International Journal of Cardiovascular Sciences. 2019; [online].ahead print, PP.0-0

ORIGINAL ARTICLE

Cardiovascular Risk Factors and Risk Measurement in Patients with Psoriatic Arthritis in a University Hospital

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Abstract

Background: Psoriatic Arthritis is the spondyloarthritis associated with psoriasis, which is often related to high mortality due to cardiovascular causes.

Objectives: To quantify cardiovascular risk factors (hypertension, diabetes, dyslipidemia, obesity and smoking) and to measure risk by the Global Cardiovascular Risk Score in patients with psoriatic arthritis.

Methods: Patients with psoriatic arthritis according to the Classification Criteria for Psoriatic Arthritis, aged between 30 and 74 years and without any other clinically manifest chronic inflammatory disease, atherosclerotic disease or heart failure were included. After an interview, clinical examination and data extraction from medical records, risk stratification was performed using a calculator available on the online platform of the Framingham Heart Study. We considered $p < 0.05$ as significant. Chi-square test and Fisher's exact test were used to compare frequencies, as well as correlation measurements.

Results: 45 patients were included, 68,9% of which were women and the mean age was 53,94 years. Dyslipidemia was confirmed in approximately 93%, hypertension in 46%, obesity in 40%, 33.3% were diabetics and, 13.3%, smokers; 95% had increased abdominal circumference. It was observed that 53% had high cardiovascular risk, 29% had intermediate risk and 18% had low risk. Individuals with altered C-reactive protein and erythrocyte sedimentation rate presented, respectively, higher levels of LDL-C and total cholesterol.

Conclusions: There was a high occurrence of risk factors and the majority of the sample was stratified into high or intermediate cardiovascular risk. (Int J Cardiovasc Sci. 2019; [online].ahead print, PP.0-0)

Keywords: Cardiovascular Diseases; Risk Factors; Obesity; Dyslipidemias; Inflammation; Arthritis, Psoriatic.

Introduction

Psoriasis is a chronic immune-mediated inflammatory disease, which classically involves the skin and affects 1.3% of the Brazilian population.[1-3] Psoriatic arthritis (PsA) is an inflammatory joint pathology that occurs in association with psoriasis, present in 10 to 30% of those with cutaneous manifestations.[4,5] The course of PsA ranges from mild manifestations to a debilitating picture. Skin injuries usually precede arthropathy and severity of cutaneous disease is unrelated to joint disease activity.[6] Its pathogenesis is not well established, but genetic, immunological, environmental factors — infections and traumas — obesity and smoking are likely to be involved.[7-14]

The CASPAR (Classification Criteria for Psoriatic Arthritis) criteria are those recommended by the Brazilian Society of Rheumatology for PsA classification and diagnosis. It takes into account the presence of inflammatory joint disease associated with some of the following: current psoriasis, personal or family history of psoriasis, dactylitis, juxta-articular bone formation (in hands or feet), negative rheumatoid factor and psoriasis

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DOI: 10.5935/2359-4802.20190079

Manuscript received on March 18, 2019; reviewed on March 27,2019; accepted on April 03, 2019.

onychodystrophy. Sensitivity and specificity of this method are 99.7% and 99.1%, respectively.[15]

Inflammatory rheumatologic diseases are associated with high mortality, largely due to cardiovascular causes. It may be justified by an increase in inflammatory cytokines, atherosclerosis, endothelial dysfunction, individual genetics, use of medications with a negative effect on the cardiovascular system, in addition to traditional risk factors.[16] Psoriasis is related to increased risk of acute myocardial infarction (AMI), especially in severe cases.[17-20]

However, unlike other inflammatory diseases, these patients are more often obese. The pathophysiology of psoriasis and obesity involves many common cytokines that contribute to the components of metabolic syndrome: hypertension, dyslipidemia and insulin resistance.[14,18] In addition to the presence of comorbidities that act as a cardiovascular risk (CVR) factor, many studies detected increased rates of cardiovascular disease in this group.[19,21,22] Only one in every seven patients with psoriasis is aware of the atherosclerotic disease and metabolic syndrome risk they present.[23] Characterization of an association between PsA and increased CVR would justify automatic reclassification of patients with this condition in high CVR, without the need for scores that could attribute different risk.

Objectives

To quantify cardiovascular risk factors (hypertension, diabetes, dyslipidemia, obesity and smoking) and to measure risk by the Global Cardiovascular Risk Score in patients with psoriatic arthritis.

Methods

Cross-sectional study carried out between September 2016 and June 2017 at the Rheumatology outpatient clinic of *Hospital Universitário Lauro Wanderley* (HULW), João Pessoa - PB.

Population and sample

Study population consisted of all PsA patients followed at the rheumatology outpatient clinic of a reference hospital. Sample was chosen for convenience and a non-probabilistic stratified sample was adopted, due to the low prevalence of the disease.

Inclusion criteria

The study included patients classified according to the CASPAR criteria[24] (evaluated by a rheumatologist); aged between 30 and 74 years, since the Global Cardiovascular Risk Score (GCRS) used is restricted to individuals of this age group.[25] After adequate information, the patients signed the informed consent form (ICF).

Exclusion criteria

Patients with clinically manifest heart failure or atherosclerotic cardiovascular disease (coronary, cerebrovascular or peripheral occlusive disease) were excluded, until assessment, since the score used estimates the risk of onset and does not apply to patients with manifested cardiovascular disease.[25] Individuals diagnosed with another chronic inflammatory disease, other than PsA, were also eliminated.

Instruments for data collection

The CASPAR[24] criteria were used to confirm PsA classification/diagnosis; sociodemographic and clinical questionnaire based on the Framingham score[25] was used for global CVR; and a specific calculator was used for risk assessment, available on the online platform of the Framingham Heart Study; in addition to medical records data.

Procedures for data collection

This study was approved by the Research Ethics Committee of HULW - João Pessoa, PB - under protocol number 56336216.1.0000.5183.

Psoriatic arthritis patients underwent an interview and clinical examination for data collection and risk stratification according to the Framingham score[25] for global CVR. The most recent data of laboratory results were used with a maximum delay of six months between testing and evaluation.

This score considers the following: age, High Density Lipoprotein Cholesterol (HDL-C), total cholesterol, untreated systolic blood pressure (SBP) or treated SBP, smoking and diabetes. Age, condition of hypertension, smoking and diabetes are self-reported by the research participant, while HDL-C, total cholesterol, triglycerides, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were obtained from the medical record. The

SBP used to calculate the CVR was measured by the researchers during the interview, as well as height and weight — for calculation of body mass index (BMI) — and abdominal circumference.

This score quantifies the percentage risk of developing the main cardiovascular events — coronary artery disease (CAD), stroke, peripheral arterial disease or heart failure — in the next 10 years. Patients with less than 5% probability of presenting any of the aforementioned outcomes were considered at low risk. Patients at intermediate risk were males with calculated risk between 5% and 20% or females with risk between 5% and 10%. High-risk individuals were men with calculated risk greater than 20% and women whose risk is greater than 10%.[26]

Data analysis

The sociodemographic and clinical characteristics were analyzed through descriptive statistics using frequencies for categorical variables, and mean and standard deviation (SD) for parametric scalar variables with a 95% confidence interval (95% CI), or median and interquartile range (IQR) for non-parametric variables. Shapiro-Wilk test was used to evaluate normality.

In inferential analysis, Chi-square and Fisher's exact test were used to compare frequencies between independent groups. To evaluate the correlation between two scalar variables, the Spearman method was used. Mann-Whitney test was used for independent samples. We considered $p < 0.05$ as significant. Statistical analysis was performed using the SPSS for MAC program (23.0 version).

Results

Among the 45 study participants, most were female (68.90%) and the mean age was 53.94 years (standard deviation 9.8). The sociodemographic data are shown in Table 1. The distribution of cutaneous psoriasis and AP forms is shown in Table 2.

Most of the sample had plaque psoriasis alone (32 individuals) and the most prevalent type of arthritis in this study was symmetrical polyarthritis (41 individuals), of which five also presented spondylitis. Most of the patients were diagnosed with cutaneous psoriasis prior to the diagnosis of PsA (66.67%), 24.44% had both diagnoses on the same occasion, and 8.89% had PsA before cutaneous manifestations. There was no difference in the types of psoriasis or the time of diagnosis of psoriasis or PsA between the different groups of CVR.

Regarding the frequency of CVR factors among the patients in this study, dyslipidemia was present in 93% of the sample, 46% were hypertensive, 40% were obese (BMI ≥ 30 kg/m²), 33.3% had type 2 diabetes mellitus, 13.3% self-reported smoking, and 95% presented increased abdominal circumference.

Among the 45 participants, 43 had increased waist circumference, that is, women with a circumference greater than or equal to 80 cm and men with an abdominal waist

Table 1 - Socio-demographic data

Variables	N	%
Sex		
Female	31	68.89
Male	14	31.11
Ethnicity		
White	08	17.78
Non-white	37	82.22

Table 2 - Absolute frequency and percentage of each type of psoriasis and PsA

Variables	N	%
Type of psoriasis		
Plaque	32	71.11
Palmoplantar	07	15.56
Plaque + Palmoplantar	03	6.67
Guttate	02	4.44
Generalized Pustular	01	2.22
Arthritis type		
Symmetrical polyarthritis	36	80.00
Symmetric polyarthritis + spondylitis	05	11.12
Spondylitis	01	2.22
Asymmetric oligoarthritis	01	2.22
Distal arthritis	01	2.22
Mutilating Arthritis	01	2.22

greater than or equal to 90 cm.[27] Patients who presented at least one of the following were considered dyslipidemic: LDL-C > 130 mg/dL or triglycerides > 150 mg/dl, values adopted by the 2017 Brazilian Dyslipidemia and Atherosclerosis Prevention Guideline.[26]

Individuals with altered serum CRP and ESR levels presented, respectively, higher levels of LDL-C (p = 0.02) and total cholesterol (p = 0.04). There was no significant difference between serum levels of CRP or ESR according to the different categories of CVR — low, intermediate or high risk.

Participants in this study had a median CVR of 13.70% (IQR 5.6-25.3). Patients at high risk for cardiovascular outcomes in the next 10 years accounted for 53% of the sample, 29% had intermediate risk and 18% were low risk.

Psoriatic arthritis medications used by the participants in this research data collection period are listed in Table 3. No association was found between the medication used and the calculated CVR compared by Fisher's exact test. Analyzing the presence of CVR factors and the type of medication used, it was evidenced that patients using leflunomide had significantly higher BMI (t = 2.41, p = 0.03)

Discussion

This study was performed to quantify risk factors and to assess the CVR of PsA patients followed at a tertiary referral hospital in northeastern Brazil. Corroborating with the high CVR found in the sample, in 2013, a systematic review evidenced increased risk of AMI, cardiovascular mortality and stroke in patients with aggressive psoriasis — those who, by definition, require hospital admission or systemic therapy which includes carriers of PsA. Other manifestations of atherosclerotic disease also have increased frequency in patients with psoriasis, such as stroke and peripheral arterial disease.[27] Although notorious, the high occurrence of CVR factors, as well as the risk estimated by GCRS[25] in patients with PsA, do not provide enough evidence to use a multiplier factor for the usual scores, as in rheumatoid arthritis, for example, in which the calculated risk is multiplied by 1.5.[28]

Prevalence of hypertension, obesity, hyperlipidemia, type 2 diabetes and the occurrence of at least one cardiovascular event were 37.1%, 30%, 20.7%, 12% and 8.2%, respectively, resulting in a 4.9% increase in the risk of cardiovascular disease, 17.5% in hypertension, 6.2% in hyperlipidemia, 5.3% in type 2 diabetes and 3.5% in obesity compared with patients with psoriasis without arthritis.[29] A 2013 systematic review found a higher prevalence of hypertension in psoriasis patients than in the control group.[30] The same occurred with diabetes in another systematic review of the same year.[31] A population study from the UK found an increased smoking frequency, and all previously mentioned risk factors in psoriasis patients compared to the control group.[32] The sample of this study also revealed a high occurrence of the main predictors of CVR, especially dyslipidemia. The prevalence of hyperlipidemia found in the Canadian study is considerably lower, which may be justified by the non-contribution of low HDL-C patients in the Canadian research statistics, in addition to the current cut-off points being more stringent.

Similar to this study, in which the majority of individuals was diagnosed with psoriasis before articular manifestations, skin disease precedes arthritis in approximately 75% of the cases, is simultaneous in 10% of the diagnoses and occurs afterwards in 15%.[33]

Studies reveal a large range of variation in the incidence of each type of joint involvement: 15%–78% of the polyarticular form, 16%–70% of asymmetric oligoarthritis, 1%–17% of the form affecting the distal interphalangeal, 2%–16% of the mutilating form and 2%–27% of spondylitis. The overlap between the several subgroups of PsA is frequent and the joint involvement can change, so that patients starting symptomatology with asymmetric oligoarthritis can develop symmetrical polyarthritis over time, for example. Thus, the current trend is to classify PsA in three main clinical presentations: polyarticular, oligoarticular and axial; it is estimated that

Table 3 - Absolute frequency and percentage of each type of medication used for PsA

Medication	N	%
Metotrexate	26	57.78
Leflunomide	10	22.22
Adalimumab	08	17.78
Infliximab	07	15.56
Corticoid	03	6.67
Ustekinumab	02	4.44
Etanercept	02	4.44
Naproxen	01	2.22
None	04	8.89

they correspond to 41%, 31% and 28% of the patients, respectively.[33] In this study, the polyarticular form was also the most prevalent, followed by the overlap of this form with spondylitis.

A 2009 retrospective cohort study using a UK database, estimated to represent 5% of the population in this region, found an increased risk of stroke in PsA, which was higher according to the severity of the disease.[34] The presence of high levels of inflammatory biomarkers —— suggestive of increased disease activity — were predictors of clinical cardiovascular events in the study by Husted J.A. et al.[29] In our study, individuals with serum alterations of CRP and ESR presented, respectively, higher levels of LDL-C and total cholesterol, factors known to be related to the development of atherosclerosis and its consequences. However, there was no significant difference between serum levels of CRP or ESR according to the different categories of CVR — low, intermediate or high risk.

Psoriatic arthritis drug therapy includes non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids and disease-modifying drugs (DMDs) — sulfasalazine, methotrexate, leflunomide and biological agents. DMDs are defined as drugs capable of preventing disease progression.[35] NSAIDs and glucocorticoids, used to alleviate PsA symptoms, are associated with an increase in unfavorable cardiovascular outcomes, such as AMI, which, in a way, may also eventually contribute to the increase of CVR.[36,37] On the other hand, in several studies, DMDs are related to reduced CVR. Risk was reduced in patients using these medications compared to those who used other systemic therapies, probably because of the greater effectiveness in reducing the disease activity, reducing inflammation and its propensity to the formation of atherosclerosis. Inflammation suppression by immunomodulatory agents represents a promising new target for the management of cardiovascular diseases both in the general population and among patients with chronic inflammatory conditions.[27,38] Methotrexate is the first-line DMD in PsA, due to its effectiveness in the treatment of cutaneous and joint involvement combined with its low cost. Its anti-inflammatory effect is mediated by adenosine and can neutralize neutrophils, T-cells and macrophages — the main agents in the pathogenesis of psoriasis and PsA.[33,39] Currently, the most widely used biological DMDs for PsA treatment, and approved by the Brazilian National Agency of Sanitary Surveillance (ANVISA), are the TNF-α inhibitors: etanercept, adalimumab, golimumab, infliximab, and certolizumab pegol.[40] However, in this study, there was no significant difference in cardiovascular parameters according to the different medications in use.

This research presented some limitations, because, although performed in a specialized outpatient clinic, the sample obtained was small and there was no comparison with the control group, thus no inferences could be made. Since it was an observational study, it was subject to memory bias. In addition, it was hampered by the lack of data in the medical records.

Conclusions

Most of the patients in the sample were stratified as high or intermediate CVR. Despite the high incidence of CVR factors, there was no parallel between them and the time of PsA diagnosis. It is recommended to use traditional CVR scores since there is not enough evidence to use a multiplier factor in this estimation, or to use a different calculator.

Authors' contributions

Research creation and design: Campos B, Gomes G, Telis A. Data acquisition: Campos B. Data analysis and interpretation: Campos B, Telis A. Statistical analysis: Telis A. Writing: Campos B, Gomes G, Braz A, Telis A. Critical revision of the manuscript for intellectual content: Braz A, Telis A. Supervision/major investigator: Telis A.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of *Universidade Federal da Paraíba* under protocol number CAAE: 56336216.1.0000.5183. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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