



Influence of disease activity on functional capacity in patients with rheumatoid arthritis

Uticaj aktivnosti bolesti na funkcijski status bolesnika sa reumatoidnim artritismom

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Abstract

Background/Aim. Progressive erosive changes in cartilage and bone in rheumatoid arthritis (RA) ultimately lead to joint deformities and disability which may be early, severe and permanent. Consequently, there is the reduction of functional ability and changes in the quality of life. The aim of this study was to estimate the impact of disease activity on functional status of patients with RA. **Methods.** A prospective investigation included 74 patients with RA who were treated in the Rheumatology Clinic of the “Niška Banja” Institute. Assessment of functional status (capacity) was measured by the Health Assessment Questionnaire (HAQ) with the values from 0 to 3 that patients fill out on their own. The patients were then divided into three groups: the group I with the HAQ values from 0.125 to 1.000, the group II with the values from 1.125 to 2.000 and the group III with the values from 2.125 to 3.000. Disease activity was measured by Disease Activity Score (DAS28). The assessment also included sedimentation rate (SE) influence, IgM rheumatoid factor (RF) and C-reactive protein (CRP) positivity, age, and disease duration. **Results.** The patients with the most severe functional damage estimated by the HAQ – the group III, had the highest values of DAS28 SE (7.4 ± 0.8) compared to the group II (6.5 ± 1.2) and the group I (3.4 ± 1.2). The group

III also showed the highest values of DAS28 CRP (7.1 ± 0.8) compared to the group II (6.7 ± 0.8) and the group I (3.6 ± 0.4). Compared with the patients with small and moderate functional damage, the patients in the group III had positive IgM RF and CRP as well as higher SE values more frequently and the difference was statistically significant. In the univariate logistic model, the tested parameters of DAS28 SE, DAS28 CRP, SE, RF and CRP represent significant predictors of functional disability. The most significant factors that increase the odds of patient having the most severe functional damage include DAS28 SE which increases the odds by 5.5 times (OR = 5.450, 95% CI = 3.211–7.690, $p = 0.001$), DAS28 CRP by 5.1 times (OR = 5.111, 95% CI = 2.123–10.636, $p < 0.01$), and the presence of increased CRP (OR = 5.219, 95% CI = 1.305–18.231, $p = 0.019$) by 5.2 times. **Conclusion.** Functional status evaluated by the HAQ is a standard for assessment of RA due to its convenience and good correlation with parameters of disease activity. The most significant factors that increase the odds that the patient has the greatest functional damage are DAS28 SE, DAS28 CRP and the presence of CRP.

Key words: arthritis, rheumatoid; severity of illness index; questionnaires; prognosis.

Apstrakt

Uvod/Cilj. Progressivne erozivne promene hrskavice i kosti u reumatoidnom artritisu (RA) u krajnjem ishodu dovede do deformacije zglobova i invalidnosti koja može biti rana, teška i trajna. Posledično dolazi do smanjenja funkcijske sposobnosti i kvaliteta života. Cilj rada bio je ispitati uticaj aktivnosti bolesti na funkcijski status bolesnika sa RA. **Metode.** Prospektivnim ispitivanjem obuhvaćeno je 74 bolesnika sa RA, lečenih bolnički u Klinici za reumatologiju Instituta „Niška Banja“. Procena funkcijskog sta-

tusa (sposobnosti) merena je upitnikom Health Assessment Questionnaire (HAQ), koji su bolesnici samostalno popunjavali (Health Assessment Questionnaire sa vrednostima od 0-3), a zatim su podeljeni u 3 grupe: grupa I sa vrednostima HAQ 0,125–1,000; grupa II sa vrednostima HAQ 1,125–2,000 i grupa III sa vrednostima HAQ od 2,125–3,000. Aktivnost bolesti procenjavana je indeksom aktivnosti bolesti (*Disease Activity Score* – DAS28). Analiziran je i uticaj brzine sedimentacije eritrocita (SE), pozitivnosti IgM reumatoidnog faktora (RF) i C-reaktivnog proteina (CRP), godina života i trajanja bolesti. **Rezultati.**

Bolesnici koji su imali najteže funkcijsko oštećenje procenjeno HAQ-om (grupa III) imali su najviše vrednosti DAS28 SE ($7,4 \pm 0,8$) u odnosu na grupu II ($6,5 \pm 1,2$) i grupu I ($3,4 \pm 1,2$), kao i najviše vrednosti DAS28 CRP ($7,1 \pm 0,8$) u odnosu na grupu II ($6,7 \pm 0,8$) i grupu I ($3,6 \pm 0,4$). Ispitanici grupe III imali su statistički značajno češće pozitivan IgM RF i CRP, višu vrednost SE, u odnosu na ispitanike sa manjim i umerenim funkcijskim oštećenjem. U univarijantnom logističkom modelu, ispitivani parametri DAS28 SE, DAS28 CRP, SE, RF i CRP predstavljali su značajne prediktore funkcijske nesposobnosti. Najznačajnije faktore koji povećavaju šansu da ispitanik ima najteže funkcijsko oštećenje predstavljali su DAS28 SE i to 5,5

puta (OR = 5,450, 95% CI = 3,211–7,690, $p = 0,001$), DAS28 CRP 5,1 puta (OR = 5,111, 95% CI = 2,123–10,636, $p < 0,01$), i prisustvo povišenog CRP-a (OR = 5,219, 95% CI = 1,305–18,231, $p = 0,019$) 5,2 puta. **Zaključak.** Funkcijski status procenjen upitnikom HAQ pokazao se kao standard pri oceni reumatoidnog artritisa zbog praktičnosti i dobre korelacije sa parametrima aktivnosti bolesti, gde su se kao najznačajniji faktori izdvojili indeks aktivnosti bolesti DAS28 SE, DAS28 CRP prisustvo CRP.

Ključne reči:

artritis, reumatoidni; bolest, indeks težine; upitnici, prognoza.

Introduction

Rheumatoid arthritis (RA) is a chronic, inflammatory, systemic autoimmune disease which is characterised by symmetric inflammatory changes of synovial joints. During the course of the disease, progressive erosions in cartilage and bone appear, finally leading to characteristic deformities of joints and possible disability, which can be early one, severe and permanent¹. Consequently, the patients' quality of life deteriorates including both self care and everyday activities and there is also a decrease in functional ability and productivity concerning professional activities, which leads to economical consequences because of treatment, rehabilitation and possible surgical methods of treatment. Success in the treatment of RA significantly depends on good and prompt assessment of disease activity². RA activity determines the speed of the disease advancement and its potential for the development of anatomical and functional disorders³.

Because of the variables of signs and symptoms manifestations, clinical trials use summary indices which overcome the problems of validity, reliability and sensitivity to changes, noticed in some characteristics^{4,5}. For the time being, the best tools for this assessment in individual patients are the Disease Activity Index and its validated modifications which include the Disease Activity Score (DAS) and DAS28⁴ developed by the European League Against Rheumatism (EULAR)⁶. Those indexes show a significant correlation with functional abilities, as well as with the outcome of the disease – radiographic progression of the disease³⁻⁵.

The aim of this study was to examine the influence of disease activity on the functional status of RA patients.

Methods

This prospective study included 74 RA patients with the diagnosis established according to a revised American College of Rheumatology (ACR) criteria from 1987. The patients were hospitalized at the Rheumatology Clinic of the "Niška Banja" Institute. There were 57 (77%) women and 17 (23%) men. The average age of patients was 58.3 ± 8.6 years, and the average duration of the disease 7.8 ± 6.6 years. Assessment of the functional status (ability) was performed by the Health Assessment Questionnaire (HAQ) with the

values from 0 to 3, which the patients filled out themselves. The patients were then divided into three study groups: group I – the subjects with smaller degree of functional damage with HAQ values 0.125–1.000, the group II with HAQ values 1.125–2.000 – subjects with moderate functional damage and the group III – subjects with complete functional disability and HAQ values from 2.125–3.000. The disease activity was assessed by the disease index activity DAS28, calculated on the basis of the number of painful and swollen joints out of a total of 28 examined, sedimentation rate (SE) for DAS28 SE, C-reactive protein (CRP) values for DAS28 CRP and assessment of general state of the patients by the use of the visual analogue scale (VAS, 0–100). DAS 28 values higher than 5.1 suggest a high disease activity, the values from 3.2 to 5.1 suggest moderate disease activity and the values from 2.6 to 3.2 suggest low disease activity. DAS28 value less than 2.6 suggests remission. Analysis also included SE rate, positivity of IgM Rheumatoid factor (RF) and CRP, age and disease duration. Analyzed data were presented by absolute and relative numbers (category variables), arithmetic mean and standard deviations (continuous numeric features). Comparison of numeric variables distributed by the type of normality, was performed by analysis of variance (ANOVA) test, while variables which were not distributed by the type of normality were compared by Kruskal-Wallis test. Mann Whitney *U*-test and Bonferroni test were used in the *Post hock* procedure. The definition of risk factors was done by univariate logistic regression. Statistical significance is regarded to be at the level of $p < 0,05$, defined by the statistical package SPSS (version 18).

Results

A statistically significant difference (ANOVA), was noticed in the DAS 28 SE variable ($F = 53.797$, $p < 0,001$), and in SE variable ($F = 8.253$, $p = 0,001$). *Post hock* analysis showed that DAS28SE and DAS28 CRP values were statistically significantly higher in the group III, as compared to the group II and the group I, as well as that the values of the same parameters in the group II were higher than in the group I.

A significance of SE value difference was also noticed, but only between the group III and the group I ($F = 8.253$, $p = 0,001$).

In the univariate logistic model, the examined parameters of DAS28 SE, DAS28 CRP, SE, RF and CRP represent significant predictors of functional disability. The most significant factors which increase the chance for a patient to be in the HAQ III group, i.e. to have the most severe functional damage include DAS 28 SE which increases the odds by 5.5 times (OR = 5.450, 95% CI = 3.211–7.690, $p = 0.001$), DAS28 CRP by 5.1 times (OR = 5.111, 95% CI = 2.123–10.636, $p < 0.01$), and the presence of CRP (OR = 5.219, 95% CI = 1.305–18.231, $p = 0.019$) by 5.2 times. As the significant risk factor at the level $p < 0.001$, RF singled out by increasing the odds that the patient has functional disability by 2.1 times.

ties, as well as with the disease outcome – radiographic disease progression^{3–5}.

The interaction between the disease activity and joint damage are the main factors which influence the functional ability.

Investigation of the relationship between the disease activity, joint destruction and functional capacity is very common in clinical investigations. This provides data on the degree to which the disease activity and current joint damage influence the functional ability of RA patients and their quality of life which has certain psychosocial and economic significance². Functional capacity measured by Health Assessment Questionnaire Disability Index (HAQDI) deterioro-

Table 1
Patient characteristics, significance of numerical differences of continuous variables between the examined groups (I–III) with respect to the Health Assessment Questionnaire (HAQ)

Variables	Groups of patients ($\bar{x} \pm SD$)						F	p
	I		II		III			
Age (years)	55.9	7.7	58.5	8.6	60.5	9.4	1.205	0.306
Disease duration (years)	5.5	3.8	7.7	6.9	10.2	9.1	1.541	0.221
DAS28 CRP	3.6	0.4	6.7	0.8	7.1	0.8	10.084	† < 0.001 ^{A,B,C}
DAS28 SE	3.4	0.9	6.5	1.2	7.4	0.8	53.797	† < 0.001 ^{A,B,C}
SE	15.1	7.5	36.4	20.3	50.8	28.5	8.253	‡ 0.001 ^B

DAS – disease activity score; CRP – C-reactive protein; SE – sedimentation rate;

Group I – HAQ values from 0.125 to 1.000

Group II – HAQ values from 1.125 to 2.000

Group III – HAQ values from 2.125 to 3.000

A (I vs II), B (I vs III), C (II vs III)

†p-value of ANOVA test, ‡p-value of Kruskal-Wallis test.

Table 2

Univariate logistic regression, predictors of functional disability

Factors	OR	95% CI	p	
DAS28 SE	5.45	3.211–7.690	0.001	
DAS28 CRP	5.111	2.123–10.636	0.01	
SE	1.561	1.021–3.156	0.04	
CRP	[0]	/	/	
	1	5219	1.305–18.231	0.019
RF	[0]	/	/	
	1	2.111	1.210–4.150	< 0.001

[] – The reference category; OR – odds ratio, 95% CI – 95% confidence interval;

p – statistical significance at the level $p < 0.05$; DAS – disease activity score;

SE – sedimentation rate; CRP – C-reactive protein; RF – rheumatoid factor.

Discussion

Success in RA treatment largely depends on the right evaluation of the disease activity, when efficient administration of medicaments is possible, which change the disease course².

Accurate measurement of the RA activity is not at all simple, and in the last 15 years it has become obvious that due to the variability of symptoms and signs manifestation⁴, it is not sufficient to determine only the number of painful and swollen joints and perform the basic laboratory analysis. It is necessary to monitor the collective indexes of the disease activity which overcome the problems with validity, reliability and sensitivity to changes noticed in some characteristics^{4,5}. For the time being, the best tools for its assessment in individuals are the disease activity Score and its validated modifications DAS and DAS28 developed by the European League Against Rheumatism (EULAR)⁶. Those indexes show a significant correlation with functional abili-

ties during the disease, If left untreated, 20–30% of RA patients will become permanently disabled for work within 3 years from the diagnosis, and after 10 years with the disease 80% of patients will be permanently incapable for work and become handicapped.

Functional disability assessment is the fundamental measurement in RA⁷, considering the chronic nature of this disease. The influence of the changes developed in RA on everyday activities, working ability, need for surgical treatment, increased mortality rate, suggest the convenience of the use of such investigation and is a significant addition to physical examination of the patient.

The HAQ, filled out by patients themselves, is a measure of the functional loss of everyday activities, such as dressing up, eating, using the toilet, shopping or house work. HAQ usually increases faster at the beginning of the disease⁸. Among the early reports, HAQ becomes a regular measure of the progression, damage and limited range of motion in RA, especially during the years of follow-up.

Investigations which deal with the influence of the disease activity on functional status often have controversial results, and this diversity of the results is explained by the variability of symptoms and signs manifestations in patients with RA, prone to frequent and even daily variations.

Drossaers-Bakker et al.⁹ investigated the relationship of the functional status which is represented by the HAQ score and the disease activity measured by DAS during the period of 12 years in 132 patients. At the beginning of the investigation there was a strong correlation of HAQ and DAS, that was maintained even after three years. In the following years, joint damage presented by Sharp's score had greater influence on HAQ, but at the end of the investigation, after 12 years of follow-up, the disease activity presented by DAS was the main factor of the functional disability represented by HAQ⁹.

Our results also show that subjects with the most severe functional damage estimated by HAQ – the group III, have the highest disease activity presented by DAS 28 SE with the values 7.4 ± 0.8 compared to the group II (6.5 ± 1.2) and the group I (3.4 ± 1.2), as well as the highest values of DAS 28 CRP 7.1 ± 0.8 compared to the group II (6.7 ± 0.8) and the group I (3.6 ± 0.4). The findings have a high statistical significance. The subjects in the group II have a higher disease activity in comparison to those in the group I (statistically significant difference ANOVA, DAS28 SE ($F = 53.797, p < 0.001$) and DAS28 CRP ($F = 10.084, p < 0.001$)).

In the univariate logistic model, the most significant factor which increases the odds for a patient to be in the HAQ group III, i.e. to have the most severe functional damage is DAS 28 SE which increases these chances by 5.5 times (OR = 5.450, 95% CI = 3.211–7.690, $p = 0.001$). DAS28 CRP increases the odds for the subject to have the most severe functional damage by 5.1 times (OR = 5.111, 95% CI = 2.123–10.636, $p < 0.01$), and presence of CRP (OR = 5.219, 95% CI = 1.305–18.231, $p = 0.019$) by 5.2 times. RF was singled out as a significant risk factor at the level of $p < 0.001$, increasing the odds for the subject to have functional disability by 2.1 times.

In the five-year follow-up, Combe et al.¹⁰ concluded that the final HAQ disability is caused by the initial value of the HAQ, pain, Ritchie index, the number of painful joints, disease activity score, SE, CRP and erosions. Using a multivariate analysis, they emphasized the following prognostic risk factors of HAQ disability: initial HAQ score, Ritchie index, SE, CRP, and the presence of erosions as the most significant prognostic factors of the functional disability.

Investigation by Courvaisir et al.¹¹ in a 10-year follow-up, defined the correlation between HAQ and disease activity which was presented by DAS and pain, both at the beginning and after five and 10 years.

The significance of investigation of the functional ability is also suggested by the Early Rheumatoid Arthritis Study (ERAS) which included 732 patients and showed that deterioration of the functional status later in the course of the disease was caused by a high HAQ at the beginning of the investigation¹².

Some studies showed that functional status at the early stages of the disease was first of all influenced by the disease activity, and that in later stages poor functional status was the consequence of joint damage².

Our results suggest that the subjects with the most severe functional damage, the group III, have a statistically significantly higher SE value (increases the odds for the subject to be in the HAQ group III by 56%), frequently positive RF as significant risk factor at the level of $p < 0.001$, increasing the odds for the subject to be in the HAD group III by 2.1 times, compared to subjects with smaller and moderate functional damage. Gender did not significantly influence the functional ability.

Investigation of the influence of age and duration of the disease on the functional ability showed that older age and longer disease significantly contribute to the loss of the functional ability (patient's age observed as continued variable), increases the odds for the patient to be in the HAQ group III by almost 60% (OR = 1.572, 95% CI = 1.111–1.946, $p < 0.001$), disease duration (continuously) by 80% (OR = 1.792, 95% CI = 1.550–1.930, $p < 0.001$). These results are in accordance with investigations by Sokka et al.¹³ who concluded that older age contributed to the decrease of the functional ability and with a study by Scott et al.¹⁴ who compared the results of several research centers and showed that functional disability increases with longer disease and the increase is constant.

Investigation that involved 706 patients, studied the influence of demographic, laboratory and radiology parameters on HAQ. The loss of functional ability was significantly influenced by the number of painful and swollen joints, older age, longer disease duration and higher SE values. The crucial factor for the functional ability loss was female gender. RF and joint damage did not have significant influence¹⁵.

A study on 110 patients with RA showed a statistically highly significant correlation between HAQ with older patients, longer disease duration, progress on the walking path, longer morning stiffness, as lower values of Erythrocyte number and statistically significant correlation between HAQ and lower hemoglobin values and higher SE and CRP values¹⁶.

HAQ index was proved to be one of the best indicators of the long-lasting prognosis in RA-patients with high HAQ score who have increased mortality rate, working disability, pain and psychosocial changes.

Original DAS and DAS28 remain valid, reliable and sensitive indicators of the disease activity that can be used for the estimation of the total RA activity. They are relatively successful in determining the number of patients who will actually be affected by the consequences of RA³.

Conclusion

The Health Assessment Questionnaire proved to be the standard in the evaluation of the functional status of rheumatoid arthritis patients due to its practicality and good correlation with parameters of disease activity, where the disease activity index DAS28 is singled out as the most significant factor.

R E F E R E N C E S

1. *Marković Z.* Rheumatoid arthritis. In: *Ilić S*, editor. Internal medicine. Niš: Faculty of Medicine University of Niš; 2009. p. 1018–28. (Serbian)
2. *Welsing PM, van Gestel AM, Swinkels HL, Kiemeneij LA, van Riel PL.* The relationship between disease activity, joint destruction, and functional capacity over the course of rheumatoid arthritis. *Arthritis Rheum* 2001; 44(9): 2009–17.
3. *Radunović G.* Monitoring of disease activity in patients with rheumatoid arthritis. *Acta Rheumatologica Belgradensia* 2008; 38(Suppl 2): 30–5. (Serbian)
4. *Ward MM.* Clinical and laboratory measures. In: *St Clair EW, Pisetsky DS, Haynes BF.* Rheumatoid arthritis. 1st ed. Philadelphia: Lippincott Williams & Wilkins; 2004. p. 51–63.
5. *van Riel PL, van Gestel AM.* Clinical outcomes measures in rheumatoid arthritis. *Ann Rheum Dis* 2000; 59(Suppl 1): 28–31.
6. *Smolen JS, Breedveld FC, Schiff MH, Kalden JR, Emery P, Eberl G*, et al. A simplified disease activity index for rheumatoid arthritis for use in clinical practice. *Rheumatology* 2003; 42(2): 244–57.
7. *Wolfe F.* A reappraisal of HAQ disability in rheumatoid arthritis. *Arthritis Rheum* 2000; 43(12): 2751–61.
8. *Sherrer YS, Bloch DA, Mitchell DM, Young DY, Fries JF.* The development of disability in rheumatoid arthritis. *Arthritis Rheum* 1986; 29(4): 494–500.
9. *Drossaers-Bakker KW, de Buck M, van Zeben D, Zwinderman AH, Breedveld FC, Hazes JM.* Long-term course and outcome of functional capacity in rheumatoid arthritis: the effect of disease activity and radiologic damage over time. *Arthritis Rheum* 1999; 42(9): 1854–60.
10. *Combe B, Cantagrel A, Goupille P, Bozonnat MC, Sibilia J, Eliaou J*, et al. Predictive factors of 5-year health assessment questionnaire disability in early. *J Rheumatol* 2003; 30(11): 2344–9.
11. *Courvoisier N, Dougados M, Cantagrel A, Goupille P, Meyer O, Sibilia J*, et al. Prognostic factors of 10-year radiographic outcome in early rheumatoid arthritis: a prospective study. *Arthritis Res Ther* 2008; 10(5): R106.
12. *Young A, Dixey J, Cox N, Davies P, Devlin J, Emery P*, et al. How does functional disability in early rheumatoid arthritis (RA) affect patients and their lives?, Results of 5 years follow-up in 732 patients from the early RA Study (ERAS). *Rheumatology (Oxford)* 2000; 39(6): 603–11.
13. *Sokka T, Krishnan E, Häkkinen A, Hannonen P.* Functional disability in rheumatoid arthritis patients compared with a community population in Finland. *Arthritis Rheum* 2003; 48(1): 59–63.
14. *Scott DL, Pugner K, Kaarela K, Doyle DV, Woolf A, Holmes J*, et al. The links between joint damage and disability in rheumatoid arthritis. *Rheumatology* 2000; 39(2): 122–32.
15. *Smedstad LM, Moum T, Guillemin F, Kvien TK, Finch MB, Suurmeijer TP*, et al. Correlates of functional disability in early rheumatoid arthritis: a cross-sectional study of 706 patients in four European countries. *Br J Rheumatol* 1996; 35(8): 746–51.
16. *Jovanović J.* Modern diagnostics and the assessment of functional ability of the knee with rheumatoid arthritis [thesis]. Niš: Faculty of Medicine University of Niš; 2005. (Serbian)

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