Original Article

Quality of life and functional capacity in patients with rheumatoid arthritis – Cross-sectional study

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ABSTRACT

Objectives: To analyze the Health related Quality of Life (HRQoL) and physical function in rheumatoid arthritis (RA) patients and compare it with the general population. We also intended to analyze about disease activity influence in HRQoL and functional capacity, as well as determine potential determinants for these outcomes.

Material and methods: A cross-sectional study was conducted in RA patients from a university hospital of Portugal. We obtained Short Form 36, EuroQol 5D, health assessment questionnaire, visual analog scale for pain and patient’s assessment of disease activity. Comparisons between SF-36 and EQ-5D values with our population reference values were conducted using the Mann–Whitney test. Data were compared in different levels of disease activity, using Kruskal Wallis test and Fisher’s exact test. A multiple regression analysis was conducted to identify the potential determinants of outcomes.

Results: RA sample showed significantly lower values than the portuguese general population on physical summary measure of SF-36 (median = 32 vs. 50, p < 0.001) and EQ-5D (median = 0.620 vs. 0.758 respectively; p < 0.001). Lower disease activity levels had better PROs and this was true even when compared patients achieving remission with those in low disease activity. The HAQ ($r^2 = 67%$), VAS-P ($r^2 = 62%$) and VAS-DA ($r^2 = 58%$) were the variables that strongly related to SF-36. Considering HAQ, the strongest related was found with VAS-P, VAS-DA and age ($r^2 = 60%, 61%$ and $33%$, respectively). Multiple regression analysis identified HAQ, VAS-P and educational status as determinants of the HRQoL; age, female gender, employment, VAS-P and VAS-DA as determinants of physical function.

Conclusion: Impairment of HRQoL in RA patients is enormous. We found significant differences between different levels of disease activity, showing higher HRQoL and functional capacity at lower disease activity levels.

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Calidad de vida y capacidad funcional en pacientes con artritis reumatoide – Estudio transversal

RESUMEN

Objetivos: Analizar la evaluación del Health related Quality of Life (HRQoL) y la función física en pacientes con artritis reumatoide (AR) y compararla con la población general. También se pretende analizar la influencia de la actividad de la enfermedad en el HRQoL y la capacidad funcional, así como definir los determinantes potenciales de estos resultados.

Material y métodos: Se realizó un estudio transversal en pacientes con AR de un hospital universitario de Portugal. Se obtuvieron los cuestionarios Short Form 36, EuroQol 5D, Health Assessment Questionnaire,
**Introduction**

The prevalence of RA has been estimated at about 0.5–1.0% worldwide\(^1\) and 0.7% in Portugal\(^2\) and the majority of patients are in a working age.\(^3\)

RA is associated with pain, fatigue, functional disability and deterioration of emotional state and if not treated early, can lead to irreversible structural and functional damage. For these reasons RA represents health-related quality of life (HRQoL) and economic burden to patients and society.\(^4\)

Currently, there are many treatment options although none of them completely treat RA. Thus, the aim of treatment is not only to achieve remission but minimize the disease consequences on patients by increasing the HRQoL and physical function.\(^5\) HRQoL is an additional metric to assess patients’ subjective perspective on their experience of pain and its adverse impact on their lives.\(^5\,9\)

With the advent of the biologic therapy, a growing attention was dedicated by physicians to the precise evaluation of outcomes of therapy.\(^10\) Disease activity is the strongest predictor of disability and that clinical and laboratory markers are important in their assessment and treatment response. However, patient’s perspective of RA disease worsening or flare represents an experience extending beyond standard clinical outcome measures.\(^11\,12\) Some authors consider that outcomes of a clinical intervention obtained by the patient i.e., patient-reported outcomes (PRO) are seemed to be of more importance than any other outcomes like clinical-reported. Several data as impact of disease on condition on daily life can be obtained only from patient.

Thus, PROs are not only an important aim of treatment but also an important long-term prognostic factor.\(^13,14\) Beyond this, increased emphasis is given to the fact that these tools also allow a cost-effectiveness analysis of treatments.\(^15\) Thus, we assisted a growing interest by an assessment not only based on objective parameters, but also an assessment that includes the patient’s subjective well-being.\(^16\)

Various generic and specific scales are used for evaluating PROs. These scales not only measure the effectiveness of the treatment as well as assess whether this effectiveness is truly significant in the patient’s perspective.

With disease modifying antirheumatic drugs (DMARDs), clinical symptoms as well as radiological joint damage are prevented. Achieving clinical remission would ideally be associated with achieving PROs comparable to those in the general population. To date, there have been limited studies about how the changes in the disease activity and classical clinical data relate with changes in the various PROs.\(^17\) Furthermore, it is not clear yet whether aiming for remission is worthwhile, especially when compared with low disease activity.

The present study aims (1) to analyze the HRQoL in a sample of patients with RA under biological therapy; (2) to compare HRQoL of patients with RA to that of the Portuguese general population; (3) to inquiry about disease activity influence in HRQoL and functional capacity; (4) to determine potential determinants for these outcomes.

**Methods**

**Study design and patients**

We performed a cohort cross-sectional study. The evaluating period was between October 2013 and July 2014 from a university hospital in the north of Portugal. Consecutive RA patients were recruited by participating study physicians during routine clinical visits. We included adult RA patients, diagnosed according to the 2010 ACR/EULAR classification criteria, under biological therapy. Patients lacking ability to answer the questionnaires were excluded. Additional exclusion criteria were not applied. A total of 154 patients were included. The medical ethics committee approved the study protocol.

**Outcomes measures**

HRQoL was captured by the Short Form Health Survey (SF-36) and EQ-5D.

SF-36 measures physical and mental health on eight subscales (physical functioning – PF, physical role functioning – PRF, bodily pain – BP, general health perceptions – GH, vitality – VT, social role functioning – SRF, emotional role functioning – ERF, mental health – MH), which are summed up in two scales, the physical and mental summary measures (PSM and MSM). Each scale comprises four dimensions scored from 0 to 100, with higher scores indicating better HRQoL. We calculated summary scores of the PCS and MCS, as well as single domain scores. These component scores are standardized on the basis of worldwide population norms to a mean of 50 and a standard deviation of 10.\(^18,19\)

EQ-5D is applicable to a variety of different illnesses and treatments and provides a simple descriptive profile and a single
index value for health status. The five dimensions included in the EQ-5D are: mobility; self-care; usual activities; pain/discomfort and anxiety/depression. Each dimension has three levels (none, some or major problems) and together defines 243 health states (3 to the power of 5 gives the 243 possible combination), to which has been added “unconscious” and “dead” for a total of 245 health states. EQ-5D scores range between −0.594 and 1 (full health).20

Limitations in activities of daily life were assessed by por-
tuguese version of the Health Assessment Questionnaire (HAQ) which comprises eight categories. A score of 0 (no difficulty), 1 (some difficulty), 2 (much difficulty or need of assistance) or 3 (unable to perform) is given to each question; the highest score in each category represents the score for that category. The sum of scores is then divided by the number of categories, yielding a total score ranging from 0 (best) to 3 (worst).21

Visual Analog Scales (VASs) were used, on which patients had to indicate on a scale from 0 (none) to 100 (worst) their rating of disease activity (VAS-DA) and pain (VAS-P).

**Data collection**

Data collection was performed in the rheumatology day-care hospital unit and through the longitudinal national database “reuma.pt”. The collected variables were C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), numbers of swollen and tender joints by using a 28-joint count (SJC28, TJC28); VAS-P and VAS-DA, and HAQ. Composite indices, such as the simpli-
fied disease activity index (SDAI) and the Disease Activity Score using 28-joint counts (DAS28-4V) were calculated by informatic system. Age, gender, level of education, marital and employment status as well as additional disease characteristics – disease duration, rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (anti-ACCP) status, extra-articular manifestations (rheumatoid nodules, ocular, rheumatoid vasculitis and pleuropulmonary) and DMARDs use – were also recorded. The application of questionnaires, available in the computer system, was held through face-to-face interviews.

**Statistical analyses**

In the description of socio-demographic and clinical character-
istics as well as in the description of PROs (eight domains of SF-36, PSM, MSM, EQ-5D, HAQ, VAS) were used means and standard devi-
ations for continuous variables with symmetrical distribution and median and range (minimum and maximum) for the variables con-
tinuous with asymmetric distribution. Categorical variables were expressed as proportions. To compare HRQoL of our RA patients to that of the portuguese general population, we used SF-36 published data by Ferreira et al.22 Measures of central tendency were compared using the Mann–Whitney test. To investigate whether outcomes are different at different levels of disease activity we divided sample according to level of disease activity by SDAI: remis-
son (REM) SDAI ≤ 3.3, low disease activity (LDA) 3.3 < SDAI ≤ 11, moderate disease activity (MDA) 11 < SDAI ≤ 26 and high disease activity (HDA) SDAI > 26. The comparison of outcomes was performed using Kruskal Wallis test and Fisher’s exact test, for medians and categorical variables, respectively. To assess the relationship between clinical data and the PROs, Spearman correlations (ρ) were performed. To identify explanatory variables of HRQoL and func-
tional capacity we conducted a multiple linear regression (stepwise selection) and included variables statistically significant in univariate analysis and those considered clinically relevant. We assessed correlations between the continuous variables and HRQoL with Spearman correlation to check for collinearity. Linear regression model assumptions were examined and satisfied. Residual plots

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic and clinical patient data.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients (n = 154)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>55.69 ± 10.72</td>
</tr>
<tr>
<td><strong>Age at diagnosis (years)</strong></td>
<td>37.99 ± 12.24</td>
</tr>
<tr>
<td><strong>Female (%)</strong></td>
<td>87.7</td>
</tr>
<tr>
<td><strong>Smoking (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td>8.5</td>
</tr>
<tr>
<td>No</td>
<td>80.6</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>10.9</td>
</tr>
<tr>
<td><strong>Education (%)</strong></td>
<td></td>
</tr>
<tr>
<td>≤4th grade</td>
<td>48.2</td>
</tr>
<tr>
<td>5–9th grade</td>
<td>27.3</td>
</tr>
<tr>
<td>10–12th grade</td>
<td>13.7</td>
</tr>
<tr>
<td>&gt;12th grade</td>
<td>10.8</td>
</tr>
<tr>
<td><strong>Work (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>33.8</td>
</tr>
<tr>
<td>Retired (due to disability)</td>
<td>49</td>
</tr>
<tr>
<td>Retired</td>
<td>11.7</td>
</tr>
<tr>
<td>Unemployed</td>
<td>5.5</td>
</tr>
<tr>
<td><strong>Disease duration (years)</strong></td>
<td>16(2–50)</td>
</tr>
<tr>
<td><strong>With EAM (%)</strong></td>
<td>42.9</td>
</tr>
<tr>
<td><strong>Antibodies (%)</strong></td>
<td></td>
</tr>
<tr>
<td>RF and/or ACCP</td>
<td>87</td>
</tr>
<tr>
<td>RF and ACCP –</td>
<td>13</td>
</tr>
<tr>
<td>Previous DMARDs</td>
<td>1(0–6)</td>
</tr>
<tr>
<td>Previous bDMARDs</td>
<td>0(0–3)</td>
</tr>
<tr>
<td>Current DMARDs</td>
<td>1(0–3)</td>
</tr>
<tr>
<td><strong>TJC 28</strong></td>
<td></td>
</tr>
<tr>
<td>1 ≤ TJC 28 &lt; 10</td>
<td>0.28(0.01–5.14)</td>
</tr>
<tr>
<td>10 ≤ TJC 28 &lt; 20</td>
<td>0.28(0.01–5.14)</td>
</tr>
<tr>
<td>20 ≤ TJC 28</td>
<td>0.28(0.01–5.14)</td>
</tr>
<tr>
<td>**ESR (mm/1h) **</td>
<td>17(1–91)</td>
</tr>
</tbody>
</table>

were examined for goodness of fit. Analyses were performed using the program SPSS Version 21. The p-values below 0.05 were con-
sidered significant.

**Results**

Socio-demographic, clinical and laboratory characteristics are documented in Table 1. At the moment of this study we found that 8.4% (n = 13) were in REM, 53.2% (n = 82) had LDA, 33.8% (n = 52) had MDA and 4.5% (n = 7) had HDA. Most patients (n = 107) were under the first biological agent and the median time under the drug was 6 years (range 0–10). Eight patients (5.2%) were under the current drug for 10 years and 27 (17.5%) for 2 years or less.

**HRQoL and functional status of RA patients**

After analysing all domains of the SF-36 we observed that the domain with lowest score was the “Physical Performance” (median 25) followed by the domain “General Health” and “Physical Func-
tioning” (median 40 for both). Mental domains showed higher values; among them, domain “Social Functioning” showed the low-
est score (median 40; range 3–53). The domain “Role-Emotional” had a median of 100 (range 0–100) (Table 2).

Likewise, we found that in SF-36 summary measure, PSM was lower than MSM (median 32 vs. 52). With the application of EQ-5D also observed a low score (median 0.620, range −0.349 to 1.000). In our sample, 5% of patients (n = 6) had scores on the EQ-5D less than zero (states worse than dead). Median score was 1.250 (range 0.000–2.875) for HAQ (Table 2).

When comparing primary outcomes between genders we found significant statistical differences only for the HAQ in which woman
Values reported: SF-36, EQ-5D, HAQ, PRF, VT, GHP, PH, MSM, PRF, SRF, ERF, MH, PSM, SRF. Differences between the groups were compared using Mann-Whitney test. Results showed that RA patients had worse scores in all domains compared to the general population. RA patients reported significant differences in emotional role functioning (p < 0.001) and physical role functioning (p = 0.0079) compared to the general population. RA patients had lower scores in all domains except for general health, which did not show significant differences. Regarding the SF-36, the scores in physical functioning, role limitations due to physical health, and vitality were significantly lower in RA patients compared to the general population. RA patients also had lower scores in the mental health domain. The EQ-5D results showed that RA patients had lower VAS-P and VAS-P scores compared to the general population. RA patients also had lower scores in the EQ-5D dimensions of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. RA patients also had lower scores in the HAQ, PRF, VT, GHP, PH, MSM, and SRF. The differences in scores were statistically significant for all instruments except for SRF. RA patients reported lower HRQoL scores compared to the general population, indicating lower quality of life for RA patients. RA patients had lower scores in all domains of the SF-36, EQ-5D, and HAQ compared to the general population. RA patients had lower scores in the emotional role functioning, physical role functioning, physical functioning, general health, vitality, bodily pain, and general health domains. RA patients also had lower scores in the EQ-5D dimensions of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. RA patients had lower scores in the HAQ, PRF, VT, GHP, PH, MSM, and SRF. The differences in scores were statistically significant for all instruments except for SRF. RA patients had lower HRQoL scores compared to the general population, indicating lower quality of life for RA patients.
The SF-36 summary measures, i.e., decreasing scores of PSM with increasing levels of disease activity ($p < 0.001$) and overlapping MSM values (Table 2). When we assessed potential differences in HRQoL by other measures, such as EQ-5D, we found very similar results ($p < 0.001$) (Table 2).

Comparing functional disability by HAQ at the four levels of disease activity, we observed significant differences between groups, showing a HAQ increase with increasing disease activity ($p < 0.001$) (Table 2).

In order to compare the benefit of remission with state of low disease activity with respect to the PRO we directly compared REM group with LDA (Table 2). In this analysis we observed a statistically significant difference in all PRO (SF-36, EQ-5D, HAQ and VAS) except in “Vitality” and “Social role functioning” domains and mental summary measure of the SF-36.

**HRQoL and functional disability have a weak correlation with clinical and laboratory data**

We evaluated the relationship between the various clinical and laboratory parameters with the PRO through the Spearman correlation ($\rho$).

The analyzed clinical and laboratory variables were: current age and age at disease onset, disease duration, education level, CRP, ESR, tender and swollen 28-joint count, DAS28 change, VAS-P and VAS-GH. We also studied the relationship between the PSM of SF-36 and initial and actual HAQ.

For PSM we concluded that variables with strongest relationship were those that correspond to other PRO, namely current and initial HAQ ($\rho = -0.67$ and $-0.48$, respectively), VAS-P ($\rho = -0.62$) and VAS-GH ($\rho = -0.58$) ($p < 0.001$ for all analyses). The relationship with tender and swollen 28-joint count, although significant, was much lower ($\rho = -0.35$ and $-0.20$, respectively). There was no correlation with ESR ($\rho = 0.02$, $p = 0.84$) nor with CRP ($\rho = 0.07$, $p = 0.365$). For MSM no significant correlations were identified.

The HAQ also showed weak correlation with ESR, CRP and 28-joint count. The strongest correlations were observed with PSM of SF-36 ($\rho = 0.674$), VAS-GH ($\rho = 0.609$), VAS-P ($\rho = 0.601$) and initial HAQ ($\rho = 0.595$) ($p < 0.001$ for all analyses).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient $\beta$</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSM</td>
<td>Higher education 3.887*</td>
<td>0.424–7.350</td>
</tr>
<tr>
<td></td>
<td>Higher HAQ $-9.119$</td>
<td>$-11.788$ to $-6.451$</td>
</tr>
<tr>
<td></td>
<td>Higher VAS-P $-0.165$</td>
<td>$-0.233$ to $-0.097$</td>
</tr>
<tr>
<td>MSM</td>
<td>$R^2$</td>
<td>54.6</td>
</tr>
<tr>
<td>EQ-5D</td>
<td>Higher HAQ $-0.208*$</td>
<td>$-0.271$ to $-0.145$</td>
</tr>
<tr>
<td></td>
<td>Higher VAS-GH $-0.003$</td>
<td>$-0.005$ to $-0.001$</td>
</tr>
<tr>
<td>HAQ</td>
<td>Higher age 0.011*</td>
<td>$0.003$–$0.018$</td>
</tr>
<tr>
<td></td>
<td>Female gender 0.247*</td>
<td>$0.014$–$0.480$</td>
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<tr>
<td></td>
<td>Current employment $-0.313$</td>
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</tr>
<tr>
<td></td>
<td>Higher VAS-GH 0.010</td>
<td>$0.004$–$0.016$</td>
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<tr>
<td></td>
<td>Higher VAS-P 0.006*</td>
<td>$0.001$–$0.011$</td>
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We used physical summary measures; HAQ, Health Assessment Questionnaire; VAS-P, visual analog scales of pain; MSM, mental summary measures; EQ-5D, EuroQol five dimensions questionnaire; VAS-GH, visual analog scale for general health.

Again, we verified that variables with strongest correlation with EQ-5D were other PRO (VAS-GH $\rho = -0.573$ and VAS-P $\rho = -0.560$, $p < 0.001$ for both) and not the clinical or laboratory classics data. There was not a significant association between the SF-36, EQ-5D and HAQ with the variation of DAS28-4V.

**Determinants of HRQoL**

The potential explanatory variables considered for summary measures of the SF-36, EQ-5D and HAQ were age, gender, level of education, employment status, disease duration, VAS-GH, VAS-P, tender and swollen 28-joint count, ESR, CRP and DAS28-4V change. For SF-36 and EQ-5D we also included HAQ questionnaire. The regression coefficients are documented in Table 3.

<table>
<thead>
<tr>
<th>Variable</th>
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<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
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There was not a significant association between the SF-36, EQ-5D and HAQ with the variation of DAS28-4V.

**Discussion**

The present study provides information on the effect of RA on HRQoL and functional capacity, in a real world setting.

Our results corroborate previous studies showing that patients with RA had not only significant physical function and mental...
health impairment but also poor HRQoL when compared to general Portuguese population.\textsuperscript{23} Differences are particularly notable on physical domains of SF-36 however, RA patients also present levels of mental health subscales significantly lower than general population.

In our study we verified values of EQ-5D corresponding to states of “full health”. Several factors may explain this finding. One of the disadvantages of the EQ5D is that may suffer from ceiling effect. The questionnaire is not sensitive enough to discriminate between different levels of health because the dimensions are probably not sufficiently disaggregated, leading individuals to respond at the highest level. These finding may indicate that individuals with significant morbidity are misclassified as in full health on the EQ-5D descriptive system.

When we evaluated disease activity influence in HRQoL and functional capacity, we found significant negative correlation (HRQoL and functional impairment with higher disease activity levels). A interesting finding in our study was to note a stronger correlation between SF-36 and measures of disability and pain (HAQ and VAS-P) than with measures directly related to disease process (ESR, CRP, joint count). Another finding was the benefit found in these outcomes when REM status was compared directly with LDA. Thus, indicators of quality of life, functional capacity, pain and appreciation of global health patient-reported complementing the clinical evaluation.

With regard to the potential determinants of these outcomes, we verified that older age and female gender was associated with higher HAQ score. This data confirms previous results.\textsuperscript{24} Physical function declines with age and it is known that women have lower threshold for pain and that men have more physical strength than women. Current employment was also related to better HAQ scores.

With regard to HQLq, we identified higher education level and functional capacity as potential determinants.

Unlike other results,\textsuperscript{18} the duration of disease showed no significant linear relationship with none of the outcomes.

Several limitations of our study should be addressed. We studied a non-representative sample of the Portuguese population. Although the sample was from a reference center of Portugal, this is a convenience sample and the sample size is potentially small. This is a cross-sectional analyses; therefore, prevents to establish directionality of interpretation, i.e., unknown if group of patients in remission and low disease activity showed better SF-36, EQ-5D and HAQ when presented higher levels of disease activity. Other limitation is the fact that the joint damage was not assessed. This becomes relevant for two reasons. We observed that most patients studied have disease for over 10 years and we know that in late disease the functional capacity is most associated with joint damage.\textsuperscript{18} The other reason is when we compare our sample with general population and observed that although all domains that compose the PSM were significantly lower, the difference is more pronounced for “physical functioning” and “physical role functioning” domains than for the “bodily pain” domain. Many patients with inactive disease but with important damage have functional limitations but do not refer pain complaints. Finally, the Portuguese population used to compare the HRQoL presents some characteristics that may affect the validity of the results. About 40% of the people interviewed report some type of pathology (namely musculoskeletal). However, this data has not been clinically confirmed based solely on patient-reported. Data such as gender and age were similar. Most were female and were between 30 and 69 years of age. In this way, we believe that there was no great influence on the results.

Strengths of the present analyses were the inclusion of a sample of patients with a broad range of clinical characteristics, rather than the more homogeneous populations of the trials; the focus on the more-stringent SDAI remission criteria, which allowed the recognition of the differences between REM and all other states, including LDA; it addressed quality of life not only through the state of health (SF-36) but also by assessing the value of health (EQ-5D) reported by the patient. The fact that it included the utility measure will enable future cost-effectiveness studies. Finally, analysis of summary measures of SF-36 as well as each of the domains provides a clearer picture of the dimensions affected by the disease.

We consider our results useful to better understand the impact of disease and establish a basis for future prospective studies with larger samples to assess the efficacy of therapeutic interventions. The focus on seriously ill patients in need of costly therapy may also be useful for cost-utility analysis studies of biotech drugs.

**Conclusion**

RA has considerable impact on quality of life and functional capacity being the impairment of HRQoL enormous when compared to general population. We verified lower HRQoL and functional capacity with higher disease activity levels and we saw that reaching remission seems to be a desirable state also from patient perspective. Since the clinical and laboratory data are weakly correlated with HRQoL and functional capacity, we believe that access to PROs is very important in order to complete the disease assessment.

**Ethical disclosures**

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

**Funding**

Not applicable.

**Authors contributions**

All authors make substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data. All critically revise it for important critical content and give final approval of the version of the article accepted for publication.

**Conflicts of interest**

None of the authors has any conflicts of interest to declare.

**Acknowledgments**

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**References**


