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Original article

Physical activity and energy expenditure in rheumatoid arthritis patients and matched controls

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Abstract

Objectives. To compare daily energy expenditure between RA patients and matched controls, and to explore the relationship between daily energy expenditure or sedentariness and disease-related scores.

Methods. One hundred and ten patients with RA and 440 age- and sex-matched controls were included in this study. Energy expenditure was assessed using the validated physical activity (PA) frequency questionnaire. Disease-related scores included disease activity (DAS-28), functional status (HAQ), pain visual analogue scale (VAS) and fatigue VAS. Total energy expenditure (TEE) and the amount of energy spent in low- (TEE-low), moderate- (TEE-mod) and high-intensity (TEE-high) PAs were calculated. Sedentariness was defined as expending <10% of TEE in TEE-mod or TEE-high activities. Between-group comparisons were computed using conditional logistic regression. The effect of disease-related scores on TEE was investigated using linear regression.

Results. TEE was significantly lower for RA patients compared with controls [2392 kcal/day (95% CI 2295, 2490) and 2494 kcal/day (2446, 2543), respectively, $P = 0.003$]. A significant difference was found between groups in TEE-mod ($P = 0.015$), but not TEE-low ($P = 0.242$) and TEE-high ($P = 0.146$). All disease-related scores were significantly poorer in sedentary compared with active patients. TEE was inversely associated with age ($P < 0.001$), DAS-28 ($P = 0.032$) and fatigue VAS ($P = 0.029$), but not with HAQ and pain VAS.

Conclusion. Daily energy expenditure is significantly lower in RA patients compared with matched controls, mainly due to less moderate-intensity PAs performed. Disease activity and fatigue are important contributing factors. These points need to be addressed if promoting PA in RA patients is a health goal.

Trial registration. ClinicalTrials.gov, http://clinicaltrials.gov, NCT01228812.

Key words: rheumatoid arthritis, exercise, physical activity, energy expenditure, matched controls.

CLINICAL SCIENCE

Introduction

RA is a chronic inflammatory autoimmune disease leading to joint damage and bone destruction. In North America and northern Europe, incidence and prevalence are estimated at around 0.02–0.05% and 0.5–1%, respectively [1]. RA is most prevalent among people aged between 40 and 60 years and affects primarily women, with a gender ratio of 3 : 1 [1]. Mortality rates were found to be higher among RA patients than in the general population, with a life expectancy likely to be shortened by 3–10 years depending on the severity of the disease and the age of disease onset [2]. More specifically, RA is associated with a higher risk of cardiovascular events due to both an increased prevalence of traditional risk factors and the

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inflammatory milieu of RA itself [3]. The European League Against Rheumatism (EULAR) recently recommended annual cardiovascular risk assessment using national guidelines for all patients with RA [4]. Among cardiovascular risk factors, sedentariness has a central place in the general population and in RA patients in particular [5].

Physical activity (PA) is defined as any body movement that generates muscle contractions and an energy consumption over that of the resting state [6]. PA is not limited to sports and exercise but includes everyday PAs during work, leisure time, housework, personal care and travel. For example, it is estimated that 100 kcal/day should be expended through walking [7]. It is now evident that regular PA has numerous health benefits [8]. The American College of Sports Medicine and the American Heart Association recommend the practice of moderate PA (e.g. brisk walking) for a minimum of 30 min 5 days a week or vigorous PA (e.g. jogging) for a minimum of 20 min 3 days a week [9].

It is easily conceivable that RA can render patients less physically active than healthy subjects. This question has been addressed by a few recent studies. A case–control study measured total energy expenditure (TEE) using the reference method of doubly labelled water [10]. Significantly lower energy expenditure was found for 20 women with RA compared with 20 healthy women matched for age and BMI, a difference mainly due to a lower PA level among RA women. A cross-sectional study found a significantly lower weekly PA in 232 RA patients compared with the general Dutch population [11]. However, the proportion of RA patients meeting PA recommendations (moderate PA for a minimum of 30 min for 5 days each week) was similar to the general population. Finally, Mancuso *et al*. [12] compared energy expenditure from lifestyle PA in 121 RA patients and 120 healthy controls. PA was significantly lower in RA patients (1474 kcal/week) than controls (1958 kcal/week), with most of the difference accounted for by less walking as opposed to high-intensity activities.

Although PA was demonstrated to be lower in RA patients compared with controls, the reported differences did not translate into a lower percentage of patients meeting PA recommendations. None of the previous studies focused on a possible association between PA and disease-related scores such as functional status and disease activity. Therefore, the purpose of the present study was to compare TEE between RA patients and matched controls, and explore the relationship between daily energy expenditure or sedentariness and disease-related scores.

Patients and methods

Participants

RA patients were recruited from April to September 2010 at the Department of Rheumatology, Lausanne University Hospital, Switzerland. Inclusion criteria were as follows: RA according to the 1987 ACR criteria (ACR, formerly the ARA) [13]; ACR functional classes I–III [14]; age 40–80 years; and stable disease-modifying anti-rheumatic drug regimen during the last 3 months. All RA patients fulfilling these criteria were invited to take part in the study by one of the authors (Y.H.) while they attended their regular office visits with their rheumatologists. All patients gave their written informed consent to participate according to the Declaration of Helsinki. Ethical approval for the study was granted by the Ethics Committee of the University Medical School of Lausanne, Switzerland.

Controls obtained from the CoLaus study (www.colaus.ch, Lausanne, Switzerland), a population-based study that has been described previously [15], were randomly matched (4 : 1) to RA patients on 5-year age group and gender. The number of controls per case was chosen to provide adequate statistical power [16].

Measures

Energy expenditure was calculated according to the PA frequency questionnaire (PAFQ), a self-administered measure of the total and activity-specific energy expenditure [17]. The PAFQ was validated and has been thoroughly described previously [17, 18]. Briefly, it lists 70 PAs categorized by general type (e.g. occupational, housework, leisure time, sports, etc.). Completion of the questionnaire takes ~20 min. Respondents are requested to indicate the number of days (0–7) and the duration per day (0–10 h with 15 min precision) they performed each activity over the past 7 days. The intensity of each PA is expressed according to the basal metabolic rate (BMR), which is the rate of energy expended at rest during quiet sitting [19]. The gender-, age-, weight- and height-specific BMR was calculated for each participant. PAs corresponding to less than four times the energy required for sleeping (<4 BMR) were classified as low-intensity activities [e.g. driving a car (2 BMR), walking slowly (2.5 BMR), vacuuming (3.5 BMR)]. Moderate-intensity activities corresponded to 4–5.9 BMR [e.g. painting (4.5 BMR), bowling (5.0 BMR), kayaking (5.0 BMR)], whereas PAs expending $\geqslant 6$ BMR were classified as high-intensity activities (e.g. uphill walking at 3.5 mph (6 BMR), level running at 6 mph (10 BMR)]. Sedentary people were defined as those expending $<10\%$ of TEE in $\geqslant 4$ BMR PAs. The rationale for this definition has been previously reported in detail [20].

Other measures included gender, age, BMI [under/normal weight (<25), overweight (25 to <30), obese ($\geqslant 30$)], marital status (single, married, divorced or widowed), work (working or not working) and smoking status (never, former or current smoker). For RA patients only, disease-related scores included duration of RA, self-reported pain and fatigue using visual analogue scales (VASs) [21], functional capacity using the French version of the HAQ [22, 23] and disease activity measured using the DAS-28, based on the number of tender and swollen joints and the ESR [24]. Participants with difficulties in understanding and/or completing the questionnaires (e.g. for language reasons) were helped by a research assistant. In case the questionnaires were not returned within 2 weeks or were incomplete, up to five

attempts were made at different hours of the day to contact patients by phone.

Statistical analysis

The sample size was based on a previous study [12] that reported an energy expended in PAs of 1474 kcal for RA patients and 1958 kcal for controls. To detect a 484-kcal difference with an S.D. of 1569 kcal, 80% power and at the 5% significance level, 104 RA patients and 416 controls were required. Baseline characteristics, TEE and sedentariness were compared between RA patients and matched controls using conditional logistic regression. The comparison of TEE and sedentariness was corrected for sex, age, weight and height. Within RA patients only, disease-related scores were compared between sedentary and active patients with a *t*-test. The association of TEE with age, RA duration, DAS-28, HAQ, pain VAS and fatigue VAS was analysed using Pearson's correlation coefficient and simple linear regression analyses. These variables were also entered in a multiple linear regression model. Data analysis was performed using Stata 11.0 (Stata Corporation, College Station, TX, USA). The significance level was set at 0.05.

Results

Subjects' characteristics

Over the recruitment period, 115 patients with RA met inclusion criteria and were invited to participate in the study (Fig. 1). Five (4%) patients refused to participate for lack of time ($n = 1$), language difficulties ($n = 2$) and anxiety or negative feelings ($n = 2$). Hence, a total of 110 (96%) patients with RA and 440 age- and gender-matched controls were included in this study. Their characteristics are displayed in Table 1. Significantly fewer RA patients were currently working compared with controls ($P < 0.001$). BMI tended to be higher in RA patients ($P = 0.094$). There was no difference in marital status ($P = 0.190$) and smoking status ($P = 0.664$).

The questionnaires were returned by 99 (90%) out of 110 RA patients and 436 (99%) controls. RA patients who returned the questionnaires shared similar characteristics to the 11 who did not, with the exception of a younger age [59.5 (95% CI 57.7, 61.3) and 51.8 (95% CI 46.5, 57.1) years, respectively, $P = 0.009$] and a higher disease activity [DAS-28 2.80 (95% CI 2.54, 3.05) and 3.87 (95% CI 2.83, 4.91), respectively, $P = 0.011$). The RA population was selected to be representative of the full range of the disease spectrum in terms of duration, disease activity and functional status, but were not in an acute flare state. RF was positive in 48% of patients, and the majority was on biologic therapies, reflecting the current practice in Switzerland.

Comparison between RA patients and controls

TEE was significantly different between RA patients and controls ($P = 0.003$, Table 2). The difference was significant for both females ($P = 0.0.019$) and males ($P = 0.041$), as well as for patients aged under ($P = 0.038$) or over ($P = 0.032$) 60 years. It was also significant for overweight ($P = 0.036$), married ($P = 0.030$) subjects and subjects not working ($P = 0.012$). Sedentariness was higher in RA patients compared with controls but the difference did not reach significance ($P = 0.085$). As shown in Table 3, patients with RA differed significantly from controls in moderate-intensity PAs ($P = 0.015$), and the differences were not significant in low- ($P = 0.242$) and high-intensity ($P = 0.146$) PAs.

Fig. 1 Flow chart of recruitment and data collection.

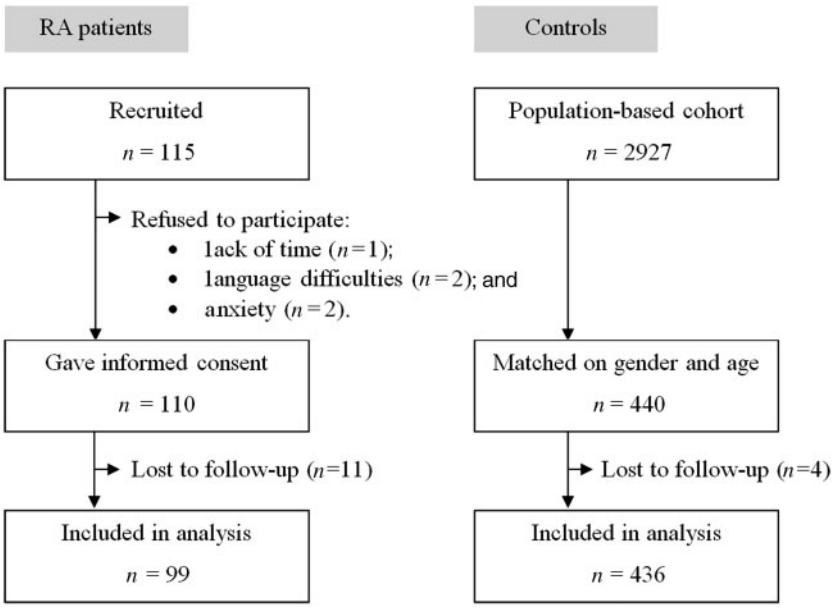

Table 1 Characteristics of study participants matched on gender and age

Characteristics	RA patients ($n = 110$)	Controls ($n = 440$)	P
Gender			NR
Female	83 (75)	332 (75)	
Male	27 (25)	108 (25)	
Age, years			NR
40–59	58 (53)	232 (53)	
60–80	52 (47)	208 (47)	
BMI			0.094
Under/normal weight	45 (41)	218 (50)	
Overweight	41 (37)	148 (34)	
Obese	24 (22)	74 (17)	
Marital status			0.190
Single	7 (6)	86 (20)	
Married	74 (67)	225 (51)	
Divorced	20 (18)	96 (22)	
Widowed	9 (8)	33 (7)	
Work			<0.001
Working	30 (28)	237 (54)	
Not working[a]	77 (72)	201 (46)	
Smoking status			0.664
Never smoker	47 (47)	182 (41)	
Former smoker	31 (31)	168 (38)	
Current smoker	23 (23)	90 (20)	
RA duration, years	9.3 (7.6, 11.0)	NR	NR
RF positive	52 (48)	NR	NR
Erosive status	62 (56)	NR	NR
Current treatment			
MTX	59 (54)	NR	NR
Biologics	91 (83)	NR	NR
Oral CSs	20 (18)	NR	NR
Functional status			
HAQ	0.93 (0.78, 1.07)	NR	NR
Disease activity			
DAS-28	2.91 (2.65, 3.16)	NR	NR
Pain VAS	3.63 (3.07, 4.19)	NR	NR
Fatigue VAS	4.76 (4.17, 5.34)	NR	NR

Values are expressed as n (%) or mean (95% CI). [a]Including part-time work <50%. HAQ: 0 = no disability to 3 = great disability; DAS-28: 0.14 = no activity to 9.3 = high activity; VAS: 0 = no pain/fatigue to 10 = high pain/fatigue; NR: not reported.

Analyses within RA patients

The comparison between sedentary and active RA patients (Table 4) showed that the two groups had similar disease duration ($P = 0.736$). Significant differences in HAQ ($P = 0.010$), DAS-28 ($P = 0.013$), pain VAS ($P = 0.004$) and fatigue VAS ($P = 0.023$) were observed. Simple regression analyses showed that TEE was significantly correlated to age ($r = -0.20$, $P < 0.001$), DAS-28 ($r = -0.22$, $P = 0.032$) and fatigue VAS ($r = -0.22$, $P = 0.029$), but not to RA duration ($r = -0.16$, $P = 0.120$), HAQ ($r = -0.10$, $P = 0.325$) or pain VAS ($r = -0.13$, $P = 0.208$) (supplementary Fig. S1, available as supplementary data at *Rheumatology* Online). Multiple linear regression showed that TEE was negatively associated with age ($P = 0.027$) and fatigue VAS ($P = 0.028$) (supplementary Table S1, available as supplementary data at *Rheumatology* Online).

Discussion

The aim of this cross-sectional study was to measure the daily energy expenditure through PA in RA patients and to compare the results with a matched control group from the same population. We went on to determine the relationship between energy expenditure and disease-related scores in RA patients. Our patients present the typical picture of long-standing RA in a hospital-based population and were on stable therapy and many of them were on biologics. Our results indicate that RA patients expend on average 100 kcal (~4% of TEE) less per day compared with controls, and this is accounted for by a lower level of moderate-intensity PA. Sedentariness is more prevalent in RA patients than the control population, but does not reach statistical significance. Population characteristics that were associated with significant TEE difference included work and a BMI between 25 and 30 (overweight group). Possible explanations for the work status results are that RA patients who were not working probably had more severe disease, thus hindering PA (see further). We observed that overweight and obese (BMI >30) patients had a lower TEE compared with controls, though in only the overweight group did it reach statistical significance. The smaller number of obese RA subjects could explain the lack of statistical significance. These findings suggest that being overweight constitutes an additional and independent barrier to PA in RA.

We also studied whether disease-related factors contribute to these differences by analysing the relationship between energy expenditure and different disease activity scores. By linear regression, significant associations between TEE and age, DAS-28 and fatigue VAS were found. However, disease duration, HAQ and pain VAS were not associated with TEE. The lack of association with pain and HAQ is surprising, and suggests that while these factors may contribute to loss of function, their role in PA is less prominent. Multiple linear regression analysis showed a significant relationship between age and fatigue on TEE. In healthy subjects, the effect of age on TEE has previously been demonstrated [25]. Fatigue, on the other hand, is an important barrier to PA in RA patients. It is interesting to note that 83% of patients were receiving various biologic therapies in the present study, and claims have been made of their efficacy in relieving fatigue in RA. Despite this type of therapy, fatigue still appears as a major factor that impacts on PA. A recent systematic review reported that biotherapies only had a small effect on fatigue [26]. Fatigue in RA is insufficiently addressed in clinical practice [27] and continues to play a central role in the downward spiral perpetuating pain, disability and physical deconditioning in many patients, as supported by the significantly poorer disease-related scores in sedentary compared with active RA patients.

Table 2 Between-group comparison of TEE and sedentariness according to patients'/subjects' characteristics

Characteristics	RA patients ($n = 110$)			Controls ($n = 440$)			P^b	
	n	TEE, kcal/day	Sedentary, %	*n*	TEE, kcal/day	Sedentary, %	TEE	Sedentary
Total	99	2392 (2295, 2490)	70 (60, 79)	436	2494 (2446, 2543)	59 (54, 64)	0.003	0.085
Gender								
Female	73	2268 (2179, 2356)	68 (58, 79)	328	2328 (2289, 2366)	60 (55, 66)	0.019	0.347
Male	26	2743 (2506, 2980)	73 (55, 91)	108	3002 (2887, 3116)	55 (45, 64)	0.041	0.056
Age, years								
40–59	50	2496 (2343, 2649)	64 (50, 78)	232	2573 (2501, 2644)	56 (50, 62)	0.038	0.373
60–80	49	2287 (2169, 2405)	76 (63, 88)	204	2406 (2342, 2469)	62 (56, 69)	0.032	0.110
BMI								
Under/normal weight	41	2263 (2153, 2373)	59 (43, 74)	216	2319 (2265, 2373)	55 (48, 61)	0.539	0.461
Overweight	37	2467 (2262, 2673)	78 (64, 92)	147	2664 (2570, 2759)	59 (50, 67)	0.036	0.050
Obese	21	2512 (2320, 2705)	76 (56, 96)	73	2672 (2552, 2793)	73 (62, 83)	0.139	0.485
Marital status								
Single	7	2281 (2036, 2527)	71 (26, 117)	85	2462 (2355, 2570)	60 (49, 71)	0.574	0.842
Married	65	2453 (2326, 2580)	69 (58, 81)	223	2570 (2494, 2646)	58 (51, 64)	0.030	0.170
Divorced	18	2261 (2065, 2457)	72 (49, 95)	96	2402 (2327, 2477)	64 (54, 73)	0.672	0.891
Widowed	9	2307 (1856, 2758)	67 (28, 105)	32	2331 (2168, 2494)	50 (32, 68)	0.504	0.809
Work								
Working	29	2622 (2369, 2875)	55 (36, 74)	237	2593 (2520, 2667)	55 (48, 61)	0.776	0.991
Not working[a]	70	2297 (2212, 2382)	76 (65, 86)	197	2376 (2319, 2433)	64 (57, 71)	0.012	0.535
Smoking status								
Never smoker	46	2429 (2270, 2589)	70 (56, 83)	181	2495 (2420, 2569)	61 (54, 68)	0.657	0.110
Former smoker	31	2464 (2296, 2631)	61 (43, 79)	167	2504 (2427, 2582)	56 (49, 64)	0.443	0.342
Current smoker	21	2231 (2053, 2409)	81 (63, 99)	88	2475 (2357, 2593)	60 (50, 71)	0.263	0.594

Values are mean (95% CI). [a]Including part-time work <50%. [b]Conditional logistic regression, corrected for age, sex, weight and height.

Table 3 Energy expenditure according to PA intensity in RA patients and controls

PA intensity	RA patients ($n = 99$), kcal/day	Controls ($n = 436$), kcal/day	P*
Low (<4 BMR)	2198 (2130, 2265)	2198 (2161, 2234)	0.242
Moderate (4 to <6 BMR)	107 (69, 145)	171 (150, 191)	0.015
High (⩾6 BMR)	88 (49, 127)	126 (102, 151)	0.146

Values are mean (95% CI). *Conditional logistic regression, corrected for age, sex, weight and height.

Table 4 Disease-related scores in sedentary and active RA patients

Variables	*n*	Sedentary, mean (95% CI)	*n*	Active, mean (95% CI)	P*
RA duration, years	69	9.5 (7.4, 11.6)	30	8.9 (5.9, 11.8)	0.736
HAQ	69	1.05 (0.87, 1.22)	30	0.63 (0.40, 0.87)	0.010
DAS-28	67	3.01 (2.70, 3.31)	30	2.32 (1.88, 2.76)	0.013
Pain VAS	69	4.16 (3.45, 4.87)	30	2.39 (1.56, 3.22)	0.004
Fatigue VAS	69	5.19 (4.46, 5.91)	30	3.72 (2.74, 4.71)	0.023

*t-test. HAQ: 0 = no disability to 3 = great disability; DAS-28: 0.14 = no activity to 9.3 = high activity; VAS: 0 = no pain/fatigue to 10 = high pain/fatigue.

Regular PA in RA has health benefits in terms of functional capacity and may also impact on cardiovascular risk. In healthy subjects, higher levels of TEE significantly lowered the risk of cardiovascular disease [28, 29]. A recent meta-analysis showed that the recommended 150 min/week of moderate-intensity PA is associated with a 14% lower coronary heart disease risk compared with no PA [30]. Although the dose response between PA and risk of cardiovascular disease has not been investigated specifically in RA patients, the difference of 100 kcal/day found in the present study between RA patients and matched controls could have substantial consequences on the risk of cardiovascular disease. Moreover, it is estimated that an energy imbalance of 50–100 kcal/day may be sufficient to cause the gradual weight gain seen in most people [31]. Some authors have suggested that only high-intensity PAs are associated with reduced risk of coronary heart disease [32, 33]. However, most studies found that not only vigorous but also moderate-intensity PAs are protective [9, 28, 34–37]. This is of major interest, since the lower TEE in RA patients found in the present study compared with matched controls was mainly due to less moderate-intensity PAs.

Participation of RA patients in regular PA is hindered by multiple factors that have been addressed by several qualitative studies using focus group discussions [38–40]. These studies were recently reviewed by Cooney *et al*. [41]. Physical barriers include pain, fatigue, physical capabilities and further comorbidities. Psychological barriers include a lack of enjoyment, motivation and confidence and the belief that exercise would have detrimental effects on joints. Finally, many patients with RA are uncertain about which exercises are adequate for them. In contrast, they are generally aware of physical, psychological and social benefits associated with exercise in the context of RA. Individual differences should be taken into account in the prescription or promotion of PA in clinical practice. The Transtheoretical Model of health promotion has been demonstrated to be relevant to a broad range of health-related behaviours, including PA [42, 43], and appears to be a promising way of promoting PA in clinical practice. Although its full applicability to RA patients remains to be investigated, a recent longitudinal investigation focusing on self-efficacy observed that higher levels of self-efficacy for PA increase the likelihood that patients will achieve their PA goals [44].

A major strength of the current study is its matched case–control design, which prevented confounding effects of age and gender. Recruitment bias was limited, since both cases and controls were recruited from the same local population. A minor percentage of patients refused (4%) or did not return the questionnaires (10%), thereby preventing attrition bias. A limitation of the study is that PA was self-reported by the participants and not assessed using an objective measure. However, the PAFQ was proven previously to accurately estimate TEE using a heart rate monitor [17]. The assessment of fatigue using a VAS was demonstrated to be as well correlated with clinical variables as longer fatigue questionnaires in RA patients [45]. However, considering fatigue is a common complaint in this population, the use of a more substantial measure like the Multidimensional Assessment of Fatigue scale should be encouraged in future studies focusing on the interaction between fatigue and PA.

In conclusion, RA patients expend fewer kilocalories daily compared with matched controls, which is mainly due to less moderate-intensity PA. Since sedentariness is associated with poor clinical scores in RA patients, exercise and PA should be better promoted in clinical practice, given their physical, psychological, functional and social benefits. Further research is needed to demonstrate whether this would reduce cardiovascular risk.

Rheumatology key messages

- Energy expenditure is lower in RA patients on stable therapy compared with matched controls.
- Lower energy expenditure in RA patients results from performing fewer PAs of moderate intensity.
- Sedentariness is associated with poor clinical scores in RA patients.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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