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ORIGINAL ARTICLE

Clinical predictors of remission and low disease activity in Latin American early rheumatoid arthritis: data from the GLADAR cohort

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Abstract

Objectives To identify baseline predictors of remission and low disease activity (LDA) in early rheumatoid arthritis (RA) from the GLADAR (*Grupo Latino Americano De estudio de la Artritis Reumatoide*) cohort.

Methods Patients with 1- and 2-year follow-up visits were included. Remission and LDA were defined by DAS28-ESR (< 2.6 and ≤ 3.2, respectively). Baseline predictors examined were gender, ethnicity, age at diagnosis, socioeconomic status, symptoms' duration, DMARDs, RF, thrombocytosis, anemia, morning stiffness, DAS28-ESR (and its components), HAQ-DI, DMARDs and corticosteroid use, and Sharp-VDH score. Multivariable binary logistic regression models (excluding DAS28-ESR components to avoid over adjustment) were derived using a backward selection method (α-level set at 0.05).

Results Four hundred ninety-eight patients were included. Remission and LDA/remission were met by 19.3% and 32.5% at the 1-year visit, respectively. For the 280 patients followed for 2 years, these outcomes were met by 24.3% and 38.9%, respectively. Predictors of remission at 1 year were a lower DAS28-ESR (OR 1.17; CI 1.07–1.27; $p = 0.001$) and HAQ-DI (OR 1.48; CI 1.04–2.10; $p = 0.028$). At 2 years, only DAS28-ESR (OR 1.40; CI 1.17–1.6; $p < 0.001$) was a predictor. Predictors of LDA/remission at 1 year were DAS28-ESR (OR 1.42; CI 1.26–1.61; $p < 0.001$), non-use of corticosteroid (OR 1.74; CI 1.11–2.44; $p = 0.008$), and male gender (OR 1.77; CI 1.2–2.63; $p = 0.036$). A lower baseline DAS28-ESR (OR 1.45; CI 1.23–1.70; $p < 0.001$) was the only predictor of LDA/remission at 2 years.

Conclusions A lower disease activity consistently predicted remission and LDA/remission at 1 and 2 years of follow-up in early RA patients from the GLADAR cohort.

Key Points
- *In patients with early RA, a lower disease activity at first visit is a strong clinical predictor of achieving remission and LDA subsequently.*
- *Other clinical predictors of remission and LDA to keep in mind in these patients are male gender, non-use of corticosteroids and low disability at baseline.*
- *Not using corticosteroids at first visit is associated with a lower disease activity and predicts LDA/remission at 1 year in these patients.*

Keywords Early RA outcomes · Early RA remission · Early RA response predictors · Latin America early RA

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Introduction

Rheumatoid arthritis (RA) is an inflammatory joint disease associated with adverse clinical consequences and high rates of disability if not adequately controlled [1–3]. An early diagnosis and timely interventions have been shown to improve clinical, radiological and

functional outcomes in these patients. Current guidelines recommend intensive treatment to achieve clinical remission for early RA and clinical remission or low disease activity (LDA) for established disease [4, 5]. These objectives can be achieved in a substantial number of patients applying a treat-to-target (T2T) strategy; however, many challenges may be encountered in daily clinical practice in Latin America [6] and other low-middle income countries around the world, making it difficult for many patients to achieve these objectives. These difficulties include limited access to health care and to appropriate medications and poor adherence [7, 8]; thus, implementing an effective care management model under these circumstances is a true challenge [9–11].

Information about local rates of remission, LDA and their prognostic factors in patients with early RA might permit a better management strategy, with an appropriate stratification of subjects at risk of adverse clinical outcomes; however, regional RA studies have mainly aimed at characterizing the clinical and epidemiological features of the disease [12–15]. Available data from these studies have demonstrated that Latin American RA patients exhibit high disease activity at baseline or cohort entry, poor rates of remission and high to moderate disability with a modest use of conventional (c) disease-modifying antirheumatic drugs (DMARDs) and very limited use of biologic therapy [12–16].

Most studies about factors predictive of remission and treatment response in early RA have been performed primarily in Caucasian patients from North America and Europe [17–20] while information from Latin America, except for single-center studies [16, 21], is lacking. The GLADAR (*Grupo Latino Americano De estudio de la Artritis Reumatoide* or Latin American group for the study of rheumatoid arthritis) cohort was initially constituted to describe the clinical profile and DMARD use in patients with early RA from the region [13]; we have previously identified deleterious features in patients from this cohort [12, 13]. The aim of the present study was to identify baseline demographic and clinical predictors of response in these patients by examining disease activity status (remission and LDA) at 1 and 2 years of follow-up as the outcome.

Materials and methods

Patients

The GLADAR cohort is a longitudinal, observational, multicenter, and multinational inception cohort constituted by 1093 RA patients with early disease (< 1 year of disease duration) from 46 medical centers in 14 Latin American countries. Patients were included if they were at least 18 years of age and had met the 1987 American College of Rheumatology (ACR) classification criteria [22]. Enrollment began on April 2004 and was completed on July 2005; yearly follow-up visits were planned. Demographic and clinical assessments were performed with validated measures in all centers, following a previously approved common protocol [12, 13]. These measurements included the socio-demographic characteristics, clinical features, laboratory tests and autoantibodies, medication, disability, and joint damage as assessed radiographically. To this end, standard posteroanterior radiographs of the hands/wrists and feet were taken; these radiographs were assessed at each participating center by an expert rheumatologist or radiologist using the Sharp modified by Van Der Heijde (Sharp-VDH) score [23].

For the study, only patients with complete clinical and laboratory baseline assessments and who had 1- and/or 2-year follow-up visits were included.

Predictors of remission and LDA/remission

Baseline demographic and clinical variables examined as potential predictors of remission and LDA/remission were gender, age at diagnosis, socioeconomic status (measured by the Graffar scale) [24], ethnicity (as per GLADAR definition) [12], symptoms' duration, delay on initiation of DMARDs, rheumatoid factor (RF) positivity, erythrocyte sedimentation rate (ESR), anemia, thrombocytosis, morning stiffness of > 1 h, baseline disease activity (as measured by the disease activity score of 28 joint count with erythrocyte sedimentation rate, DAS28-ESR), tender joint count (TJC), swollen joint count (SJC), patients' visual analogue scale (patient's VAS), baseline disability (measured by Health Assessment Questionnaire-Disability Index, HAQ-DI), and baseline use of cDMARDs (monotherapy or in combination), biologic DMARDs (bDMARDs), corticosteroids, and the Sharp-VDH score. The original protocol considered anti-citrullinated protein antibodies (ACPA) measure, but we were not able to obtain them in the large majority of patients and thus this variable could not be included as a predictor.

Outcomes

Remission and LDA were defined with DAS28-ESR [25]. Remission was defined as a DAS28-ESR < 2.6 and LDA as a value between 2.6 and ≤ 3.2 as a single time-point measure, at 1 and 2 years of follow-up after enrollment. LDA/remission category included patients who achieved either LDA or remission (two acceptable outcomes in the treatment of RA) [4].

Statistical analyses

ARTRHOS 6.0 was used for data collection. Continuous variables were expressed as means and standard

deviations (SD), and categorical variables as numbers and percentages with their corresponding 95% confidence intervals (95% CI). Univariable and multivariable binary logistic regression models were examined to determine the predictors of remission and LDA/remission at 1 and 2 years after cohort entry. For each outcome, a multivariable binary logistic regression model was derived using a backward selection method with α-level to stay in the model set at 0.05. All variables included in the descriptive analysis were considered candidates for inclusion in the multivariable model (except for the DAS28-ESR components—TJC, SJC, patient's VAS, and ESR—in order to avoid an over-adjustment bias).

Two alternative models were examined. In the first, baseline categories of disease activity (remission, < 2.6; low, 2.6 to 3.2; moderate, > 3.2 to 5.1; and high disease activity, > 5.1, respectively) instead of the DAS28-ESR value were examined as predictors. In the second, the components of the DAS28-ESR (TJC, SJC, the patient's VAS, and the ESR) were included rather than the DAS28-ESR in order to explore their impact.

Results

General characteristics and remission rates

Four hundred ninety-eight GLADAR cohort patients (with complete clinical and laboratory baseline assessments) were included in these analyses. Four hundred twenty-four (85.1%) patients were female; the mean (SD) age at diagnosis was 45.9 (13.6) years. Three hundred eighty-four (77.1%) patients were RF positive. At the baseline visit, remission was reached by 18 (3.6%) patients, LDA by 14 (2.8%), moderate activity by 106 (21.3%), and high disease activity by 360 (72.3%). Three hundred thirty-one (66.5%) patients at baseline were receiving glucocorticoids, 396 (79.5%) cDMARDs (49.4% one cDMARD, and only 30.1% cDMARDs in combination); only five (1.0%) patients had received at least one bDMARDs (see Table 1).

Remission by DAS28-ESR was met by 96 (19.3%) patients and LDA/remission by 162 (32.5%) at the 1-year follow-up visit. Two hundred eighty patients were followed for at least 2 years; remission and LDA/remission were met by 68 (24.3%) and 109 (38.9%) of these patients, respectively.

Remission and LDA/remission predictors: univariable analysis

In the univariable analysis, predictors of remission at 1 year were anemia: 24.6% vs. 11.0%, $p = 0.005$; a lower baseline of the DAS28-ESR: 6.3 (1.6) vs. 5.1 (1.6), $p < 0.001$; all components of the DAS28-ESR (SJC—12.2 (6.8) vs. 8.1 (7.6), $p < 0.001$; TJC—18 (12.3) vs. 45.3 (28.2), $p < 0.001$; patients' VAS—56.4 (28.3) vs. 45.3 (28.2), $p = 0.001$); HAQ-DI: 1.5 (0.8) vs. 1.00 (0.8), $p < 0.001$; and corticosteroid use: 276 (83.4%) vs. 55 (57.3), $p = 0.034$. Predictors of LDA/remission at 1 year were male gender: 42 (12.5) vs. 32 (19.8), $p = 0.03$; anemia: 26.6% vs. 14.8%, $p = 0.007$; DAS28-ESR: 6.3 (1.6) vs. 5.4 (1.7), $p < 0.001$; all components of DAS28-ESR (patient's VAS—57.3 (28.5) vs. 48.0 (27.9), $p = 0.001$; SJC—12.6 (8.6) vs. 9.0 (7.8), $p < 0.001$; TJC—18.5 (12.4) vs. 13.3 (10.7), $p < 0.001$; ESR—41.0 (25.5) vs. 30.6 (221.9), $p < 0.001$); HAQ-DI: 1.6 (0.8) vs. 1.2 (0.8), $p < 0.001$; and

Table 1 Clinical baseline characteristics of 498 patients from the GLADAR cohort

Variables	Values
Male, *n* (%)	74 (14.9)
Age at diagnosis, years (SD)	45.9 (13.6)
Ethnicity, *n* (%)	
Mestizo	238 (47.8)
Caucasian	143 (28.7)
African	98(19.7)
Indigenous	14 (2.8)
Symptoms' duration, months (SD)	5.3 (2.9)
Delay of DMARDs intervention, months (SD)	4.3 (3.8)
Rheumatoid factor positivity, *n* (%)	384 (77.1)
Erythrocyte sedimentation rate, mm/h (SD)	37.6 (24.8)
Anemia, *n* (%)	110 (22.1)
Thrombocytosis, *n* (%)	81 (16.3)
Morning stiffness of more than 1 h, *n* (%)	489 (98.2)
DAS 28-ESR at baseline, *n* (SD)	6.1 (1.7)
Baseline disease activity status, *n* (%)	
Remission	18 (3.6)
Low disease activity	14 (2.8)
Moderate disease activity	106 (21.3)
High disease activity	360 (72.3)
Tender joint count, *n* (SD)	16.8 (12.1)
Swollen joint count, *n* (SD)	11.4 (8.5)
Patient's visual analogue, mm (SD)	54.3 (28.6)
HAQ-DI, value (SD)	1.43 (0.84)
First visit anti-rheumatic medications prescribed	
Corticosteroid use, *n* (%)	321 (66.5)
cDMARDs use, *n* (%)	396 (79.5)
Monotherapy, *n* (%)	246 (49.4)
Two cDMARDs combination, *n* (%)	150 (30.1)
bDMARD use at baseline, *n* (%)	5 (1.0)
Sharp-VDH score at baseline, *n* (SD)	24.5 (46.1)

DMARDs disease-modifying rheumatic drugs, *DAS28-ESR* disease activity score of 28-joint count with erythrocyte sedimentation rate, *HAQ-DI* Assessment Questionnaire-Disability index, *cDMARDs* conventional DMARDs, *bDMARDs* biologic DMARDs, *Sharp-VDH score* Sharp score modified by Van der Heijde

corticosteroid use: 71.3% vs. 58.6%, $p < 0.001$. See Tables 2 and 3.

Remission and LDA/remission predictors: multivariable analysis

Independent predictors of remission at 1 year were a lower baseline DAS28-ESR (OR 1.17, 95% CI 1.07–1.27, $p = 0.001$) and a lower baseline HAQ-DI (OR 1.48, 95% CI 1.04–2.10, $p = 0.028$). At 2 years of follow-up, the only predictor of remission was a lower baseline DAS28-ESR (OR 1.40, 95% CI 1.170–1.66, $p < 0.001$).

Predictors of LDA/remission at 1 year of follow-up were male gender (OR 1.77, 95% CI 1.2–2.63, $p = 0.036$), a lower DAS28-ESR (OR 1.42; 95% CI 1.26–1.61, $p < 0.001$), and baseline non-use of corticosteroids (OR 1.74, 95% CI 1.11–2.44, $p = 0.008$). Baseline DAS28-ESR (OR 1.45, 95% CI 1.23–1.70, $p < 0.001$) was the only independent predictor of LDA/remission at 2 years. Data are depicted in Table 4.

Alternative analyses

When disease activity categories by DAS28-ESR (low, moderate, and high disease activity) at baseline were used as potential predictor instead of the numeric values, remission at baseline was found to be an independent predictor of remission at 2 years but not at 1 year of follow-up and lower categories of activity were predictors of LDA/remission at 1 and 2 years (data not shown). In the alternative multivariable analyses considering the components of DAS28-ESR instead of DAS28-ESR score value, ESR and MDHAQ predicted both remission and LDA/remission (data not shown).

Table 2 Univariable analyses of remission at 1 year of follow-up in 498 patients from the GLADAR cohort

Variables	No remission	Remission	*p* value*
Male, *n* (%)	56 (13.9)	18 (18.8)	0.233
Age at diagnosis, years (SD)	46.1 (13.8)	45.0(12.5)	0.478
Ethnicity, *n* (%)			
Mestizo	192 (48.1)	46 (48.9)	0.543
Caucasian	112 (28.1)	31 (33.0)	
African	84 (21.1)	14 (14.9)	
Indigenous	11 (2.8)	3 (3.2)	
Symptoms duration, months (SD)	5.3 (2.8)	5.3 (2.8)	0.954
Delay of DMARDs intervention, months (SD)	4.4 (3.9)	4.1 (3.7)	0.496
Rheumatoid factor positivity, *n* (%)	313 (77.9)	71 (74.0)	0.414
ESR	40.4 (25.0)	26.0 (20.3)	< 0.001*
Anemia	99 (24.6)	11 (11.5)	0.005
Thrombocytosis	69 (17.2)	12 (12.5)	0.266
Morning stiffness > 1 h	395 (98.3)	94 (97.9)	0.821
DAS 28-ESR at baseline, value (SD)	6.3 (1.6)	5.1 (1.6)	< 0.001*
TJC	18.0 (12.3)	12.0 (10.1)	< 0.001*
SJC	12.2 (8.6)	8.1 (7.6)	< 0.001*
Patient's VAS	56.4 (28.3)	45.3 (28.2)	0.001*
HAQ-DI, value (SD)	1.5 (0.8)	1.0 (0.8)	< 0.001*
Anti-rheumatic medications prescribed at first visit			
Glucocorticoid, *n* (%)	276 (83.4)	55 (57.3)	0.034*
cDMARDs, *n* (%)	320 (79.5)	76 (9.2)	0.390
Monotherapy	204 (82.9)	42 (43.8)	
Combination	116 (28.9)	34 (35.4)	
No DMARDs prescribed, *n* (%)	82 (20.4)	20 (19.6)	0.924
bDMARD use at baseline, *n* (%)	4 (1.0)	1 (1.0)	0.967
Sharp-VDH score	24.3 (18.7)	25.4(23.1)	0.682

DMARDs disease-modifying rheumatic drugs, *ESR* erythrocyte sedimentation rate, *DAS28-ESR* disease activity score of 28-joint count with erythrocyte sedimentation rate, *TJC* tender joint count, *SJC* swollen joint count, *VAS* visual analogue scale, *HAQ-DI* Assessment Questionnaire-Disability Index, *cDMARDs* conventional DMARDs, *bDMARDs* biologic DMARDs, *Sharp-VDH* Sharp score modified by Van der Heijde

*Significant statistical difference with χ^2 or Student's *t* test, at convenience

Table 3 Univariate analyses of LDA/remission at 1 year of follow-up in the GLADAR cohort

Variables	No LDA/remission	LDA/ remission	*p* value
Male, *n* (%)	42 (12.5)	32 (19.8)	0.033
Age at diagnosis, years (SD)	46.1 (13.8)	45.0(12.5)	0.102
Ethnicity, *n* (%)			
Mestizo	148 (44.3)	90 (56.6)	0.029*
Caucasian	100 (29.9)	43 (27.0)	
African	77 (23.1)	21 (13.2)	
Indigenous	9 (2.7)	5 (3.1)	
Symptoms' duration, months (SD)	5.2 (2.9)	5.5 (2.8)	0.319
Delay of DMARDs intervention, months (SD)	4.4 (3.9)	4.3 (3.8)	0.876
Rheumatoid factor positivity, *n* (%)	262 (78.0)	122 (75.3)	0.507
ESR, mm/h (SD)	41.0 (25.5)	30.6 (21.9)	< 0.001*
Anemia, *n* (%)	86 (25.6)	24 (14.8)	0.007*
Thrombocytosis, *n* (%)	60 (17.9)	21 (13.0)	0.166
Morning stiffness > 1 h, *n* (%)	330 (98.2)	159 (98.1)	0.959
TJC, *n* (%)	18.5 (12.4)	13.3 (10.7)	< 0.001*
SJC, *n* (%)	12.6 (8.6)	9.0 (7.8)	< 0.001*
VAS, mm (SD)	57.3 (28.5)	48.0 (27.9)	0.001*
DAS 28-ESR at baseline, value (SD)	6.3 (1.6)	5.4 (1.7)	< 0.001*
HAQ-DI, value (SD)	1.6 (0.8)	1.2 (0.8)	< 0.001*
Anti-rheumatic medications prescribed at first visit			
Glucocorticoid, *n* (%)	236 (71.3)	95 (58.6)	0.010*
cDMARDs, *n* (%)	266 (79.2)	130 (70.2)	0.221
Monotherapy	173 (51.5)	73 (45.1)	
Combination	93 (27.7)	57 (35.2)	
No DMARDs prescribed, *n* (%)	70 (20.8)	32 (19.8)	0.780
bDMARD use at baseline	3 (0.9)	2 (1.2)	0.720
Sharp-VD, value (SD)	24.9 (18.9)	23.9 (21.0)	0.667

DMARDs disease-modifying rheumatic drugs, *ESR* erythrocyte sedimentation rate, *TJC* tender joint count, *SJC* swollen joint count, *VAS* visual analogue scale, *DAS28-ESR* disease activity score of 28-joint count with erythrocyte sedimentation rate, *HAQ-DI* Assessment Questionnaire-Disability Index, *cDMARDs* conventional DMARDs, *bDMARDs* biologic DMARDs

*Significant statistical difference with χ^2 or Student's *t* test, at convenience

Discussion

We have identified a lower baseline disease activity status as the most relevant predictor of good clinical outcomes achieving either remission or LDA/remission at 1 and 2 years of follow-up in patients with early RA from the GLADAR cohort. These observations are concordant with those reported in several other studies. In observational real-world cohorts, lower baseline disease activity, in addition to other predictors (such as scheduled therapy, being male, non-use of alcohol, being of low weight, or being young), has been associated with remission [26, 27] or sustained remission [28] at 1 year. In clinical trials, similar results have been found; for example, in the Netherlands IMPROVED (Induction therapy with Methotrexate and Prednisone in Rheumatoid Or Very Early Arthritic disease) study (375 in remission and 221 patients in non-remission), low disease activity (DAS28-ESR), a low HAQ, along with short symptom duration, ACPA positivity, male sex, and low body mass index were found to be predictors of early remission in patients with early RA and undifferentiated arthritis [29]. Furthermore, in an analysis of several clinical trials evaluating the efficacy of tumor necrosis factor (TNF) inhibitors, a lower baseline activity score was found to be predictive of remission after 1 year of treatment [30]. On the other hand, in a multicenter longitudinal study from France, the level of baseline disease activity, particularly, during the first 3 months of treatment, has been significantly associated with disease activity at 1 year, when different scores of disease activity were used [31]. In our region, a study of 107 early RA Mexican patients under a T2T intervention strategy revealed a lower level of

Table 4 Multivariate analyses of remission and low disease activity at 1 and 2 years of follow-up in the GLADAR cohort

Variables	At 1 year of follow-up $N = 498$		At 2 years of follow-up $N = 280$	
	OR	p value	OR	p value
Predictors of remission				
Anemia	0.50 (0.25–0.995)	0.048		
Lower baseline, DAS28-ESR	1.17 (1.07–1.27)	0.001	1.40 (1.17–1.66)	< 0.001
Lower baseline, HAQ-DI	1.48 (1.04–2.10)	0.028	–	–
Predictors of LDA/remission				
Male gender	1.77 (1.2–2.63)	0.036		
Lower baseline, DAS28-ESR	1.42 (1.26–1.61)	< 0.001	1.45 (1.23–1.70)	< 0.001
Non-use of corticosteroids at baseline	1.74 (1.11–2.44)	0.008	–	–

DAS28-ESR disease activity score of 28-joint count with erythrocyte sedimentation rate, *HAQ-DI* Assessment Questionnaire-Disability Index, *LDA* low disease activity

disease activity, persistent use of DMARDs, younger age, and male gender as being predictive of remission [21].

Regarding the other clinical predictors of remission or LDA/remission which we found in our study (lower disability, non-use of corticosteroids, and male gender), evidence does exist about the impact of these variables in disease outcome. Respect to disability, the low levels of HAQ predicted remission at 1 year from a real-world cohort of early arthritis patients from Canada. [32] In contrast, high disability was a predictor of a lower likelihood of remission in the analysis of the open-label phase of the SWEFOT (SWEdish PharmacO Therapy) trial, conducted in 395 early RA Swedish patients [33]. In Latin America, in a study performed in Colombian patients with early RA, a lower HAQ-DI was found to be a predictor of remission [16].

In terms of medications, we found not using corticosteroids at baseline to be predictive of LDA/remission at 1 year, an association that was not found at the 2-year follow-up visits; these data apparently contrast with the reported beneficial effects of adding corticosteroids to DMARDs [34–37]; however, this strategy probably accounts for punctual but not for a sustained remission in early RA patients [38]. In our cohort, patients not receiving corticosteroids at the baseline visit had less active disease than patients using them (DAS28-ESR = 3.83 (1.65) vs. DAS28-ESR = 4.66 (1.66); $p = 0.031$; data not shown); thus, a confounding by indication could have occurred, with an increased probability of achieving remission due to a lower disease activity instead of the action of the corticosteroids, an effect that was not evident subsequently. We also identified male gender to be a predictor of LDA/remission category, but not of remission. Male gender has been well recognized as a stronger predictor of remission or sustained remission in clinical trials and real-world studies [27, 39, 40]. The same has been the case in our region; in a Colombian study, males were more likely to achieve remission than females after a T2T intervention [41].

Our data showed poor rates of remission and LDA/remission over the observation time, which contrasts with the higher rates observed in clinical trials, [29, 37] but which are comparable with data from more traditional early observational cohort studies. [28, 40] About this, a less frequent response to treatment that is to achieve remission has been observed in Latin American patients, in comparison with European, US, and Canadian patients participating in clinical trials. [42] Of note, more satisfactory rates of remission are being achieved in cohorts in which more sensitive RA classification criteria and intensive treatment strategies have been used [43–45]. In the GLADAR cohort, on the other hand, we used the ACR 1987 criteria given that this cohort was established years before the new 2010 ACR-EULAR [46] criteria were published. Finally, we did not have a standardized treatment protocol and our patients had a relative low rate of bDMARD use. An example of the impact of an intensive intervention in our region are the results of the aforementioned Colombian cohort in which patients had similar baseline clinical characteristics to those of the GLADAR cohort but achieved remission rates above 60% [41], reinforcing the notion that an intensive treatment implementation should be a reasonable objective for all patients in our region.

Our study has some limitations. Our remission rates could have been even lower because we used the DAS28-ESR score, which is considered "liberal" in comparison with other definitions [18, 31, 43]. We were also unable to examine the rate of sustained remission and of very early remission, clinical objectives which seem to be quite relevant [38, 39, 47–49]. Also, although ACPA were part of the laboratory assessments in the original GLADAR protocol, this test was not available to the majority of our patients, and consequently we were not able to examine this variable; nevertheless, the association

between the presence and fluctuations of ACPA (and RF) and remission is still controversial [50, 51]. In our patients, RF was not associated with remission. Another limitation is our loss to follow-up rate which may have affected our data. Several factors may explain this relatively high rate (such as differences in medical coverage, lack of economic support for such monitoring, time constraints for both patients and physicians alike, etc.). Also, although we used a standardized radiographic assessment and a validated and objective joint damage score (Sharp-VDH score), and the reading of the radiographs was done at each center by rheumatologists or radiologists with experience in assessing radiographs, no formal inter- and intra-rater reliability were obtained. Despite these limitations, we should point out the clear advantage of our study: data collected from a cohort constituted by patients with early RA from different centers in Latin American. In fact, GLADAR is the first multicenter study of early RA in our region, and these centers are quite homogeneous in terms of the population being served: predominantly Mestizo patients (of Amerindian and European ancestry) [11]. Furthermore, GLADAR is a real-world cohort and our results are thus applicable in clinical practice probably beyond our region.

Conclusions

We have now identified baseline demographic and clinical predictors of remission and LDA/remission in Latin American patients with early RA from the GLADAR cohort. We found modest rates of remission at the 1- and 2-year follow-up visits while a lower disease activity at baseline consistently predicted remission and remission/LDA at these time points in our patients. A lower baseline level of disability, non-use of corticosteroids, and male gender were also predictive of better outcomes but only at the 1-year follow-up visit. Our data suggest that not only an early diagnosis but also a more aggressive treatment approach at disease onset are needed to prevent the deleterious effects of active (RA) in early (diagnosed) RA Latin American patients with adverse baseline features. These data may have applicability to other regions of the world.

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Compliance with ethical standards

Disclosures None.

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