The Influence of the Definition of Patient Global Assessment in Assessment of Disease Activity According to the Disease Activity Score (DAS28) in Rheumatoid Arthritis

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ABSTRACT. ***Objective.*** Patient global assessment (PGA) is one of the 4 items included in the Disease Activity Score (DAS28) for evaluation of activity of rheumatoid arthritis (RA). We studied the influence of the use of 3 different techniques of PGA on the assessment of disease activity.

Methods. We evaluated 3 different DAS28 according to the technique of PGA in 108 patients with active RA before and after 12 weeks of etanercept therapy.

Results. The reliability (intraclass coefficient of correlation) between screening and baseline was very high and similar for the 3 DAS28. The percentage of patients in the different states of disease (from remission to higher disease activity) and the sensitivity to change across the 3 DAS28 scales were very similar.

Conclusion. The different techniques of collection of PGA to be included in the DAS calculation yield similar results. However, an accepted, unequivocal technique should be encouraged in order to reduce heterogeneity in scoring DAS among patients with RA. (J Rheumatol First Release Oct 1 2011; doi:10.3899/jrheum.110487)

Key Indexing Terms:
RHEUMATOID ARTHRITIS DISEASE ACTIVITY SCORE PATIENT GLOBAL ASSESSMENT

Systematic evaluation of activity in rheumatoid arthritis (RA) is currently recommended in order to facilitate communication between health professionals and also to support a therapeutic decision to achieve a certain threshold of such disease activity[1]. This therapeutic approach is known as the "treat to target" concept[2]. The current recommendation for optimal evaluation of disease activity is to refer to a validated composite measure such as the Disease Activity Score (DAS28)[3].

Four components are included in the DAS28: number of swollen joints, number of tender joints, erythrocyte sedimentation rate, and patient global assessment (PGA).

Despite widespread use of the DAS28, to our knowledge, there is no firm recommendation concerning the exact technique of collection of the information related to PGA[4] and in particular its exact phrasing[4,5].

The current debate addresses whether the PGA should refer to the patient's health status (considering all the different facets of all the different conditions the patient is suffering from) or to the patient's RA activity. Recently, under the umbrella of EULAR, a patient-reported outcome composite index called RAID (Rheumatoid Arthritis Impact of Disease) has been proposed and validated[6,7]. Such a composite index includes 7 domains (pain, function, fatigue, physical well-being, psychological well-being, sleep disturbances, and coping).

During the 2010 Patient-Reported Outcome session of OMERACT, the proposal was made to consider the RAID score as the PGA item of the DAS28.

In a recent trial evaluating etanercept in active RA (clinicaltrials.gov no. NCT00768053), 3 different PGA were collected (PGA-HS, PGA-DA and PGA-RAID). In this study, we evaluated the influence of the definition of PGA in the assessment of RA disease activity according to the DAS28 scale in terms of categorization of patients (from remission to high disease activity) and also in terms of psychometric properties such as reliability and sensitivity to change.

MATERIALS AND METHODS

Study design. This study was conducted as an open, single-arm therapeutic

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Supported by Pfizer SAS France.

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Accepted for publication July 11, 2011.

trial with different visits: screening, baseline, and also visits after etanercept was initiated. Patient's disease activity was supposed to be stable between the screening and baseline visits. All patients received etanercept 50 mg once weekly during the entire study period.

Inclusion criteria. To be eligible for the study, the patient had to have definite RA[8] justifying use of tumor necrosis factor (TNF) blocker therapy as recommended by the French Society of Rheumatology[9].

Collected data. Patient (age, sex) and disease (duration, anti-cyclic citrullinated peptide positivity) characteristics were collected at screening. Moreover, at screening, at baseline, and during visits after therapy the following outcome measures were also collected: number of swollen and tender joints (28-joint count), erythrocyte sedimentation rate (ESR; mm/h). PGA was evaluated using 3 different techniques: (1) PGA-HS, the patient answering the question, "In general, how would you rate your health over the last 2–3 weeks?"; (2) PGA-DA, the patient answering the question, "Please estimate your disease activity over the last 48 hours"; and (3) PGA-RAID, the patient answering the 7 questions of the RAID instrument for the last 8 days[6]. For all 3 techniques, the answer was given using a written numerical rating scale of 0–10.

Statistical analysis. The reliability of the different PGA and DAS28 scales was assessed using the intraclass correlation coefficient (ICC) and its 95% confidence interval in the data collected at screening compared to the baseline visit.

The level of correlation between the 3 different techniques was evaluated at baseline using the correlation coefficient (r) and its 95% confidence interval.

The percentage of patients in the different categories of DAS28 status (from remission to high disease activity) was calculated for the 3 different DAS28 scales at baseline and at the final visits.

Finally, the sensitivity to change was evaluated for the 6 different variables (i.e., 3 PGA and 3 DAS28 scales) according to the standardized response mean (SRM), which is the ratio of the mean change divided by the standard deviation of the change; such sensitivity to change was also evaluated by calculating the percentage of improved patients (i.e., DAS28 reduction of at least 1.2 points) in the 3 DAS28 scales.

Data presented here are from the intent-to-treat analysis.

RESULTS

Of 120 screened patients, 108 entered the study and received at least 1 etanercept injection. During the 12 weeks of the trial, 1 patient was lost to followup and 10 others withdrew because of side effects.

The main characteristics of the 108 recruited patients were the following: age 54 ± 13 years, 75% were females, 61% positive for anti-cyclic citrullinated peptide, disease duration 8 ± 7 years, CRP 18 ± 30 mg/l, and DAS28-ESR-PGA-HS 5.4 ± 0.8.

The reliability was very high for the PGA-HS, with ICC 0.75 (95% CI 0.66–0.82), for the PGA-DA, ICC 0.63 (95% CI 0.50–0.73), and for PGA-RAID, ICC 0.85 (95% CI 0.79–0.90); and even higher for the DAS28-PGA-HS, ICC 0.92 (95% CI 0.88–0.94), the DAS28-PGA-DA, ICC 0.92 (95% CI 0.88–0.94), and the DAS28-PGA-RAID, ICC 0.94 (95% CI 0.91–0.96).

The correlations at baseline between the 6 variables (3 PGA and 3 DAS28) were significantly positive (Table 1).

The influence of the choice of the technique of collection of PGA in the categorization of disease activity based on the DAS28 is summarized in Table 2. The percentages of patients achieving remission or a state of low disease activity were similar with the three DAS28 scores.

Finally, the sensitivity to change of the different measures evaluated is summarized in Table 3.

DISCUSSION

Our results suggest that the technique of collection of PGA has a minimal influence in the evaluation of disease activity according to the DAS28-ESR.

The strengths of our study include a large sample of patients with active RA disease, and more importantly, information related to PGA according to 3 different techniques.

Moreover, all patients were seen by the same investigator at the different study visits. The detailed evaluation of the psychometric properties of the 3 techniques of evaluation of PGA suggests a trend in favor of the RAID score technique. Such preference is also supported by a recent study confirming the validity of this tool[10]. The additional advantage of the RAID score composite index is the standardized phrasing of each question in it. However, based on the data observed in this study, the influence in the calculation of the different techniques of the evaluation of PGA was minimal, particularly while checking the categorization of the patients. For example, the percentage of patients in remis-

Table 1. Correlations between the 3 techniques of evaluation of patient global assessment and consequently the 3 techniques of evaluation of Disease Activity Score in 108 patients with active RA, at baseline. Values are correlation coefficients (95% CI).

	PGA-HS	PGA-DA	PGA-RAID	DAS28 PGA-HS	DAS28 PGA-DA	DAS28 PGA-RAID
PGA-HS	1					
PGA-DA	0.51 (0.35–0.63)	1				
PGA-RAID	0.77 (0.68–0.84)	0.68 (0.57–0.77)	1			
DAS28 PGA-HS	0.35 (0.17–0.5)	0.24 (0.06–0.4)	0.4 (0.23–0.55)	1		
DAS28 PGA-DA	0.13 (–0.07–0.31)	0.38 (0.2–0.53)	0.33 (0.15–0.49)	0.94 (0.91–0.96)	1	
DAS28 PGA-RAID	0.19 (0–0.37)	0.25 (0.06–0.42)	0.4 (0.23–0.55)	0.97 (0.96–0.98)	0.97 (0.95–0.98)	1

PGA-HS: patient global assessment evaluated using a question related to health status; PGA-DA: PGA evaluated using a question related to rheumatoid arthritis disease activity; PGA-RAID: PGA evaluated using the RAID questionnaire[6]. DAS28-PGA-HS: Disease Activity Score evaluated using the PGA-HS; DAS28-PGA-DA: DAS evaluated using the PGA-DA; DAS28-PGA-RAID: DAS evaluated using the PGA-RAID.

Table 2. Influence of the technique of collection of patient global assessment in the categorization of disease activity based on the Disease Activity Score definition. Data are percentages of patients.

DAS28 Definition	Baseline (before therapy)				12 Weeks (after etanercept therapy)				
	Remission*	LDAS	Moderate	High	Remission*	LDAS	Moderate	High	Improved
DAS28-PGA-HS	0	0	33	67	27	44	45	11	26
DAS28-PGA-DA	0	0	33	67	28	47	44	9	22
DAS28-PGA-RAID	0	0	34	66	27	47	46	7	21

* Remission = DAS28 < 2.6. LDAS: low disease activity score = DAS28 ≤ 3.2; moderate disease activity = DAS28 between > 3.2 and ≤ 5.1; high disease activity = DAS28 > 5.1; improved = DAS28 changes during the study of at least 1.2 point. DAS28-HS: Disease Activity Score calculated with the patient global assessment evaluated using a question related to health status; DAS28-PGA-DA: DAS calculated with the patient global assessment evaluated using a question related to disease activity; DAS28-PGA-RAID[5]: DAS calculated with the patient global assessment evaluated using the RAID[5].

Table 3. Changes after 12 weeks of etanercept therapy in the patient's global assessment with regard to the technique of collection and consequently the Disease Activity Score in 108 patients with active rheumatoid arthritis.

Outcome	Time			
	Baseline Visit*	Final Visit*	Change** (95% CI)	SRM (95% CI)
PGA-HS	5.9 ± 2.2	3.3 ± 2.5	–2.51 (–2.98; –2.03)	0.94 (0.69–1.26)
PGA-DA	6.5 ± 1.9	3.3 ± 2.3	–3.16 (–3.58; –2.74)	1.36 (1.08–1.73)
PGA-RAID	5.9 ± 1.7	3.0 ± 2.3	–2.85 (–3.25; –2.45)	1.37 (1.12–1.71)
DAS28-PGA-HS	5.4 ± 0.8	3.4 ± 1.2	–1.98 (–2.19; –1.77)	1.84 (1.54–2.28)
DAS28-PGA-DA	5.5 ± 0.8	3.4 ± 1.2	–2.08 (–2.29; –1.87)	1.94 (1.63–2.36)
DAS28-PGA-RAID	5.4 ± 0.8	3.4 ± 1.2	–2.04 (–2.25; –1.83)	1.94 (1.63–2.37)

* Mean ± SD. ** Adjusted mean change from baseline. PGA-HS: patient global assessment evaluated using a question related to health status; PGA-DA: PGA evaluated using a question related to rheumatoid arthritis disease activity; PGA-RAID: PGA evaluated using the RAID[6]. DAS28-PGA-HS: Disease Activity Score evaluated using the PGA-HS; DAS28-PGA-DA: DAS evaluated using the PGA-DA; DAS28-PGA-RAID: DAS evaluated using the PGA-RAID. SRM: standardized response mean (mean change/standard deviation of change).

sion or in a state of low disease activity after 12 weeks of therapy (that is, the thresholds that are usually considered as the target to achieve in the treatment of RA) was very similar across the 3 techniques.

Other studies are required to further analyze this question, keeping in mind that such efforts could potentially improve the validity of PGA and reduce heterogeneity in scoring the DAS28 among patients.

ACKNOWLEDGMENT

The authors thank the patients who agreed to participate in this study and the investigators who recruited and monitored the patients.

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