Physical Activity Assessment in Tunisian Patients with Rheumatoid Arthritis Compared to Controls

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is the most common rheumatic disease affecting 0.3 to 0.5% of the population worldwide [1]. Nowadays, the positive effect of PA in RA is well documented and recent guidelines on exercise prescription were set. The main objective of our study was to assess the level of PA in Tunisian RA patients.

Methods: We conducted a cross-sectional study involving 50 patients with RA according to the ACR/EULAR criteria. PA was assessed using a questionnaire about PA self-perception as well as the GPAQ (the Global Physical Activity Practice Questionnaire).

Results: The mean total PA was significantly lower in patients with RA than the controls (p=0.000). The percentage of respondents who did not meet the WHO recommendations for physical activity was 68% in RA patients and 28% in controls (p<0.001). The mean number of minutes spent in sedentary activity was significantly higher in RA patients compared with controls (p=0.000). In multivariate analysis, ESR (Erythrocyte Sedimentation rate) (p=0.06) and HAQ score (p=0.023) were the independent risk factors for a low level of PA in patients with RA.

Conclusion: PA in Tunisian RA patients was significantly lower than in the general population. Determinants of a low level of PA were HAQ score and ESR.

KEYWORDS: Physical activity; Rheumatoid arthritis; Energy expenditure

HIGHLIGHTS

i. Physical inactivity appears to be more common in RA patients than in the general population.
ii. Understanding patients’ perceptions of PA and perceived barriers towards engaging in PA is a key step in implementing PA behavior change interventions.
iii. Strategies including therapeutic patient education as well as information of the rheumatologist about different programs are important to promote and spread PA.

INTRODUCTION

Physical activity (PA) is defined as “any movement produced by skeletal muscles responsible for increased energy expenditure” [2]. It is a major determinant of the health status of individuals in the general population and specifically in patients with rheumatic diseases (RD) including rheumatoid arthritis (RA). Nowadays, the health benefits of PA are well documented, and a positive effect is reported on the quality of life of RA patients [2]. Recently, recommendations for exercise prescription during RA have been announced [3]. However, physical inactivity appears to be more...
common in RA patients than in the general population. Pain and functional impotence are most often accompanied by a reduction in the level of PA, thus leading to a state of physical deconditioning. In Tunisia, there are no trials that have evaluated PA in RA patients.

The main objective of our study was to assess the level of PA in patients with RA compared to age-matched controls. We have additionally studied the factors affecting the level of PA in RA patients.

METHODS

Study Design and Population

This is a cross-sectional case-control study including 50 patients with established RA according to the ACR/EULAR criteria (American College of Rheumatology/European League Against Rheumatism criteria) [4] recruited from the rheumatology department of Mongi Slim hospital Marsa. To demonstrate the real impact of PA in RA patients, we also included 50 subjects in the control group matched for age. They were randomly recruited from the accompaniment of patients. We’re not included in our study subjects (patients and controls) with disabling chronic disease making PA difficult to perform. This study was performed according to Helsinki Declaration. Written consent was obtained from the patients and ethical permission was granted from ethical committee of Mongi Slim hospital, number 18/20.

Data Collection

Sociodemographic characteristics (age, sex, level of education, living environment, occupation, and marital status) and comorbidities were documented for each patient and control. In patients, disease activity was evaluated by the global pain intensity visual analogue scale (VASP), patient global assessment (PGA), the duration of morning stiffness (MS), the number of night awakenings (NA), tender joint count (TJC), swollen joint count (SJC), erythrocyte sedimentation rate (ESR), the C Reactive Protein (CRP) and the Disease Activity Score (DAS28) ESR. Functional disability was assessed by the Health Assessment Questionnaire (HAQ). Disease duration, global fatigue intensity, visual analogue scale (VASF), extra-articular manifestations, and patients’ treatment were noted, as well as radiographic data and immunologic factors (rheumatoid Factor (RF) and anti-citrullinated peptide antibody (ACPA)).

Assessment of Physical Activity

Evaluation of self-perception of physical activity: In order to assess the perception of PA, we used a questionnaire comprising the following questions to the patients (P) and to the controls (C):

“How do you feel during physical activity?” (P, C): “Nothing/Pain/Fatigue/Well-being”

“Why don’t you do physical activity?” (P, C): “Not interested/Fear of disease flares/Lack of time/comorbidities”

“Do you think physical activity is good for your health?” (P, C)

“Do you know the effects of physical activity on your illness?” (P)

Evaluation of physical activity by the global physical exercise practice questionnaire: The evaluation of the physical activity of patients and controls was based on the GPAQ (The Global Physical Exercise Practice Questionnaire), which was developed by the WHO (World health organization) [5]. It contains 16 questions, assessing physical exercise in various situations: activities at work, moving from one place to another, leisure activities as well as sedentary behaviors. Metabolic equivalents (METs) were used to express the intensity of the PA. MET is the ratio of a person’s working metabolic rate relative to their resting metabolic rate. To calculate a person’s total energy expenditure, 4 METs are assigned to the time spent in moderately intense physical activity and 8 METs to the time spent in intense physical activity [5].

The GPAQ recorded the total PA in MET-minutes/week, the level of PA (low, moderate, and intense), the mean time of total PA on an average day in minutes, and the mean number of minutes spent on an average day in specific aspects of life (work, transport and recreation-related PA). We also calculated the percentage of total PA on average per day that comes from each of the three types of activity (work, transport, or recreation-related PA) as well as the number of minutes spent in sedentary activities on average per day.

Respondents were considered not meeting RECOMMENDATIONS if the Total Physical Activity MET minutes per week was less than 600.

Statistical Analysis

Data were captured using Excel 2007 software and analyzed using SPSS version 11.5 software. The comparison of the two quantitative series was made using the Mann and Whitney nonparametric test. The independent series percentage comparisons were made by Pearson’s Chi-2 test. In case of significance of the chi-square test and invalidity of the latter, the exact bilateral Fisher test was used. The link study between a qualitative variable and a qualitative variable was carried out by the student test and in case of invalidity, the nonparametric test of Mann and Whitney. The level of significance was fixed at p<0.05. To identify independent risk factors for a low level of PA, we conducted a multivariate logistic regression analysis step-by-step. In the first step, we introduced all factors with p<0.05 in univariate analyses and those with “p” ranging between 0.05 and 0.15, and step by step we removed the factor that has the least significant “p”. Adjusted Odds ratios (OR) were calculated with a confidence interval (CI) fixed at 95%.

RESULTS

Sociodemographic Characteristics and Comorbidities of Patients and Controls

The sociodemographic characteristics and comorbidities of patients with RA and controls are listed in Table 1. Some significant differences between both groups were found. There were significantly more unemployed and living in urban area patients than controls.

Disease Characteristics

The mean disease duration of RA was 9.8±6.7 years. The VASF was on average 40.9±30.1, the VASP was 57.0±25.8, and the mean GPA was 0.70±0.7. The TJC and the SJC were on average 8.3±8.2 and 3.4±4.3, respectively. Immunopositivity was found in 4 patients with RF and 14 patients with ACPA. The mean ESR, CRP, and DAS28 ESR were 43±27, 16.2±20.4, and 4.2±1.3, respectively. Erosions were found in 43 patients. Sixty-three percent of patients were on corticosteroid therapy with a mean dosage of 6mg/1±2.7 [2.5-10]. Thirty-five patients were taking csDMARDs distributed as follows: Methotrexate (n=28), Sulfasalazine (n=1), and Leflunomide (n=6). Fifteen patients were taking bDMARDs: Infliximab (n=2), Certolizumab (n=2), Adalimumab (n=2), Etanercept (n=2) and Tocilizumab (n=4).
Table 1: Sociodemographic characteristics and comorbidities of patients and controls.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients (n=50)</th>
<th>Control Group (n=50)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex-ratio</td>
<td>0.13</td>
<td>0.28</td>
<td>0.183</td>
</tr>
<tr>
<td>Age (mean±SD)</td>
<td>54.4±10.1</td>
<td>52.1±9.5</td>
<td>0.812</td>
</tr>
</tbody>
</table>

**Educational level**

| Illiterate or primary, n(%) | 33(66)         | 34(68)               | 0.832|
| Secondary or university, n(%) | 17(34)        | 16(32)               |      |

**Profession**

| Unemployed, n(%) | 35(70)         | 22(44)               | 0.031|
| Employed, n(%)   | 12(24)         | 23(46)               |      |
| Retired, n(%)    | 3(6)           | 5(10)                |      |

**Type of profession**

| Office work, n(%) | 8(66.7)        | 10(43.5)             | 0.193|
| Physical work, n(%) | 4(33.3)     | 13(56.5)             |      |

**Living environment**

| Urban, n(%) | 45(90)         | 50(100)              | 0.022|
| Rural, n(%) | 5(10)          | 0                     |      |

**Marital Status**

| Single, n(%) | 6(12)          | 6(12)                | 0.718|
| Married, n(%) | 41(82)      | 40(80)               |      |
| Divorced, n(%) | 1(2)        | 3(6)                 |      |
| Widower, n(%) | 2(4)         | 1(2)                 |      |

**Comorbidities**

| Normal BMI, n(%) | 18(36)         | 13(26)               | 0.546|
| Overweight, n(%) | 20(40)         | 24(48)               |      |
| Obese, n(%)      | 12(24)         | 13(26)               |      |
| Diabetes, n(%)   | 7(14)          | 8(16)                | 0.779|
| Hypertension, n(%) | 18(36)       | 10(20)               | 0.075|
| Dyslipidemic, n(%) | 9(18)        | 5(10)                | 0.249|
| Metabolic syndrom, n(%) | 1(2)   | 5(10)                | 0.092|

SD: Standard Deviation; n: Number of Patients; M: Male; F: Female; BMI: Body Mass Index

Self-perception of Physical Activity by Patients and Controls

Based on the subject’s personal perception about PA, 44.4% of patients declared feeling no particular sensation, 44.4% felt pain, and 11.1% had a feeling of well-being. Among the control group, 33.3% declared feeling nothing during PA, 13.3% felt pain, 20% felt tired, and 33.3% had a feeling of well-being. According to the patients, the main factors of physical inactivity were lack of time (34.1%), lack of interest in PA (26.8%), associated comorbidities (24.4%), fear of the onset of flares (12.2%), and finally lack of resources (2.4%). According to the controls, the main factors of physical inactivity were represented by the lack of time (70.5%), then by the lack of interest in the PA (17.6%), associated comorbidities (5.8%), and finally the lack of resources (5.8%). All subjects were aware of the beneficial effect of PA on their health and/or their illness.

Comparison of Physical Activity Between Patients and Controls

The mean total PA was significantly lower in patients with RA (636MET-min/week±747.2) than in controls (2606.8MET-min/week±4623.1) (p=0.000).

The percentage of respondents not meeting WHO recommendations on PA for health in RA patients was found in 68% and in controls in 28% (p<0.001). The comparison of the GPAQ variables between both groups is represented in Table 2.
Table 2: Physical activity in patients and controls according to the GPAQ.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients</th>
<th>Controls</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total PA in MET-minutes/week, mean±SD</td>
<td>636±747.2</td>
<td>2606.8±4623.1</td>
<td>0</td>
</tr>
<tr>
<td>Level of PA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low, n(%)</td>
<td>34(68)</td>
<td>14(28)</td>
<td></td>
</tr>
<tr>
<td>Moderate, n(%)</td>
<td>16(32)</td>
<td>27(54)</td>
<td>0</td>
</tr>
<tr>
<td>Intense, n(%)</td>
<td>0(0)</td>
<td>9(18)</td>
<td></td>
</tr>
<tr>
<td>Mean total PA on average/day, min±SD</td>
<td>22.7±26.6</td>
<td>78.8±110</td>
<td>0</td>
</tr>
<tr>
<td>Mean number of minutes/days spent in work±DS</td>
<td>0.2±1.3</td>
<td>20±75.2</td>
<td>0.133</td>
</tr>
<tr>
<td>Mean number of minutes/days spent in transport±DS</td>
<td>17±18.5</td>
<td>43.1±39</td>
<td>0</td>
</tr>
<tr>
<td>Mean number of minutes/days spent in recreation-related PA±SD</td>
<td>5.4±14.8</td>
<td>15.7±39.9</td>
<td>0.083</td>
</tr>
<tr>
<td>Percentage of total PA on average per day at work, %±SD</td>
<td>0.9±4.7</td>
<td>8.2±24.5</td>
<td>0.124</td>
</tr>
<tr>
<td>Percentage of total PA on average per day in transport, %±SD</td>
<td>86.6±26.3</td>
<td>77.9±31</td>
<td>0.994</td>
</tr>
<tr>
<td>Percentage of total PA on average per day spent in recreation-related PA, %±SD</td>
<td>12.6±25.9</td>
<td>13.8±22.4</td>
<td>0.175</td>
</tr>
<tr>
<td>Mean number of minutes spent in sedentary activities on average per day ±SD</td>
<td>312±143.9</td>
<td>189.9±126.6</td>
<td>0</td>
</tr>
</tbody>
</table>

SD: Standard Deviation; PA: physical Activity; min: Minutes

Determinants of PA in RA Patients

In univariate analysis, a significant association was found between a low level of PA and HAQ score (p=0.021), ESR (p=0.029), pain after performing a PA (p=0.04) and bDMARDs duration (p=0.06). However, no link was found between low levels of PA and sociodemographic data: age (p=0.512), gender (p=0.074), profession (p=0.246), level of education (p=0.618), marital status (p=0.284) or living environment (p=0.544) nor with the characteristics of the RD: disease duration (p=0.88), immunologic profile (p=0.361), comorbidities (p=0.1), extra-articular manifestations (p=0.191), VASP (p=0.076), disease activity score (p=0.377) and radiographic data (p=0.48). Similarly, PA was neither correlated to VASF (p=0.27) nor to treatment modalities (p=0.6). In multivariate analysis, ESR (p=0.06; OR=22.041, 95% CI [2.4-204.9]) and HAQ score (p=0.023, OR=1.2; 95% CI [1.4-112.8]) were the independent risk factor for low level of PA in patients with RA.

DISCUSSION

Assessment of PA in RA Patients

In our study, the total mean PA was significantly lower in patients with RA (636MET-min/week±747.2) than in controls (2606.8MET-min/week±4623.1) (p=0.000). All patients and controls were aware of the beneficial effect of PA on their health and their illness. However, the percentage of respondents not meeting WHO recommendations on physical activity for health in RA patients was significantly higher in patients with RA than in controls (68% versus 28%; p=0.001).

The impact of RA due to inflammation, disability, and more recently fatigue, has been widely described in patients, and great strides have been made in their treatment. However, the impact of RA on PA remains insufficiently considered and poorly documented [3]. In the literature, PA in RA patients ranged from 26% to 56% [6]. A cross-sectional international study conducted in 21 countries evaluating PA in RA patients showed that physical inactivity varied between 60 to 80% across countries. In the same study, only 13.8% of all patients exercised more than 3 times weekly according to the recommendations [7].

Some trials were conducted to determine if PA was hindered in RA patients compared to healthy subjects [8-11]. In a case-control study carried out in the United States, the total energy expenditure measured by the reference method of doubly labeled water indicated a limited level of PA in patients with RA (913±1335KJ/day) compared with controls (10 477±1992KJ/day) with a statistically significant correlation (p=0.02) [8]. In another study, the mean total energy expenditure in 121 RA patients compared to 120 controls using Paffenbarger questionnaire showed a total energy expenditure estimated at 1474kcal/week compared to 1958kcal/week in the control group (p=0.003) [9]. In a study including 144 patients and 144 controls matched for age and sex, PA was assessed using a questionnaire evaluating 20 domains [11]. Results showed that controls participated in more domains than the study group (p=0.001). In the study of Van den Berg el al. [11] PA was measured using a Short Questionnaire to Assess Health (SQUASH)-Enhancing PA. Both the study groups and controls engaged in PA in 58% of cases. However, the mean number of minutes of PA per week was significantly lower in the RA population compared with the general population (1836 versus 2199, respectively, p=0.001) [11]. These findings were in line with our results.

Although the positive effect of PA in RA patients compared with controls was observed in many studies, it was not always significant compared to controls. Indeed, according to Soloman et al. [12] the total energy expenditure was similar between RA patients and controls (13.4METS/week versus 15.6METS/week). In Roubenoff [8] study, statistically significant difference was found between RA patients and controls when using the objective method (double
labeled water and accelerometry). However, no differences were found when a self-reported questionnaire was used.

The disparities in these results may be explained by methodological problems related to the sensitivity of the questionnaires used, RA characteristics as well as eligibility criteria. Indeed, PA in RA can be measured using several methods. A very accurate measurement of PA can be obtained by assessing the total daily energy expenditure, heart rate monitoring, and movement sensors (mainly pedometers and accelerometers) [13]. Declarative measures include activity reminder questionnaires such as the International Physical Activity Questionnaire (IPAQ), the Global Physical Activity Questionnaire (GPAQ), as well as the Behavioral Risk Factor Surveillance (BRFSS) system [14]. In our study, we used the GPAQ which has the advantage of incorporating questions relating to sedentary activities, such as time spent sitting and leisure time.

**Barriers to PA in RA Patients**

Understanding patients’ perceptions of PA and perceived barriers towards engaging in PA is a key step in implementing PA behavior change interventions. According to the patients, the main factors of physical inactivity were the lack of time, the lack of interest in the PA, the associated comorbidities, fear of the onset of flares, and finally lack of resources. In the literature, pain, stiffness, and tender joints, as related to impaired physical function, constitute a barrier to engage in PA [15]. Moreover, pain was related to poorer emotional and physiological health, such as sleep habits, functionality in everyday life as well as the emotional status hindering PA [15]. Data from prior studies also showed that lack of communication with rheumatologists is an influential factor in patients’ decision-making regarding PA engagement [16]. Indeed, many patients mentioned the fear of movement and not being informed about the benefits of PA for the disease as a reason for not being physically active [16].

Moreover, some of the patients who do not engage in PA admit to fear of exacerbating RA symptoms through PA engagement. A review by De Jong et al. [16] showed that moderate or high intensity exercise reduced disease activity. Similarly, regarding small joints, exercise decreased the lesions and did not worsen the radiographic progression [17]. Interestingly, a beneficial effect of PA was observed on CRP and ESR levels in RA patients [11]. The exact mechanism by which these positive effects arise remains unknown but may be explained by the reduction of the adipose tissue which is the main source of IL6 [8]. In our study, a significant correlation was found between ESR, HAQ, and a low level of PA.

**Practical Applications and Exercise Recommendations**

According to the latest EULAR recommendations, the benefit of PA on RA lies in controlling the activity of the disease, preventing structural changes in the joints, avoiding undesirable effects of iatrogenic origin and achieving clinical remission if possible [3]. Typically, exercise interventions have focused on aerobic training and strength training or a combination of aerobic training and strength training [18].

However, these exercises should be adjusted according to the patients’ state in a supervised clinical environment or at home under professional guidance [17]. Although there is a lack of studies designed to evaluate the role of PA during RA flare, reduction in the duration and intensity of exercise is recommended. It should be noted that our study has some limitations. It was a monocentric study, so the results cannot be generalized to the rest of the population. Moreover, some differences were noted between patients and the control group concerning socio-professional characteristics. However, these variables were not linked to PA.

**CONCLUSION**

PA in Tunisian RA patients was significantly lower than the general population in terms of number of minutes as well as energy expenditure. Disability and disease activity were independent factors significantly associated with a low level of PA. Strategies including therapeutic patient education as well as information of the rheumatologist about different programs are important to promote and spread PA.

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**Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**Data Sharing Statement**

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

**Contributorship**

Fazaa Alia, Makhlouf Yasmine: Draft, Writing, Editing
Jallouli Syrine: Draft, Writing, Editing
Miladi Saoussen, Sellami Meriem, Ouenniche Kmar: Conceptualization, Data Collection
Souabni Leila, Kassab Selma, Chekili Selma: Conceptualization, Data Collection
Ben Abdelghani K, Laatar A: Final Draft

**Ethics Approval and Consent to Participate**

Written consent was obtained from the patient for publication purposes.

**REFERENCES**


