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VARIABILITY OF PATIENT AND PHYSICIAN GLOBAL ASSESSMENT ON VISUAL ANALOGUE AND LIKERT SCALES IN RHEUMATOID ARTHRITIS

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Abstract

Objective. The study aimed to observe the variability of rheumatoid arthritis (RA) disease activity scores according to the type of patient global assessment (PtGA) and to compare these subjective assessments with objective measurements.

Methods. Prospective study in which RA patients four types of assessments in the same day of their inclusion in the study: completing a questionnaire (including PtGA on a 100 mm visual analogue scale – VAS, and a 0-10 Likert scale), clinical interview and joint examination performed by each attending rheumatologist and peripheral venous blood sampling for acute phase reactants.

Results. The study included 110 RA patients (57.5 years average age, 9.4 years median disease duration, 90.0% women, 58.2% in remission or low disease activity). There was low concordance and agreement between PtGA and physician global assessment (PhGA): the two evaluations were significantly but poorly correlated, and in 71.8% of cases VAS and Likert PtGA were higher than PhGA with at least 2 points in average. Patients with no tender or swollen joints (27.3%) reported a median VAS-PtGA of 27 cm and a median Likert-PtGA of 4.2 points. Likert-PtGA were higher than VAS-PtGA in the general sample and for patients with normal objective measures (patients in remission according to DAS28-3v-CRP reported a median VAS-PtGA of 5 points, compared to VAS-PtGA of only 2.2 cm). The strongest correlations of PtGA on both VAS and Likert scales were recorded for mHAQ ($r = 0.521$ and 0.589, $p < 0.001$), DAS28-3v-CRP ($r = 0.419$ and 0.422, $p < 0.001$) and the presence of prolonged morning stiffness ($r = 0.361$ and 0.485, $p < 0.001$).

Conclusion. Romanian patients with RA seem to favour and understand the Likert scale better than the VAS when reporting PtGA.

Keywords: rheumatoid arthritis, patient global assessment, Likert scale, visual analogue scale

Abbreviations

ACPA – anti-citrullinated protein antibodies
bDMARDs – biologic disease-modifying anti-rheumatic drugs
CDAI – clinical disease activity index
CRP – C-reactive protein
csDMARDs – conventional synthetic disease-modifying anti-rheumatic drugs
DAS – disease activity score
ESR – erythrocyte sedimentation rate
LDA – low disease activity
MDA – moderate disease activity
mHAQ – modified health assessment questionnaire
PhGA – physician global evaluation
PRO – patient-reported outcomes
PtGA – patient global assessment
RA – rheumatoid arthritis
RF – rheumatoid factors
SDAI – simplified disease activity index
SJC28 – swollen joints count
TJC28 – tender joints count from the 28 joints
v – variable
VAS – visual analogue scale

INTRODUCTION

Therapeutic decisions in rheumatoid arthritis (RA), such as treatment intensification and tapering [1], are now based on validated composite activity scores which include subjective patient-reported outcomes (PROs) in the form of global health assessments, which have gained considerable importance in the last decades especially due to clinical

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trials showing their significant improvement in treat-to-target strategies [2]. However, results from national cohorts revealed that some PROs are poorly correlated with objective composite scores such as the Disease Activity Score or DAS28 calculated with three variables [3], which can indicate a lack of precision of either of them or the fact that PROs are able to reflect addition clinical information not captured by objective measures [4]. In current medical practice, this subjective information is collected through a visual analogue scale (VAS, 0-100 mm) or a Likert scale (0-10 points) with variable anchor questions. There are many possible confounders which can influence patient's global assessment on a VAS, some of which are patient-related (for example comorbidities [5]), while others pertain to the design of this instrument used to capture PRO. Therefore, subjective evaluations may vary and thus may not reflect the evaluations considered objective (e.g. clinical examination, acute phase reactants, composite scores). Even though inflammation is now being more thoroughly controlled using biologic and targeted drugs, this improvement seems not to translate in concordant and significant improvements of PROs [6]. In the larger context in which efforts should be dedicated to optimizing the tools for capturing PROs [7], the present study aimed to observe in a real-life clinical setting the variability of disease activity scores according to the type of global patient assessment and to compare these subjective assessments with the measurements considered objective.

METHODS

Patients

In order to reach the study objectives, all out-clinic patients with RA were included in the study between March and June 2019. The diagnosis of RA was based on the opinion of each attending physician (senior rheumatologists). Patients non-fluent in Romanian, illiterate patients, minors (aged below 18 years), patients with overlap syndromes, patients with impaired cognition and patients unwilling to participate were excluded. The study protocol was approved by the local ethics committee and, before any study procedure, each patient expressed informed consent. All patients underwent four types of assessments in the same day of their inclusion in the study: completing a questionnaire, clinical interview and joint examination performed by each attending rheumatologist and peripheral venous blood sampling for acute phase reactants and RA specific serology.

PROs

Each questionnaire collected general patient data (gender, age, dwelling, education level, work status, smoking), information on disease activity (presence and duration of morning stiffness, which was considered present if the patient reported 30 minutes or more), quality of life (using the modified Health Assessment Questionnaire - mHAQ [8], translated into Romanian) and three subjective assessments of general health and disease activity [9]: a patient global assessment on a 100 mm VAS (VAS-PtGA) related to the question "Considering all the ways in which your rheumatoid arthritis affected you, how do you feel about your arthritis today? (mark the answer on the line below by a vertical bar)", with the anchors "very good" on the left and respectively "very bad" on the right; a patient global assessment on a Likert scale with 0-10 points (Likert-PtGA) related to the question "How much did your rheumatoid arthritis affect you last week? (circle or tick a number below)", with the anchors "it did not affect me at all" on the left and respectively "it severely affected me" on the right; a Likert scale with 0-10 points related to the question "How big was the pain caused by your rheumatoid arthritis in the last week? (circle or tick a box below)", with the anchors "no pain" on the left and respectively "the worst pain ever" on the right.

Physician-reported outcomes

Each attending rheumatologist completed on the same day as the his patient/s a specific questionnaire for each patient, containing the following variables: height and body mass of the patient (body mass index was calculated as the ratio of weight in kilograms to squared height in meters); tender joints count from the 28 joints (TJC28) included in the DAS28; swollen joints count (SJC28); a physician global evaluation (PhGA) of disease activity on a 100 mm VAS (corresponding to the instruction "General evaluation of the activity of rheumatoid arthritis by the doctor", with the anchors "very good" on the left and "very bad" on the right); information from the clinical interview and medical documents concerning RA variables: date of disease onset (the duration of the disease being calculated as the difference between the date of current evaluation and the date of disease onset) and type of current anti-rheu-

matic treatment, referring to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), biological originator or biosimilar DMARDs (bDMARDs) and chronic oral glucocorticoids.

Laboratory tests and composite activity scores

Acute phase reactants were measured by the local laboratory from peripheral venous blood samples taken the same day of study inclusion and included C-reactive protein (CRP; normal < 5 mg/l) and erythrocyte sedimentation rate (ESR; normal < 15-30 mm/h depending on age and gender). Inflammation was defined as either CRP or ESR above the upper limit of normal. Serology markers were retrieved from the medical history or, if absent, were measured on the day of study inclusion using commercially available kits: rheumatoid factors (normal < 30 IU/ml) and anti-citrullinated protein antibodies (normal < 20 IU/ml). Data collected from the three sources (patient questionnaire, physician questionnaire and acute phase reactants from the local laboratory) were used to calculate composite disease activity indices: DAS28, either with 3 variables, respectively TJC28, SJC28 and CRP (abbreviated as DAS28-3v-CRP), either with 4 variables, respectively TJC28, SJC28 and CRP/ESR and PtGA on VAS/Likert scales, with the following cut-offs for activity: 2.6 for remission, 3.2 for low disease activity (LDA) and 5.1 for moderate disease activity (MDA) [10]; simplified disease activity index (SDAI), using TJC28, SJC28, CRP, PhGA and PtGA on VAS/Likert scales [11]; clinical disease activity index (CDAI), using TJC28, SJC28, PhGA and PtGA on VAS/Likert scales [12].

Statistics

Missing data were treated with multiple imputation. Distribution normality was assessed using descriptive statistics, normality and stem-and-leaf plots, and Kolmogorov-Smirnov tests. Nominal variables are reported as "absolute frequency (percent of group)". Continuous variables are reported as "mean (standard deviation)" if normally distributed or as "median (minimum-maximum)" if non-normally distributed. Correlations of two non-normally distributed continuous variables (for example age and VAS-PtGA) were studied using Spearman coefficients, while correlations of a continuous variable and a dichotomous categorical variable (for example gender and VAS-PtGA) were studied with point biserial correlations (Pearson). Mann-Whitney U tests were used to assess differences in continuous variables among study subgroups (e.g. VAS-PtGA with or without inflammation). Kappa coefficients were generated by cross-tabulation. The statistical tests were considered significant if $p < 0.05$. All the statistical analysis was performed using IBM SPSS Statistics version 25.0 for Windows (Armonk, NY, IBM Corp.).

RESULTS

Demographics and RA phenotype

The study included a sample of 110 RA patients with an average age of 57.5 years, predominantly composed of women (90.0%), with established disease judging by its median duration of 9.4 years (Table 1). The majority of patients were receiving csDMARDs (98.2%), more than half were on bDMARDs (54.5%) or on chronic doses of oral glucocorticoids (55.5%). The most commonly used csDMARD was methotrexate (53.0%), followed by leflunomide (26.8%), hydroxychloroquine (12.0%) and sulfasalazine (6.0%). The most commonly used bDMARD was tocilizumab (37.2%), followed by etanercept (18.0%), infliximab (14.2%) and rituximab (9.8%). Despite treatment, average DAS28 score, irrespective of the type of acute phase reactant or PRO scale used for calculation, were situated in the MDA category, just above the LDA category (Table 2).

TABLE 1. *Demographics and RA phenotype (n = 110)*

age (y)	57.5 (13.3)
women	99 (90.0%)
smoking	19 (17.3%)
urban dwelling	74 (67.3%)
university education	34 (30.9%)
employed	37 (33.6%)
BMI (kg/m^2)	27.1 (5.3)
disease duration (y)	9.4 (0.3-40.3)
positive RF	76 (69.1%)
positive ACPA	88 (80.0%)
csDMARD*	108 (98.2%)
bDMARD&	60 (54.5%)
glucocorticoids#	61 (55.5%)

Notes: * methotrexate, leflunomide, sulfasalazine, hydroxychloroquine; & abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, tocilizumab, rituximab; # prednisone, methylprednisolone; normally-distributed continuous data are reported as "mean (SD)"; non-normally-distributed data are reported as "median (minimum-maximum)"; categorical data are reported as "absolute frequency (percentage of sample)".

Abbreviations: ACPA - anti-citrullinated protein antibodies; BMI - body mass index; b/csDMARD -biological or conventional synthetic disease-modifying anti-rheumatic drug; RA - rheumatoid arthritis; SD - standard deviation; y – years

TABLE 2. *RA activity indices (n = 110)*

morning stiffness	76 (69.1%)
PtGA-VAS (cm)	4 (0-10)
PtGA-Likert	5 (0-10)
PtPA-Likert	5 (0-10)
PhGA-VAS (cm)	1.4 (0-8)
mHAQ	0.6 (0-2.8)
TJC28	2 (0-26)
SJC28	1 (0-20)
ESR (mm/h)	22 (2-80)
CRP (mg/L)	2.8 (0.2-81.9)
inflammation[&]	49 (44.5%)
DAS28-4v-ESR-VAS	3.4 (1.5)
DAS28-4v-ESR-Likert	3.2 (1.2)
DAS28-4v-CRP-VAS	3.1 (1.3)
DAS28-4v-CRP-Likert	2.6 (1.0)
DAS28-3v-CRP	2.9 (1.1)
remission[*] and LDA[*]	64 (58.2%)
SDAI-VAS	12.3 (11.2)
SDAI-Likert	13.6 (11.0)
CDAI-VAS	11.5 (10.5)
CDAI-Likert	12.7 (10.3)

Notes: normally-distributed continuous data are reported as "mean (SD)"; non-normally-distributed data are reported as "median (minimum-maximum)"; categorical data are reported as "absolute frequency (percentage of sample)"; & defined as either ESR or CRP above the upper limit of normal; * remission and LDA according to DAS28-3v-CRP.
Abbreviations: CDAI - Clinical Disease Activity Index; CRP - C-reactive protein; DAS28 - disease activity score using 28 joints; ESR - erythrocyte sedimentation rate; LDA - low disease activity; mHAQ - modified health assessment questionnaire; PhGA - physician global assessment; PtGA - patient global assessment; PtPA - patient pain assessment; RA - rheumatoid arthritis; S/TJC - swollen/tender joint count; SD - standard deviation; SDAI - Simple Disease Activity Index; v - variables; VAS - visual analogue scale; y - years.

RA activity and PRO

Not all participants in the study reported the outcomes inquired by the questionnaire: 11 patients (10.0%) did not report their VAS-PtGA, while 3 patients (2.7%) did not report their Likert-PtGA, a frequency difference which was statistically significant (p = 0.027). Of the 11 patients who did not report their VAS-PtGA, 8 patients (72.7%) had reported however their Likert-PtGA. Education level and dwelling were not significantly associated with these discrepancies. A large proportion of the sample had prolonged morning stiffness (69.1%), despite the facts that 55.5% of the patients had normal acute phase reactants (ESR and CRP below the upper limit of normal) and 58.2% were in remission or LDA according to DAS28-3v-CRP (Table 2). Comparing activity scores calculated with the VAS-PtGA with the same scores calculated with Likert-PtGA (Table 2), DAS28 is higher (+0.2 in median for the ESR-calculated score and respectively +0.5 for the CRP-calculated score), while SDAI (-1.3 in median) and CDAI (-1.2 in median) are lower. Generally, there was low concordance and agreement between PtGA and PhGA (Table 3): the two evaluations were significantly but poorly correlated, and in more than 71.8% of cases VAS and Likert PtGA was higher than PhGA with at least 2 points in average.

Remarkably, patients with normal objective measures reported higher than expected PtGA and pain assessments (Table 4).

TABLE 3. *Comparison of patient and physician global assessments according to VAS or Likert scale (n = 110)*

	VAS-PtGA *versus* VAS-PhGA	Likert-PtGA *versus* VAS-PhGA
kappa	0.01 (p = 0.15)	0.05 (p < 0.01)
Spearman's rho	0.31 (p < 0.01)	0.34 (p < 0.01)
means difference[&]	+2.0	+3.1
medians comparison[*]	4.0; 1.4 (p < 0.01)	5.0; 1.4 (p < 0.01)
% PtGA > PhGA	71.8%	83.6%
% PtGA < PhGA	26.4%	13.6%
% PtGA = PhGA	1.8%	2.7%

Notes: & mean physician assessment subtracted from mean patient assessment; * Mann Whitey U test. Abbreviations: PhGA - physician global assessment; PtGA - patient global assessment; VAS - visual analogue scale.

TABLE 4. *Subjective patient assessments according to objective physician and laboratory measures (n = 100)*

	n (%)	*VAS-PtGA (cm)*	*Likert-PtGA*	*pain (Likert)*
TJC28 = 0	32 (29.1%)	2.8 (0-10)	4.1 (1-9)	3.8 (0-10)
SJC28 = 0	50 (45.5%)	3.0 (0-10)	4.4 (0-10)	4.0 (0-10)
TJC28=SJC28=0	30 (27.3%)	2.7 (0-10)	4.2 (0-9)	3.8 (0-10)
no inflammation[*]	61 (55.5%)	3.0 (1-10)	4.1 (0-10)	4.0 (0-10)
remission[&]	53 (48.2%)	2.2 (0-10)	5.0 (0-10)	4.0 (0-10)

Notes: continuous variables reported as "median (minimum-maximum)"; categorical data reported as "absolute frequency (percentage of sample)"; * no inflammation defined as both ESR and CRP below the upper limit of normal (20-30 mm/h; 5 mg/L); & remission defined by DAS28-3v-CRP < 2.6.
Abbreviations: CRP - C-reactive protein; ESR - erythrocyte sedimentation rate; PtGA - patient global assessment; S/TJC28 - swollen/tender joint count of the 28 evaluated joints; v - variables; VAS - visual analogue scale.

For example, patients with no tender or swollen joint on clinical examination (27.3%) reported a median VAS-PtGA of 27 cm, a median Likert-PtGA of 4.2 points and a mean RA-related pain assessment of 3.8 points on the Likert scale. As a pattern, Likert-PtGA were higher than VAS-PtGA in the general sample (Table 2) and for patients with normal objective measures (for example patients in remission according to DAS28-3v-CRP reported a median PtGA of 5 points on the Likert scale, compared to only 2.2 cm

on the VAS; Table 4). The strongest correlations of PtGA on both VAS and Likert scales were recorded for mHAQ (rho = 0.521 and respectively 0.589, $p < 0.001$ for both), DAS28-3v-CRP (rho = 0.419 and respectively 0.422, $p < 0.001$ for both) and the presence of prolonged morning stiffness (rho = 0.361 and respectively 0.485, $p < 0.001$ for both). Interestingly, PtGA was not correlated with the presence of different treatment types (csDMARDs, bDMARDs, glucocorticoids) nor with the status of remission defined by DAS28-3v-CRP (Table 5).

TABLE 5. *Correlations of patient global assessments (n = 110)*

	VAS-PtGA	*p*	*Likert-PtGA*	*p*
mHAQ	0.521	<0.001	0.589	<0.001
DAS28-3v-CRP	0.419	<0.001	0.422	<0.001
TJC28	0.384	<0.001	0.335	<0.001
morning stiffness	0.361	<0.001	0.485	<0.001
CRP	0.356	<0.001	0.388	<0.001
disease duration	0.317	0.001	0.038	0.692
SJC28	0.301	0.001	0.268	0.005
inflammation	0.253	0.008	0.262	0.006
ESR	0.235	0.014	0.2220.317	0.001
age	0.167	0.082		0.020

Notes: correlations of PtGA are reported with Spearman's rho for continuous variables and with biserial correlations (Pearson) for dichotomous variables; correlations with BMI, gender, smoking, dwelling, education, employment, RF, ACPA, csDMARDs, bDMARDs, glucocorticoids and remission status were not significant (data not shown). *Abbreviations*: ACPA - anti-citrullinated protein antibodies; BMI - body mass index; b/csDMARDs -biological or conventional synthetic disease-modifying anti-rheumatic drugs; CRP - C-reactive protein; DAS28 – disease activity score using 28 joints; ESR - erythrocyte sedimentation rate; mHAQ - modified health assessment questionnaire; PtGA - patient global assessment; RF - rheumatoid factors; S/TJC28 - swollen/tender joint count of the 28 evaluated joints; v - variables; VAS - visual analogue scale.

DISCUSSION

In summary, the study observed a higher prevalence of missing data for VAS-PtGA than for Likert-PtGA and the fact that, generally, Likert-PtGA was higher than VAS-PtGA for the same patient. These observations may indicate that, compared to VAS, Likert scales are better understood by Romanian RA patients and better reflect PtGA (which is concordant with patient experience, since in the Romanian educational system, evaluations are graded from 1, for "very bad", to 10, for "very good"). This hypothesis may be influenced by the design of our study, since different phrasing was used for capturing PtGA on VAS and Likert scales (see Methods). In this regard, relevant literature offer proof that, for capturing PtGA, Likert scales seem stable regardless of the wording of the accompanying question addressed to the patient [13], unlike VAS, which varies according to different phrasing [9,14,15].

The observation that DAS28 calculated with VAS-PtGA is generally higher than DAS28 calculated with Likert-PtGA, while CDAI and SDAI are lower respectively, can be explained by the presence of PhGA in the formula for CDAI and SDAI, knowing that generally PhGA was significantly lower than corresponding PtGA, irrespective of the scale used.

Another set of important observations of the study is the fact that PtGA had relatively strong correlations with the quality of life and the presence of prolonged morning stiffness and that patients with normal objective measures (no inflammation, no tender of swollen joints) report relatively high PtGA, pain assessment and high prevalence of morning stiffness. Most practitioners recognize a natural and frequent tendency of some patients to consider their general health less optimal than suggested by objective measures. Other patients recognize a good health but nonetheless report high PtGA considering the fact that they are diagnosed with a chronic incurable illness which implies that their health is not normal even in the absence of symptoms. However, our observations could also imply that PtGA can capture additional information which surpasses the information gained from clinical examination and acute phase reactants, especially if patients complain of prolonged morning stiffness, sleep disturbance, chronic fatigue or depression, conditions which can be a result of an underlying pathogenic process mediated by tissue inflammation [16] and cytokines [17]. Over time, with new pharmacological molecules and more tight treatment strategies, objective inflammatory markers have substantially improved in RA, but even though PROs can be improved with treat-to-target strategies [2], they have not experienced a similar magnitude of change [6], due to their poor association with objective measures [3,18,19] and with physician-reported outcomes [20,21] or due to the fact that they are not particularly taken in consideration and properly estimated when taking therapeutic decisions (e.g. morning stiffness [16], latent pain, depression, anxiety, inability to participate, fibromyalgia, old age, osteoarthritis [22], sleep disturbance [21] and comorbidities [5], with emphasis on pain [23]), but are left to aggregate under the PtGA, reducing the chance of reaching remission [24]. This suggests that controlling inflammation does not equate with controlling the disease or even

with controlling pain. In line with this conjecture, the authors who developed the CDAI showed that acute phase reactants bring few additional information regarding disease activity defined by strictly clinical (tender and swollen joints) and patient-reported variables [12], and the authors who reported the results of the DUO study concluded that changes in treatment (for example augmentation of doses or addition of new pharmacological principles) were predominantly based on PRO rather than physician-reported outcomes [1].

There are certain limitations of the study which can influence the relevance of our results, such as low sample size (a further research direction would be to analyse data from the Romanian Registry of Rheumatic Diseases, which is a mandatory nation-wide electronic database of all patients receiving treatment with biological and targeted synthetic DMARDs), single centre design and exclusive inclusion of Romanian-speaking patients which can introduce a cultural bias, knowing that PRO and PRO-physician discordance vary by country [25].

CONCLUSIONS

RA patients understand VAS and Likert scales differently and frequently report disease activity even when objective measures are normal and physician reports are favourable, which could influence therapeutic decisions based on composite scores and which could represent either a failure of understanding the principle of PtGA, either an ability of PtGA to capture additional information regarding the disease state. Romanian patients with RA seem to favour and understand the Likert scale better than the VAS when reporting PtGA. An instrument with a higher ability to discern RA morbidity, including latent manifestations such as morning stiffness and fatigue, is needed in order for patients to report this outcome more accurately.

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