IMPACT OF MORNING STIFFNESS, EDUCATION, AND AGE ON THE FUNCTIONAL STATUS OF PATIENTS WITH RHEUMATOID ARTHRITIS

UTJECAJ JUTARNJE UKOČENOSTI, OBRAZOVANJA I DOBI NA FUNKCIONALNI STATUS BOLESNIKA S REUMATOIDNIM ARTRITISOM

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Abstract

The purpose of this study was to explore the relationship between disability status and duration of morning stiffness in hands with regard to age, level of education, and gender in patients with rheumatoid arthritis (RA). Also, the authors wanted to investigate this relationship with regard to the presence of rheumatoid factor, i.e., the serological status.

A retrospective study was conducted in 250 patients with the classic form of RA (186 females, 64 males, mean age Xb = 49.96 years, range 25-60 years, disease duration 1-27 years, Xb = 6.41) previously diagnosed with RA according to the ACR (American College of Rheumatology 1987 criteria). All patients were in Steinbrocker functional classes II and III. The probability level was expressed by $p < 0.01$ and $p < 0.05$. The relationship between the variables was measured by point-biserial correlation.

The correlation between duration of morning stiffness and functional class was positive but low [($r = 0.10$, $y = 0.00x + 2.37$, $p > 0.05$) seronegative, ($r = 0.12$, $y = 0.00x + 2.30$, $p > 0.05$) seropositive]. High positive values were obtained for the linear correlation coefficient between duration of the disease and functional class ($p < 0.01$). Also, high values were obtained regarding the coefficient of correlation between age and functional class [($r = 0.29$, $p < 0.01$) seronegative, ($r = 0.47$, $p < 0.01$) seropositive]. Uneducated patients were significantly more represented in functional class III [23 (50%) seronegative, 19 (42.2%) seropositive] than in functional class II [16 (20.3%) seronegative, 22 (27.5%) seropositive].

In conclusion, in this study of patients with rheumatoid arthritis, increased duration of morning stiffness was associated with functional disability. Functional disability increased with the duration of the disease, depended on age and educational level, and was more pronounced in older age, regardless of RA serological status. With regard to serological status and sex, the differences were non-significant.

Keywords: rheumatoid arthritis, functional status, morning stiffness, age, education.

Sažetak

Svrha istraživanja bila je proučiti i usporediti odnos između funkcionalnog statusa i trajanja jutarnje zakočenosti u šakama s obzirom na dob, razinu obrazovanja i spol u bolesnika s reumatoidnim artritisom (RA). Istražena je povezanost tih čimbenika u odnosu na postojanje reumatoidnog faktora, odnosno seroloski status.

Ova retrospektivna studija provedena je u 250 bolesnika s klasičnim oblikom RA (186 žena, 64 muškarca). Ispitanici su bili u dobi između 25 i 60 godina, ($\bar{x}$=49.96) s trajanjem bolesti od jedne do 27 godina ($\bar{x}$ =6.41) i nisu ispunjavali revidirane dijagnostičke kriterije ACR-a (American College of Rheumatology – 1987). Svi ispitanici pripadali su II. i III. funkcionalnom razredu prema Steinbrockerovoj klasifikaciji. Odnos između funkcionalnih razreda i odabranih varijabli (trajanje jutarnje ukočenosti u rukama, spol, dob i stupanj obrazovanja) u odnosu na serostatus

mjeren je point-biserijalnim koeficijentom korelacije. Nađena je pozitivna, iako niska korelacija između trajanja jutarnje ukočenosti i funkcionalnih klasa [(r=0.10, y=0.00x 2.37, p> 0.05) seronegativni, (r=0.12, y=0.00x 2.30, p>0.05) seropozitivni]. Visoke pozitivne vrijednosti dobivene su pri određivanju koeficijenta linearne korelacije između trajanja bolesti i funkcionalnih klasa (p<0.01). Također su visoke vrijednosti dobivene za koeficijent korelacije između dobi i funkcionalnih klasa [(r=0.29, p<0.01) seronegativni, (r=0.47, p<0.01) seropozitivni]. Slabije obrazovani bolesnici bili su znatno više zastupljeni u III. funkcionalnom razredu [23 (50%) seronegativni, 19 (42.2%) seropozitivni] nego u II. funkcionalnom razredu [16 (20.3%) seronegativni, 22 (27.5%) seropozitivni]. Zaključno, prema ovoj studiji bolesnika s reumatoidnim artritisom dulje trajanje jutarnje zakočenosti bilo je povezano sa stupnjem funkcionalne nesposobnosti. Funkcionalna nesposobnost bila je povećana s trajanjem bolesti, ovisna o dobi i obrazovnoj razini te je izraženija u starijoj dobi, bez obzira na RA serološki status. U odnosu na serološki status i spol, razlike nisu znatne.

Ključne riječi: reumatoidni artritis, funkcionalni status, jutarnja zakočenost, dob, obrazovanje.

Introduction

Rheumatoid arthritis (RA) is an autoimmune inflammatory disease which primarily involves the synovial tissue of peripheral joints in a symmetrical fashion. The disease presents a broad spectrum of clinical phenotypes, with characteristic progressive symmetric polyarthritis which is nonspecific and destructive (1,2,3). The pathogenesis of the disease is complex, chronic, and multifactorial (4). The presence of the rheumatoid factor (RF) IgM, detected by conventional hematological method (Waaler-Rose and Latex tests), can be used to divide RA patients into subpopulations of seropositive and seronegative. This evidence was a starting premise in many studies (5). Rheumatoid arthritis causes premature disability, mortality, and compromised quality of life in the industrialized and developing world (6). The simplest, widely used criteria to classify patients with RA are comprised in the Steinbrocker classification into 4 functional classes, which was later accepted by the American Rheumatogy Association (ARA), today's American College of Rheumatology (7,8). The most important factor affecting functional disability in early disease is joint tenderness, while erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are useful markers of inflammatory activity. In patients with advanced disease, declining functional disability is more related to the degree of joint structural changes (9,10). Nevertheless, although the importance of joint damage increases with time, disease activity remains a significant factor which influences the functional capacity throughout the course of RA (11).

The purpose of this study was to explore the relationship between the level of functional status and the duration of morning stiffness in hands with regard to age, level of education, and gender in patients with established RA. Also, we wanted to investigate this relationship with regard to serological status.

Materials and Methods

This was a retrospective study conducted in 250 consecutive adult patients with an established diagnosis of RA according to the American College of Rheumatology (ACR) criteria from 1987 (12). The patients were treated in the period 2010-2014 at the Clinic for Physical and Sport Medicine in Prishtina and at the Internal Medicine Services of Kosovo. The study was approved by the Ethics Committee. The subjects were 186 females and 64 males, the mean age was Xb = 49.96 years (range 25-60 years), and the disease duration was Xb = 6.41 (range 1-27 years). The patients completed a structured questionnaire specifically designed for this study, which included relevant clinical parameters. Apart from the diagnosis of RA, the inclusion criterion was a II or III functional class based on the Steinbrocker classification. The Steinbrocker functional index comprises 4 classes: I - complete ability to carry out all the usual duties without handicaps; II - adequate for normal activities despite handicap of discomfort or limited motion of one of the joints; III - limited to little or none of the duties of usual occupation or self-care; and IV - incapacitated, largely or wholly bed-ridden or confined to a wheelchair with little or no self-care. Consequently, patients with Steinbrocker functional class I and IV were excluded from the study. The presence of RFIgM in the patients was determined by standard agglutination methods (Waaler-Rose and Latex RF tests). A titer lower than 1:64 for Waaler-Rose test and a titer of 1:40 for the Latex RF test were considered to be seronegative. The study group consisted of 125 seronegative (93 female, 32 male) and 125 seropositive (93 female, 32 male) patients. Considering disease duration, there was no difference regarding serological status (seronegative Xb = 6.4 ± 5.9, seropositive Xb = 6.3 ± 6.9) or age (seronegative Xb = 46.6 ± 10.3, seropositive Xb = 47.3 ± 10.4).

Apart from descriptive statistics, T-test and χ^2 test were used to determine the differences between factors or features. In the cases when one variable was dichotomous while the other was continuous, the point biserial correlation coefficient was used. The level of significance was set up at $p < 0.05$.

Results

When divided into two categories regarding the duration of morning stiffness (less than 120 minutes and equal or more than 120 min), there were more seronegative (82 - 79.6%) than seropositive (71 - 67.6%) patients in the group of patients with lesser morning stiffness duration, whereas in the over-120-minute group, seropositive (34 - 32.4%) patients were more represented than seronegative (21 - 20.4%) in both Steinbrocker functional classes II and III (Table 1). Morning stiffness (Table 2) was more frequent in seropositive patients who belonged to the functional

Table 1 Morning stiffness in hands (in minutes) and functional classes II and III (Steinbrocker) regarding RA serological status.

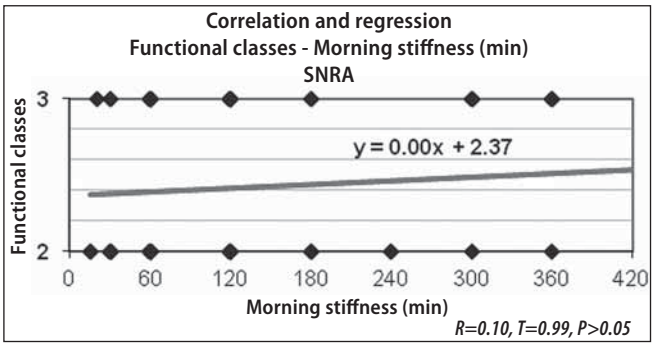
Tablica 1. Jutarnja zakočenost (u minutama) i funkcionalna klasifikacija II i III (prema Steinbbrockeru) u odnosu na serolpški status RA.

Functional class	Morning stiffness		Seronegative RA		Seropositive RA	
			N	%	N	%
II	up to 120′		50	83.3	47	69.1
		>120′	10	16.7	21	30.9
III	up to 120′		32	74.4	24	64.9
		>120′	11	25.6	13	35.1
Total	up to 120′		82	79.6	71	67.6
		>120′	21	20.4	34	32.4

RA- rheumatoid arthritis

class II [68 (85%) seropositive, 60 (75.9%) seronegative], while in seronegative patients morning stiffness was more frequent in those who belonged to functional class III [43 (93.5%) seronegative, 37 (82.2%) seropositive]. However, these differences were not statistically relevant. The mean values of morning stiffness were higher in seropositive patients in both functional classes, without a statistically significant difference ($t = 1.05$, $p > 0.05$). There was a positive but low level of correlation between duration of morning stiffness and functional class [($r = 0.10$, $y = 0.00x + 2.37$, $p > 0.05$) seronegative, ($r = 0.12$, $y = 0.00x + 2.30$, $p > 0.05$) seropositive]. Increased duration of morning stiffness was associated with functional disability, but without a statistical significance (Figures 1 and 2).

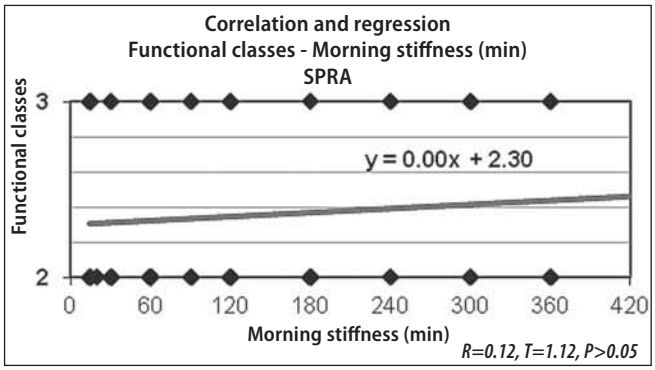
Our data showed the dominance of seropositive patients in functional class III when the duration of the disease was up to 10 years (28.6% vs. 22.4%). On the contrary, this



SNRA - seronegative rheumatoid arthritis.

Figure 1 Correlation and regression analysis between morning stiffness and functional classes in seronegative RA patients.

Slika 1. Korelacija i regresijska analiza između trajanja jutarnje zakočenosti (u minutama) i funkcionalnih klasa u seronegativnih bolesnika s RA.



SPRA - seropositive rheumatoid arthritis.

Figure 1 Correlation and regression analysis between morning stiffness and functional classes in seronegative RA patients.

Slika 1. Korelaci ja i regresijska analiza između trajanja jutarnje zakočenosti (u minutama) i funkcionalnih klasa u seronegativnih bolesnika s RA.

Table 2 Correlation between duration of morning stiffness in hands (in minutes) (MS*) and functional classes II and III (Steinbrocker) regarding RA serological status.

Tablica 2. Korelacija između trajanja jutarnje zakočenosti u šakama (u minutama) i funckionalnih klasa II i III (prema Steinbrockeru) u odnosu na seroloski status bolesnika s RA.

Functional class	Seronegative RA				Seropositive RA				Total				T-test	
	Subjects		Duration MS*		Subjects		Duration MS*		Subjects		Duration MS*		t	p
	N	%	Xb	SD	N	%	Xb	SD	N	%	Xb	SD		
II	60	75.9	114	131	68	85	130	129	128	80.5	123	130	0.71	P>0.05
III	43	93.5	137	106	37	82.2	167	173	80	87.9	151	140	0.9	P>0.05
Total	103	82.4	124	121	105	84	143	146	208	83.2	134	134	1.05	P>0.05
T-test	t =	0.99	P>0.05		t =	1.12	P>0.05		t =	1.44	P>0.05			
Correlation	r =	0.1	P>0.05		r =	0.12	P>0.05		r =	0.1	P>0.05			
Regression	Y=0.00x+2.37				Y=0.00x+2.30				Y=0.00x+2.34					

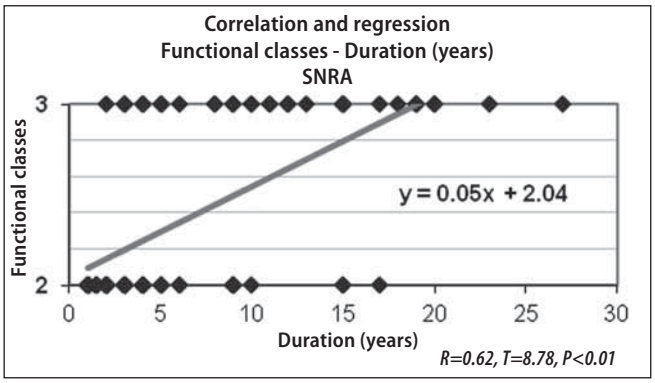
RA - rhematoid arthritis.

Table 3 Correlation between functional classes II and III (Steinbrocker) and duration (years) regarding RA serological status and sex.

Tablica 3. Korelacija između funckionalnih klasa II i III (prema Steinbrockeru) i trajanja bolesti (u godinama) u odnosu na seroloski status i spol bolesnika s RA.

Duration (years)	Functional class	Female				Male				Total			
		SNRA		SPRA		SNRA		SPRA		SNRA		SPRA	
		N	%	N	%	N	%	N	%	N	%	N	%
	II	55	79.7	55	72.4	21	72.4	20	69.0	76	77.6	75	71.4
1-10	III	14	20.3	21	27.6	8	27.6	9	31.0	22	22.4	30	28.6
	II	3	12.5	4	23.5			1	33.3	3	11.1	5	25.0
>10	III	21	87.5	13	76.5	3	100.0	2	66.7	24	88.9	15	75.0
Correlation		r=	0.64	r=	0.5	r=	0.58	r=	0.46	r=	0.62	r=	0.48
		p=	**<0.01**	p=	**<0.01**	p=	**<0.01**	p=	**<0.01**	p=	**<0.01**	p=	**<0.01**

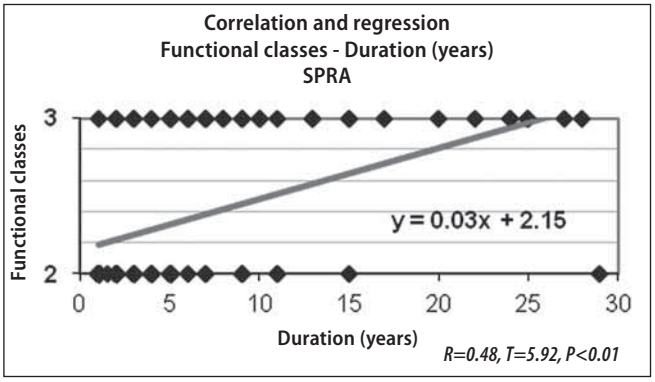
SNRA - seronegative RA; SPRA - seropositive RA.



SNRA - seronegative rheumatoid arthritis.

Figure 3 Correlation and regression analysis between functional classes and duration of the disease (in years) in seronegative RA patients.

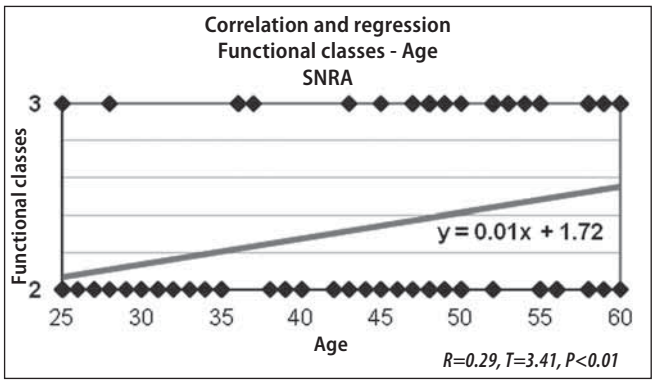
Slika 3. Korelacija i regresijska analiza između funkcionalnih klasa i trajanja bolesti (u godinama) u seronegativnih bolesnika s RA.



SPRA - seropositive rheumatoid arthritis.

Figure 4 Correlation and regression analysis between functional classes and duration of the disease (in years) in seropositive RA patients.

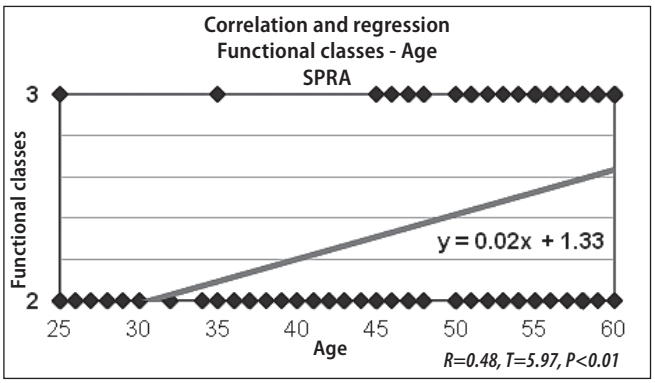
Slika 4. Korelacija i regresijska analiza između funkcionalnih klasa i trajanja bolesti (u godinama) u seropozitivnih bolesnika s RA.



SNRA - seronegative rheumatoid arthritis.

Figure 5 Correlation and regression analysis between functional classes and age of seronegative RA patients.

Slika 5. Korelacija i regresijska analiza između funkcionalnih klasa i dobi u seronegativnih bolesnika s RA.



SPRA - seropositive rheumatoid arthritis.

Figure 6 Correlation and regression analysis between functional classes and age of seropositive RA patients.

Slika 6. Korelacija i regresijska analiza između funkcionalnih klasa i dobi u seropozitivnih bolesnika s RA.

Table 4 Correlation between functional classes II and III (Steinbrocker) and age regarding RA serological status.

Tablica 4. Korelacija između funkcionalnih klasa II i III (prema Steinbrockeru) i dobi u odnosu na serološki status bolesnika s RA.

Functional class	Serostatus		Age				Age
			25-34	35-44	45-54	55-60	(Xb)
II	SNRA	N	19	16	22	22	44.3
		%	24.1	20.3	27.8	27.8	
	SPRA	N	17	23	26	14	43.6
		%	21.3	28.8	32.5	17.5	
III	SNRA	N	2	4	24	16	50.6
		%	4.3	8.7	52.2	34.8	
	SPRA	N	1	1	14	29	53.9
		%	2.2	2.2	31.1	64.4	
Correlation	SNRA		r =0.29		**P<0.01**		
	SPRA		r =0.47		**P<0.01**		

SNRA - seronegative RA; SPRA - seropositive RA

ratio changed in favor of seronegative patients in the cases of a disease duration greater than 10 years (88.9% vs. 75%). These findings suggest that seronegative patients need more time to decline into functional class III (Table 3).

High and positive values were obtained for the linear correlation coefficient between duration of the disease and functional class ($p < 0.01$). Functional disability increased with the disease duration (Figures 3 and 4).

Patients of both serological groups who belonged to functional class II (Table 4) were younger than those of functional class III. High values were obtained regarding the coefficient of correlation between age and functional classes [($r = 0.29$, $p < 0.01$) seronegative, ($r = 0.47$, $p < 0.01$) seropositive]. This means that functional disability in both serological groups increases with age (Figures 5 and 6). Uneducated patients were significantly more represented in functional class III [23 (50%) seronegative, 19 (42.2%) seropositive] than in functional class II [16 (20.3%) seronegative, 22 (27.5%) seropositive] (Table 5). In the category of uneducated subjects and those with a low level of education, seropositive patients were more frequent in functional class II, whereas seronegative patients were in the majority in class III. Seronegative patients with middle and high levels of education dominated in functional class II, while seropositive patients were more numerous in functional class III. There were no statistically significant differences between the functional class and educational level categories, which was valid for both serological groups.

Table 5. Functional classes II and III (Steinbrocker) and level of education regarding RA serological status

Tablica 5 Funkcionalne klase II i III (prema Steinborckeru) i stupanj obrazovanja u odnosu na serološki status bolesnika s RA.

Functional class.	Serostatus		Education				Total	X^2-test
			high	medium	low	uneducated		
II	SNRA	N	10	26	27	16	79	
		%	12.7	32.9	34.2	20.3	100.0	X^2=5.78
	SPRA	N	5	17	36	22	80	p>0.05
		%	6.3	21.3	45.0	27.5	100.0	
III	SNRA	N	1	9	13	23	46	
		%	2.2	19.6	28.3	50.0	100.0	X^2=1.60
	SPRA	N	2	13	11	19	45	p>0.05
		%	4.4	28.9	24.4	42.2	100.0	

SNRA - seronegative RA; SPRA - seropositive RA

Discussion

Although the decrease in working ability is continuous and varies during the course of the disease, it has been observed to be most rapid during the early years of RA (13-17). In many studies, poor functional class has been the strongest predictor of functional outcome (18). Long-lasting sick leave and coming to terms with having a lifelong and incurable condition cause substantial changes in the patients' way of life, mostly in the form of lack of motivation at work and a reduction of social contacts (19). Not only the activity of the disease, but also the patient's age at the onset of RA, as well as his/her education level and the type of work, have been proposed as predictors for work disability (14,20).

In our data set, the correlation coefficient between duration of the disease and functional class had high and positive values. Increased duration of the disease increases the functional disability ($p < 0.01$). Similar results presented by Scott DL, et al. (18) in a long-term prospective study stated that functional disability increases constantly.

Synovitis persistence leads to damage of the joints whose progression, according to some authors, in 44% of the patients results in functional disability 10 years after the first clinical symptoms (17). Results from a prospective follow-up study of 681 RA patients showed that only 10% of them did not develop significant disability during a follow-up of approximately 11.9 years (21). Smedstad LM, et al. found that gender, ESR, and duration of disease were correlated with functional disability (22). Krol B, et al. confirmed that the longer the patient suffers from this condition, the greater the number of restrictions due to pain, inflammation, and fatigue will be, and that the pain level is slightly related to duration of the disease (23). Also, Liang MH, et al. have found that with increasing disease duration, a considerable number of RA patients are forced to live rather restricted lives (24). Restrictions are due to the nature of the disease, with consequences affecting the quality of life (QoL). Our seropositive patients with a duration of the disease up to 10 years passed into the third functional class earlier, while seronegative patients were in the group of disease duration over 10 years.

We found higher mean values of morning stiffness in seropositive patients in both functional classes, without a statistically significant difference with regard to serological status. The correlation between duration of morning stiffness and functional class was positive, but of a low level. Similar results were presented in a study by Yazici et al., performed in a total of 337 patients with recent-onset RA, who found that morning stiffness in patients with early rheumatoid arthritis was associated with functional disability (25).

In their retrospective study, Terkeltaub R, et al. showed that, although functional capacity at the final visit was equal in both older and younger RA patients, at some point older patients tended to have greater functional incapacity than younger patients (26). Kaarela K, et al. confirmed that the risk of work disability increased with increasing age, more severe disease (measured by the number of deformed joints or the number of joints with flare), greater complexity of work tasks, reduced working hours, and wanting to be home (27). In terms of age and functional disability, our data are in accordance with the findings of the aforementioned authors (26,27). Different results were obtained by Sherrer YS, et al. and Gurcay E, et al. (21,28). They found that disability did not correlate with age at the onset of the disease, and those results led the authors to conclude that gender, ESR, and duration of the disease were correlated with functional disability. The same authors pointed out that in early RA female gender correlated significantly with functional disability, but not with RF. On the other hand, based on their results some other authors inferred that seropositive patients end up with the most limited functional abilities (29-32).

The findings of a large retrospective hospital-based study from Finland in which 405 RA patients were analyzed confirmed that patients with heavy work and/or lower educational levels were at greater risk of losing their work capacity (20). This is in accordance with our findings, because uneducated patients were significantly more represented in the functional class III. Regarding serological status, seronegative patients with middle and high education levels mostly fell into functional class II, while seropositive patients belonged to functional class III.

There are a few limitiations of our study, mostly due to the lack of data and the restrospective character of the study. The most prominent factor that we did not take into account was the disease avticity (i.e., DAS 28).

In conclusion

Increased duration of morning stiffness is associated with functional disability. Functional disability increases with duration of the disease, depends on age and educational level, and is more pronounced in older age, regardless of RA serostatus. With regard to serostatus and sex, the differences are non-significant.

Declaration on conflict of interest: The author declares that there is no conflict of interest.

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