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Artículo original

Comparación entre artritis reumatoide seronegativa y artritis psoriásica poliarticular: estudio transversal en una cohorte brasileña

A comparative study between seronegative rheumatoid arthritis and polyarticular psoriatic arthritis: cross-sectional report in a Brazilian cohort

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Palabras clave: artritis reumatoide; artritis psoriásica; calidad de vida; depresión; riesgo cardiovascular

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RESUMEN

Objetivos: comparar el riesgo cardiovascular, la calidad de vida, la depresión y la funcionalidad entre pacientes con artritis reumatoide (AR) seronegativa y artritis psoriásica (APs) poliarticular.

Materiales y métodos: se analizaron datos de 45 pacientes con AR seronegativa y 36 con APs poliarticular. Se utilizaron cuestionarios para depresión (CES-D), funcionalidad (*Health Assessment Questionnaire*, HAQ) y calidad de vida (SF-12). Se midió el espesor íntima-media carotídea (cIMT) para valorar el riesgo cardiovascular.

Resultados: las frecuencias de hipertensión, diabetes y dislipidemia fueron similares entre ambos grupos. Los pacientes con APs tuvieron un índice de masa corporal (IMC) y una circunferencia abdominal más elevados. El cIMT fue equivalente entre los grupos. La depresión y la calidad de vida no mostraron diferencias significativas. Los pacientes con AR presentaron peor funcionalidad según el HAQ.

Conclusiones: en nuestra serie los pacientes con AR y APs seronegativos tuvieron similitudes en calidad de vida, depresión y riesgo cardiovascular, excepto por diferencias en el IMC y la circunferencia abdominal, más elevados en APs. La funcionalidad fue peor en AR en comparación con APs.

ABSTRACT

Objectives: *the study compared seronegative RA and polyarticular psoriatic arthritis (APs) in terms of cardiovascular risk, quality of life, depression, and functionality.*

Materials and methods: *data from 45 patients with seronegative RA and 36 with polyarticular APs were analyzed. Questionnaires were used to assess depression (CES-D), functionality (Health Assessment Questionnaire-HAQ), and quality of life (SF-12). Carotid intima-media thickness (cIMT) was measured to assess cardiovascular risk.*

Key words: *rheumatoid arthritis; psoriatic arthritis; quality of life; depression; cardiovascular risk*

Results: *the results showed similar rates of hypertension, diabetes, and dyslipidemia between both groups. However, patients with APs had higher BMI and abdominal circumference. cIMT was equivalent between groups. Depression and quality of life did not show significant differences. Patients with RA presented worse functionality, according to the HAQ.*

Conclusions: *in our cohort, patients with RA and seronegative APs had similarities in quality of life, depression, and cardiovascular risk, except for differences in BMI and abdominal circumference, which were higher in APs. Functionality was worse in AR compared to APs.*

INTRODUCTION

At first glance, seronegative rheumatoid arthritis (RA) and polyarticular psoriatic arthritis (APs) may look clinically similar, with diagnoses that can be confused. Their pathophysiological pathways are quite distinct; however, both diseases are chronic inflammatory polyarticular conditions affecting the wrist and finger joints. They are seronegative and erosive[1]. Without prompt identification and treatment, they can lead to joint damage and functional loss[2].

These two entities share some comorbidities. Cardiovascular diseases and depression are common in both situations, although their prevalence from each other has no consensus. Fragoulis et al.[3]. revealed the same cardiovascular risk in RA and APs, but patients with APs had more depression. Later in their work, these authors included all APs subtypes and both seropositive and seronegative RA. A review of the Dutch population in 2012-2016 showed that the most commonly reported comorbidity in these two diseases was depression, accounting for 25.7% in patients with RA and 25.1% in APs. A Spanish study with 151 subjects (75 RA and 76 APs)[4] did not find any differences in cardiovascular risk scores. However, Labitigan et al.[5] compared the prevalence of metabolic syndrome in these two diseases in an American sample and revealed that patients with APs have higher rates of dyslipidemia, obesity, and diabetes than those with RA. Ethnic and environmental background as well as differences in the access to health care may have played a role in these variances.

The treatment of these two diseases has also been compared, which revealed that patients with RA are more promptly treated and more frequently achieve remission than those with APs. This happens perhaps because APs has been considered a milder disease compared to RA, and this perception was associated with less aggressive treatment[6].

A sample of Brazilian patients with seronegative RA and polyarticular APs was studied to obtain comparative data on cardiovascular risk factors and depression as well as the influence of both diseases on the functionality and quality of life.

MATERIALS AND METHODS

A total of 81 subjects (45 with seronegative RA and 36 with polyarticular APs) were studied. A convenience sampling of patients who came for regular consultation in one year (from October 2020 to October 2021) was conducted in a single rheumatology unit, and inclusions were according to appointment order and willingness to participate in the study. Inclusion criteria were: a) for the RA patients: the fulfillment of the classification diagnosis criteria from the American College of Rheumatology/European League Against Rheumatism for RA classification from 2010[7] and be seronegative; b) for APs: the CASPAR criteria for APs[8] and be polyarticular.

Data collection included: a) clinical and epidemiological data: sex, age, age disease diagnosis, tobacco or alcohol use, autodeclared ethnic background, comorbidities, and medications use, arterial blood pressure value, weight and height for body mass index (BMI) calculation, and abdominal circumference measurement; b) data on laboratory test: blood cell count, C reactive protein, lipid profile (total cholesterol, high-density lipoprotein, low-density lipoprotein, cholesterol, and triglycerides), and fasting glycemia were simultaneously obtained with the other data collection; c) Center for Epidemiological Study

Depression Scale (CES-D). This is a 20-item self-report measure of those accesses depression symptoms on a Likert scale (0 = rarely or none of the time; 1 = some or little of the time; 2 = occasionally or a moderate amount of the time, and 3 = most or all the time). Values under 15 are normal, 15–21 mild to moderate depression, and over 2 possible major depression[9]; d) Health Assessment Questionnaire (HAQ). This is a questionnaire on 20 specific activities from daily life that are assessed on a 4-point Likert scale where 0 = without difficulty, 1 = with some difficulty, 2 = with much difficulty, and 3 = unable to do. They are grouped into 8 functional groups; each category receives a single score equal to the maximum value of their component activities. The final value goes from 0 = no damage to 3 = maximum damage[10]; e) Short Form Health Survey with 12 questions (SF-12). It is a 12-item questionnaire that assesses the physical and mental domains of the quality of life that goes from 0 to 100; high values are related to better quality of life[11]; f) Carotid intima-media thickness (cIMT) measurement. It was performed using a high-resolution ultrasound apparatus Esaote®, model MyLab40, in B-mode and with a linear transducer of 18 MHz by a single investigator, blind to clinical data.

Patients were studied in an environment at 22 °C, in the supine position, with the neck extended and rotated at 45 degrees contralateral to the examined side. The carotid artery was studied in transverse and longitudinal planes; the measurements were done at 10 to 20 mm of the carotid bifurcation in the distal vessel wall[12]. The exam was executed on both sides, and the highest value was considered for statistical purposes. The reference values used were 0.4-0.7 mm as normal IMT; 0.8-1.4 mm as thickened IMT (subclinical atherosclerosis); values ≥1.5 mm as atheroma[13].

According to the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ACT III)[14], patients were classified as having metabolic syndrome.

Data was studied through contingency and frequency tables. The Shapiro-Wilk test was used to evaluate the data distribution, and the central tendency was expressed in mean and standard deviation when data were parametric or in the median and interquartile range when data were nonparametric. The Fisher and chi-squared tests were used to compare nominal data, and the unpaired t-test and Mann-Whitney test were used for the numeric data. The adopted significance was 5%. Tests were performed using GraphPad Prism version 8.0.0 for Windows, GraphPad Software, San Diego, California USA.

This study was approved by the local Committee of Ethics in Research of Mackenzie Evangelical School of Medicine Paraná, under protocol 4.106.681. All included patients should be older than 18 years and with a signed informed consent form.

RESULTS

Forty-five (45) RA patients and 36 psoriatic arthritis patients were included. RA sample had 87.8% females with a mean age of 56.3 ±9.5 years; the mean age at disease onset was 45.5±13.1 years old. The psoriatic arthritis sample had 66.6% females with a mean age of 53.5±10.7 years old with a mean age at disease onset of 45.9±11.8 years old. Disease duration had a mean value of 10.9±7.1 years in the RA group and 9.0±.7.2 in APs group. Table 1 describes the studied sample and compares the two groups. Glucocorticoid use was more common in the RA group.

The Table 2 compares cardiovascular risk factors and cIMT values. The only differences observed were in BMI and abdominal circumference, which were higher in APs; all other parameters were similar in the two groups. This table also shows that hemoglobin levels were lower in patients with RA.

The Table 3 compares the results of CES-D, SF 12, and HAQ in both groups. HAQ was higher in patients with RA than those with APs, indicating that the first group had worse functionality.

Table 1: Description and comparison of studied sample: 45 patients with seronegative rheumatoid arthritis (RA) and 36 patients with polyarticular psoriatic arthritis (APs).

			RA n=45	APs n=36	P
Female sex (n)			36 (87.8%)	24 (66.6%)	0.17
Mean age (years)±SD			56.3±9.5	53.5±10.7	0.13
Mean age at disease onset (years) ±SD			45.5±13.1	45.9±11.8	0.89
Mean disease duration (years)±SD			10.9±7.1	9.0±7.2	0.17
Exposed to tobacco (n)			21 (46.6%)	19 (52.7%)	0.65
Treatment (n)					
	Methotrexate		25 (55.5%)	18 (50%)	0.61
	Leflunomide		23 (51.1%)	5 (13.8%)	0.39
	Biologic drugs		11 (24.4%)	15 (41.6%)	0.09
		Anti-TNF	7 (15.5%)	11 (30.5%)	
		Anti-IL 6	3 (6.6%)	-	
		Anti-IL 17	-	4 (11.1%)	
		Abatacept	1 (2.2%)	-	
	Tofacitinib		1 (2.2%)	-	-
	Prednisone		14 (31.1%)	2 (5.5%)	**0.004**

N= number; SD= standard deviation.

Table 2: Comparison of cardiovascular risk factors and carotid intima media thickness in seronegative rheumatoid arthritis (RA) and polyarticular psoriatic arthritis (APs).

	RA n=45	APs n=36	P
Mean BMI (kg/m^2) ± SD	28.2±5.5	31.5±6.09	**0.01**
Median abdominal circumference (cm) (IQR)	99 (91.5-106.0)	108.5 (98.5-114.8)	**0.01**
Median systolic blood pressure (mm) (IQR)	130 (110-140)	120 (112-140)	0.65
Mean diastolic blood pressure (mm) (IQR)	80 (70-85)	80 (70-80)	0.64
Diabetes mellitus (n)	11(24.4%)	10 (27.7%)	0.73
Arterial hypertension (n)	24 (53.3%)	17 (47.2%)	0.51
Dyslipidemia (n)	19 (42.2%)	22 (61.1%)	0.33
History of myocardial infarction (n)	2 (4.4%)	2 (5.5%)	-
History of stroke (n)	0	2 (5.5%)	-
Mean cholesterol ± SD (mg/dL)	197.6±48.8	194.1±40.3	0.73
Mean HDL cholesterol ± SD (mg/dL)	50.5±11.8	48.6±11.7	0.47
Mean LDL cholesterol ± SD (mg/dL)	115.0±40.8	111.7±36.6	0.71
Median tryglicerides (mg/dL) (IQR)	139 (90.8-186)	128.5 (99.5-178.0)	0.80
Metabolic syndrome (n)	17/37 (45.9%)	15/35 (42.9%)	0.79
Median C reactive protein (IQR) – mg/dL	4.7 (1.1-15.4)	3.3 (0.80-5.6)	0.11
Mean hemoglobin ± SD (g/dL)	12.8±1.0	14.1±1.4	<0.0001
Hemoglobin lower than 12 g/dL (n)	9 (20%)	2 (5.5%)	0.10
Median cIMT- mm (IQR)	0.69 (0.59-0.76)	0.68 (0.52-0.85)	0.69

IQR= interquartile range; SD= standard deviation; n= number; BMI= body mass index; cIMT= carotid intima-media thickness.

Table 3: Comparison of functionality, quality of life and depression in seronegative rheumatoid arthritis (RA) and polyarticular psoriatic arthritis (APs).

	RA n=45	Aps n=36	P
Median CES-D (IQR)	14.0 (7.5-21.2)	16.5 (70-24.0)	0.72
CES-D (categorical)			0.65
. Normal	52.6%	43.3%	
. Mild to moderate	23.6%	23.3%	
. Possibility of major depression	23.6%	33.3%	
Mean SF-12 mental domain (±SD)	41.05 ± 11.61	42.62 ± 12.50	0.61
Median SF 12- physical domain (IQR)	39 (30-48)	39 (31-48)	0.21
Mean HAQ±SD	1.24 ± 0.64	0.95 ± 0.58	**0.05**

CES-D = Center for Epidemiological Studies Depression Scale; HAQ= Health assessment questionnaire; SF= Short Form Health Survey with 12 questions.

DISCUSSION

The present study's data show that the cardiovascular risk factors were similar in seronegative RA and polyarticular APs, except for BMI and central obesity, which were more common in patients with APs. Equally, a higher BMI was found in APs than RA by Reddy et al.[15] in the Consortium of Rheumatology Researchers of North America database from 2001 to 2008 and by Li et al. in the Asiatic population[16]. Obesity is considered a risk factor for psoriasis[17], and weight loss seems to control skin inflammation[18]. The median cIMT was similar and within the normal range in both groups despite a high rate of metabolic syndrome (that affected almost half of the studied sample). The current studied sample is from a Rheumatology Clinic at a University Hospital, where dyslipidemia, hypertension, and diabetes were aggressively treated, which may have contributed to a better outcome.

Depression risk was also comparable in both two groups, presenting a high frequency of depression scores with 23% and 33% at risk of major depression in the RA and APs groups, respectively. According to the literature, patients with RA and APs have higher rates of anxiety and depression than the general population, accounting for 10%–42% in RA and 9%–37% in APs. Depression not only affects the patient's quality of life, but it may reduce the possibility of achieving joint remission[19]. Different from our results, Fragoulis et al.[20] revealed that patients with APs have more depression than those with RA, but these latter authors only considered the history of having depression. The quality of life was similar in both domains (physical and mental) in the two groups despite the HAQ results being worse in RA. However, quality of life is multifactorial, and biases from unstudied variables cannot be ruled out.

Despite the similarities, RA and APs have different genetic and pathophysiological aspects. Interleukin (IL)-17, IL-23, IL-22, IL-1β, IL-6, interferon-γ and tumor necrosis factor-α (TNF-α) are produced in APs by activated T cells. IL-17 and CD8 T cell levels have been found in the joints of patients with APs but not in those with RA. The main cytokines in RA include TNF-α, IL-6, IL-1, IL-22, IL-33, chemokine ligand 11, and chemokine C-X-C motif ligand (2). Some cytokines are elevated in both situations; however, their hierarchic role may differ in these two diseases. Anti-IL 6 is effective in RA treatment but does not work for APs (2). IL-6 is one of the main cytokines involved in hepcidin induction during inflammation, which is important in the appearance of chronic disease anemia[21]. Additionally, its major importance within the RA inflammatory process may explain the lower hemoglobin levels in RA than in APs.

This study revealed higher HAQ scores in patients with RA, suggesting their worse functionality but an equal quality of life in both groups. Soccol et al.[22] revealed no significant differences between these two groups in terms of function and quality of life. These authors also comparatively studied radiographic changes and revealed that patients with RA had more radiographic damage and were taking more disease-modifying antirheumatic drugs than patients with APs, suggesting that inflammation and structural damage in RA were more severe[22]. They believed that patients with APs have an extra burn due to skin involvement, which compensates for the aggressiveness of RA[21].

Concerning the treatment approaches, the only observed difference was in the high-frequency glucocorticoid in RA. Glucocorticoid treatment is usually avoided in APs due to the fear of skin flare in individuals with psoriasis when the drug is withdrawn[23]. Additionally, it was not statistically significant in our sample; however, patients with APs used more biological drugs (41% vs. 24%) than the RA sample, similar to the findings of Reddy et al.[15].

This study is limited by its small sample and cross-sectional design. However, it has the distinction of limiting the sample to seronegative RA and polyarticular APs, aiming for a more homogeneous sample.

In conclusion, patients with seronegative RA and polyarticular APs have similar quality of life and depression rates in this series. The cardiovascular risk factors were also similar, except for BMI and abdominal circumference, which were higher in APs. Functionality was worse in patients with RA compared to those with APs.

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