywords

Rheumatoid arthritis, Biological therapy, Nurse and rheumatologist management, RADAI, DAS28

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory heterogeneous disease presenting with acute flares, showing a prevalence of 0.5% in Spanish population according to the study EPISER and an annual incidence of 8.3 cases per 100,000 population, and that in the absence of optimal and individualized treatment causes a long-term severe disability [1,2]. The therapeutic target in RA is remission and in the absence, to obtain a low sustained inflammatory disease activity, pursuing a better quality of life, through the control of symptoms, prevention of structural damage, normalization of social participation and functional capacity [3].

The treatment strategy has changed in the last decade, improving the dosage of classical drugs like methotrexate, performing double or triples combinations of DMARDs, or performing a tight control of disease. A strategy of intensive and tight outpatient monitoring, improves substantially the disease activity, radiographic progression, functional capacity, physical function and quality of life, without an increase in economic costs [4,5]. Subsequently, the advent and implementation of biological therapies has really changed course and prognosis. In addition, the progressive collaboration with specialized nursing allows us to improve patient information therapeutic target, and treatment strategy to be used [3].

To evaluate its activity, we use visual analogic scales (VAS), together with other measures validated such as Simple Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), beside the fully accepted measurement DAS28 [6]. Obviously, the

Table 1: Statistics obtained in the RADAI and DAS28 measurements.

Variable	Number of observations	Average	Standard Deviation	Median	Mínimum	Maximum
RADAI	97	2.74433	2.25716	2.20000	0	9.80000
DAS28	111	2.89324	1.18863	2.82619	0.39598	6.32000

Table 2: DAS28 and RADAI correlation.

	RADAI	DAS28
RADAI	1.00000 97	0.66451 < 0.0001 94
DAS28	0.66451 < 0.0001 94	1.00000 111

*Pearson´s correlation; Prob > |r| accepting H0: Rho = 0 Number of observations.

Table 3: Parameter estimation with standard error.

Variable	DF	Estimator parameter	Standard error	T value	P value
Intercept	1	1.92707	0.14311	13.47	< 0.0001
RADAI	1	0.34550	0.04051	8.53	< 0.0001

choice of the composite method to measure disease activity and the target value may be influenced by co-morbidity, drug and patient risk factors [3].

The progressive collaboration with specialized nurses in RA clinics, allow rheumatologists to streamline the consultation, in parallel to increase its complexity. Currently, the contribution of nurses allows using validated methods of measurement (DAS28, HAQ), assessing cardiovascular risk factors, educate patients to administer an immunomodulatory or biological therapy, and monitoring in coordination with the rheumatologist, the adverse effects of these therapies. In case of adverse events with conventional or biological DMARDs, nursing notifies the rheumatologist who decides the therapeutic approach and the measures to be taken [7]. The DAS28 index is a well implemented index nowadays, which allows a comprehensive and objective assessment of the degree of activity of RA, while the Rheumatoid Arthritis Disease Activity Index (RADAI) index measures the activity of RA perceived subjectively by the patient on a scale of 0-10 on 5 weighted questions. Includes 5 items: 1) Activity of the disease in the last six months (0-10), 2) Activity by pain and joint swelling (0-10), 3) Joint pain (0-10) 4) Duration of the morning stiffness (0-6), 5) tender joint count (0-48) with a range from 0 to 50 [8].

The aim of our project was to describe the degree of activity of RA patients receiving biological agents in clinical remission, monitored by the rheumatologist and nurses together, to assess the activity using validated methods DAS28, RADAI, visual analog scales (VAS), and to evaluate the correlation between them and the applicability in routine clinical practice.

Material and Methods

We aimed to correlate different tools of activity of a cross-sectional cohort of 114 patients with RA treated with biological agents, according to the American College of Rheumatology (ACR) 2010 criteria that were in DAS28 remission, in 12 shared nursing outpatient clinics from Catalan hospitals. We registered age, sex, and clinical data of the disease such as disease durations, rheumatoid factor, anti-CCP antibodies and steroid joint injections received the previous three months. Patients were asked for their current drug treatments. Activity was measured by the index values such as DAS28, the RADAI questionnaire and the estimated degree of pain by the patient (VAS) in a range (0-10). Statistical analysis for average comparisons, Kruskall-Wallis test and the Pearson´s correlation coefficients were used using a SPSS 17.0 package.

Results

114 patients met the inclusion criteria, with a mean age of 58.56 years (SD = 46.29), and 77% were women. A total of 90/114 patients (81.1%) had rheumatoid factor and 51/114 (55.4%) had anti-CCP antibodies.
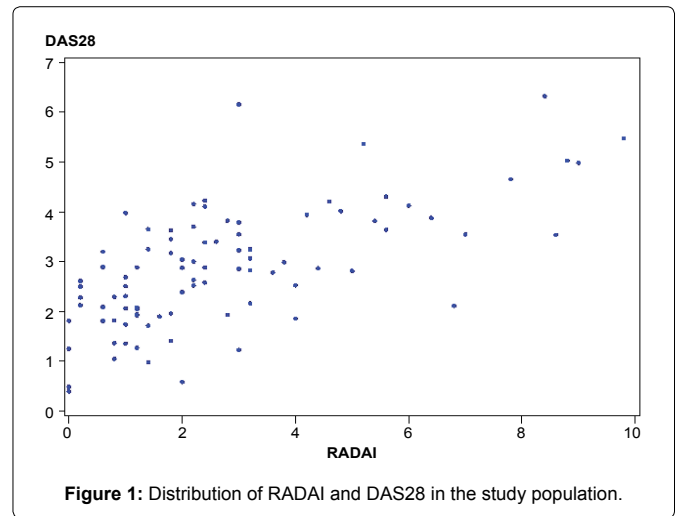
Figure 1: Distribution of RADAI and DAS28 in the study population.

The disease duration since diagnosis was 11.23 years (SD = 8.27). The treatments received at that time were: 69 (60.5%) Etanercept, 47 (41.2%) Adalimumab, 9 (7.9%) Infliximab, 3 (2.6%) Abatacept, 1 (0.9%) Anakinra. Ten patients (10.8%) received joint injections in the 3 months prior to the visit. The mean value in the VAS scale was 2.85 (SD = 2.15), the mean RADAI self-assessment questionnaire level was 2.74 and the mean DAS28 index was 2, 89. The majority of patients (63.1%) had a low disease activity (DAS28 < 3.2). 49/114 patients (44.1%) had a DAS < 2.6 (remission).

Correlation DAS28 and RADAI Index

The values of minimum and maximum RADAI observed in the study population varied range between 0.00 and 9.80 respectively, with a mean (and standard deviation) of 2.74 (2.26) (Table 1). The DAS28 index was calculated from the formula DAS28 = $0.56\sqrt{(t28)}$ + $0.28\sqrt{(SW28)}$ + $0.70\text{Ln}(VSG)$ + $0.014 \times VGP$ (t28: number of tender joints; SW28: number of swollen joints; erythrocyte sedimentation rate or ESR (mm/hr) and overall disease assessment by the patient (VGP of 0-100)). The minimum and maximum observed values of DAS28 of the study population were 0.39 to 6.32 respectively, with a mean (and standard deviation) of 2.89 (1.19) (Table 1). We analyzed whether there was good correlation between RADAI index and DAS28. It was found that although the correlation between them was significant (p < 0.0001), this correlation was not powerful (r = 0.6645) (Table 2). On the other hand a model to have an estimation of DAS28 from RADAI and vice versa index was constructed. The best model fit to the line DAS28 = $0.3455 \cdot \text{RADAI} + 1.92707$ (Table 3). However, estimation errors were high, explaining the model, only 44% of the variance. The distribution graphically of the DAS28 and RADAI self evaluated by patients is shown in figure 1.

Discussion

The RADAI index is a method of subjective assessment, easy to use to assess disease activity in RA patients, especially in observational studies or monitoring of patient groups. It is a self-completed questionnaire that combines five items into a single activity index of the current and past illness, pain, morning stiffness and joint count. In terms of practicality, a large majority of patients can complete the questionnaire in 5-7 minutes with no problems. Our results show that, DAS28 and RADAI reasonably correlated (p < 0.001), in a series of patients with low activity disease or remission treated with biological therapy, which does not mean that in a DAS28 active patient with painful and swollen joints we could replace an index for the other alternatively in clinical practice. Stucki G, et al. tried on a re-test to evaluate the applicability of monitoring RADAI in a cohort of active

rheumatoid arthritis [8]. Subsequently, Fransen J, et al. demonstrated the validity and reproducibility of RADAI, but showing that RADAI differs significantly between subgroups of RA, having different degree of disease activity measured by DAS28 [9]. If we recognize RA as a heterogeneous process, monitoring activity can differ between various types of disease, therefore, not all the measurement indexes offer objective and reproducible results in active patients. Walter MJ, et al., assessed the suitability of the "patient-Reported Outcomes (PRO) as primary indicators of identification and prediction of a subsequent change in the DAS28 > 3.2. Patients completed the PRO (HAQ, VAS, and RADAI) monthly, and were evaluated every 3 months using DAS28. Using a Bayesian model that combines changes in 3 PRO, demonstrated that provided a moderate performance after a model validation (sensitivity 0.61, specificity 0.75) [10]. That is probably due to a higher measurement by patients when they are asked about their tender and swollen joints, than if this is done by the rheumatologist [9]. Several studies have shown low or no correlation between self-completed questionnaires and biochemical parameters of inflammatory activity such as CRP and ESR. Balsa A, in a review already in 2011, comments the creation of an ACR / EULAR subcommittee that might propose new criteria for referrals based on a categorical classification and an index of activity such as the SDAI, to allow easier use in daily clinical practice [11]. This is mainly due to that in active RA, correlation RADAI / DAS28 has less validity but in patients with low activity or remission, the correlation between the two indices is more favorable.

In RA with low activity disease or remission, the increasing role developed by specialized nursing in collaboration with the rheumatologist in the management of the patients, leading educational programs and being the direct on-line contact when appears any kind of adverse event, is becoming more prominent. To support this evidence, our report demonstrates that in patients with low disease activity or remission, nursing can play a role in monitoring the patients using the available tools we have actually such as DA28, RADAI, CDAI, and SDAI. Moreover, a recent work in this line of Primdahl J, et al. designed to compare the evolution and prognosis at 2 years of monitored RA patients in remission, the nursing group, who performs alternately consultation with rheumatologist, provides favorable outcomes valued by subjective and objective methods in terms of satisfaction [12].

More recently, the development of RADAI-5 updated version of index, in clinical practice provide information from the standpoint of the patient at any time. RADAI-5 showed a significant correlation with all other composite indices [13].

The present study, however, has several limitations that should be mentioned. First, it is an observational cohort study of clinical practice, with a relatively small number of patients without any pre-established protocol. We show our results that pretended to validate DAS28/RADAI indices in a number of patients, monitored alternatively by nurses and rheumatologists. Whereas, it has a great point if interest. We consider that the increasing role that nursing plays in the management of low disease activity or in patients in clinical remission, permits rheumatologists to improve their clinics. Secondly, to date several subjective indices have been proved to be useful to measure in RA activity, such as CDAI, SDAI, RADAI, and even more the updating of the already existing, such as RADAI 5. The RADAI-5 is analogous to the RADAI with replacement of joint counts by the patient's general health assessment and change of question format to an ordered category scale. The RADAI-5 is significantly correlated with the original RADAI, CDAI, SDAI, DAS28-ESR, and DAS28-CRP. To date, translations in German and English but not in Spanish are available. Therefore, we aimed to correlate the gold standard; DAS28 to the subjective index widely extended and validated in Spanish. Third, the power of the study might be low but, we desired to correlate those indices in high activity diseases, but we performed the comparison in RA treated with biological therapy and that had already obtained clinical remission or low disease activity.

Finally, our results show that most patients treated with biologic agents have a good control of the disease, as measured by DAS28 objectively and subjectively by RADAI. The involvement of a multidisciplinary team (rheumatologist/ nursing) can coordinate patient care and establish consensus on the management of these patients. The RADAI, might in our cohort of patients be a reliable method to set the state of RA patient subjectively, but cannot replace DAS28 by RADAI in patients with increased disease activity.

In summary, emphasizing the collaboration between rheumatologists and specialized nurses, we reaffirm that, even though there are different tools of establishing the status of our patients, metrological evaluation with DAS28 is to date the most reliable, flexible and reproducible outcome measure.

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