MAEDICA – a Journal of Clinical Medicine
2014; 9(1): 19-24

MÆDICA - a Journal of Clinical Medicine

ORIGINAL PAPERS

# Cardiovascular Risk in Psoriatic Arthritis – A Cross-Sectional Study

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*ABSTRACT*

***Objectives:*** *The present study aims to estimate long term cardiovascular risk in psoriatic arthritis (PsA) patients and to identify clinical and/or laboratory features which influence this risk.*

***Materials and methods:*** *cross-sectional design; sample: 103 in-patients known with psoriatic arthritis (PsA) and 56 normal age-matched female in-patients; cardiovascular variables recorded: age, gender, arterial hypertension (AHT), ischemic heart disease (IHD), dyslipidemia (lipid profile), type II diabetes mellitus (DM; fasting plasma glucose - FPG), obesity (body mass index - BMI), smoking, cardiovascular 10-year risk (SCORE high risk charts); PsA variables recorded: age at onset, inflammation markers; phenotype (peripheral/axial disease); type of treatment.*

***Outcomes:*** *The PsA group included 44 males and 59 females ($p = 0.167$) with an average age of 52 years (23-80). SCORE was significantly correlated with age of onset, BMI, triglycerides, FPG. Among these patients, males, smokers, those with axial involvement, with IHT, with AHT and those not treated with glucocorticoids had a significantly higher SCORE. The subgroup of 56 PsA women, age-matched with 56 normal women, had a significantly higher SCORE, even after controlling for covariates.*

***Conclusions:*** *Cardiovascular risk of PsA patients estimated on SCORE charts correlates with metabolic clinical and laboratory features and is associated with classical cardiovascular risk factors. The axial involvement in PsA is associated with a higher cardiovascular risk when compared to non-axial PsA. Women with PsA have a higher cardiovascular risk than normal women, which sustains the opinion that PsA may be considered an independent cardiovascular risk factor.*

**Keywords:** psoriatic arthritis, cardiovascular risk, SCORE

## INTRODUCTION

Psoriatic arthritis (PsA) is an auto-immune chronic inflammatory disease associated with psoriasis and the lack of rheumatoid factor in most patients (1). It has been classified as a spondylarthritis (2), since it shares some clinical elements with this nosological group, namely sacroiliitis, dactylitis, enthesitis and uveitis. Compared with the general population, PsA patients have higher morbidity and mortality rates (3,4) and a higher cardiovascular risk (5). In fact, more than a third of PsA patients' deaths are caused by cardiovascular factors (3,6,7). This excess in cardiovascular mortality can be explained by the association of PsA with atherosclerosis (8), as a recent meta-analysis also

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Article received on the 20th of September 2013. Article accepted on the 25th of February 2014.

demonstrates (9). Thus, compared to normal individuals, PsA patients have a higher prevalence of ischemic heart disease (IHD),(3) arterial hypertension (AHT) (3,10), angina and myocardial infarction (11), heart failure and vascular disease (9), obesity and metabolic syndrome (12), type II diabetes mellitus (DM) and hyperglycemia (8,13,14), dyslipidemia (3,8) and inflammation (8). It has been established that PsA is equivalent to rheumatoid arthritis and DM regarding its cardiovascular risk (15,16). There are several tools used to estimate long term cardiovascular risk, such as SCORE charts (Systematic Coronary Risk Evaluation), published by the European Society of Cardiology (17). Good clinical practice requires an approximation of PsA cardiovascular risk since this disease can be considered an independent cardiovascular risk factor (7), which indicates an early detection and therapeutic management of these patients (18,19). There is insufficient and contradictory data regarding the decrease of cardiovascular risk of PsA patients using disease modifying anti-rheumatic drugs (DMARDs) (9). For example, some authors observed that methotrexate does not decrease the risk of hospitalization for IHD (20) and others showed that TNFα blockers are not cardio-protective in PsA patients (21). In this context, the present study aims to estimate long term cardiovascular risk in PsA patients and to identify clinical and/or laboratory features which influence this risk. ❑

## MATERIALS AND METHODS

The population sample was studied in a cross-sectional design and it comprised two groups of in-patients, randomly admitted to the hospital from 2012 to 2013. The first group included 103 patients known with PsA, who fulfilled the disease classification criteria (CASPAR 2006) (22). The second group included 56 normal female patients, matched with an equal number of PsA women by age, ethnicity and geographical area. Each participant in the study gave informed consent, and the study was approved by the local ethics committee.

AHT was defined as: systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg (mechanical sphygmomanometer; 5 mmHg error) or anti-hypertensive drug therapy (23). IHD was defined if the patient had suggestive electrocardiographic modifications or a history of acute coronary syndromes, angina, rhythm or conduction abnormalities, ischemic heart failure (24). Dyslipidemia was defined as triglycerides >150 mg/dL or total cholesterol >200 mg/dL or treatment with statins/fibrates (25). Type II DM was defined if the patient had fasting plasma glucose level (FPG) >126 mg/dL on two occasions or plasma glucose level ≥200 on one occasion or treatment with insulin/oral hypoglycemic drugs (26). Obesity was defined by a body mass index (BMI) ≥30 kg/m$^2$ (wall stadiometer, 0.5 cm error; mechanical scale, 100 mg error). Cardiovascular risk was estimated using high risk SCORE charts, adequate for the Romanian population (17).

Normally distributed data were reported as "mean (standard deviation; interval)", while non-normally distributed data were reported as "median (interval)". Differences were evaluated using non-parametric tests: $\chi^2$ test (with Fisher's correction were appropriate) for nominal variables; Mann-Whitney U test for scale variables. Spearman correlation coefficients were computed. Since most variables were non-normally distributed, linear regression and parametric covariance analysis could not be done. So, for testing the significance of SCORE differences between normal and PsA patients controlling for confounding variables (age, BMI etc.) the following algorithm was used: SCORE and its covariates were ranked; the ranks of SCORE were linearly regressed on the ranks of covariates, saving un-standardized residuals; a one-way analysis of variance war run on these residuals with the diagnostic grouping variable (normal/PsA) (27). All tests were two-sided, were considered significant if p ≤0.05 and were computed using SPSS Statistics v.17.0.1 for Windows (SPSS Inc., Chicago, S.U.A., 2008). ❑

## OUTCOMES

1. *General characteristics*. Table 1 summarizes the general characteristics of the PsA group. Overweight, hyperglycemia, dyslipidemia, inflammatory syndrome, peripheral disease pattern, smoking and IHD predominated in this group.

2. *Cardiovascular risk*. The SCORE value correlated significantly with age (a variable included in SCORE), age of PsA onset, triglycerides, FPG and BMI (Table 2). On average, the

following subgroups had a significantly higher SCORE compared to the respective subgroup: men, smokers, patients with IHD and AHT, patients with axial PsA (Figure 1A) and patients who did not receive glucocorticoids (GCs; see Table 3). Compared to patients without anti-TNFα, PsA patients receiving this biologic treatment had a significantly higher median disease duration (120 months compared to 48 months, p = 0.001) and a lower mean SCORE-estimated cardiovascular risk (1.35% compared to 2.52%, p = 0.077), which failed to reach statistical significance in this group. There were no significant differences between these two subgroups regarding the frequency of cardiovascular disease (p > 0.05).

3. Comparison of a PsA subgroup with normal individuals. The subgroup of 56 PsA women, age-matched with 56 normal women, had significantly lower rates of AHT and dyslipidemia, but significantly higher inflammation markers (Table 4). Compared to normal women, PsA had a significantly higher SCORE (Fig. 1B), even after controlling for the covariates recorded by the study (smoking, DM, IHD, AHT, dyslipidemia, cholesterol, triglycerides, FPG, ESR, CRP). ❑

## DISCUSSION

The present study reports a mean SCORE of 2.3% in 103 PsA patients. The main cardiovascular risk factors observed had the following prevalence in the PsA group: smoking: 23.3% (24/103); type II DM: 11.6% (12/103); AHT: 42.7% (44/103); IHD: 22.3% (23/103); obesity: 34.9% (36/103); dyslipidemia: 33.9% (35/103). The observed cardiovascular risk factors had a marked tendency to cluster. For example, patients with AHT, compared with non-AHT patients, had significantly higher age, BMI, triglycerides, FPG and significantly higher frequencies of obesity, type II DM and dyslipidemia (p <0.05). The same was true for any of these variables.

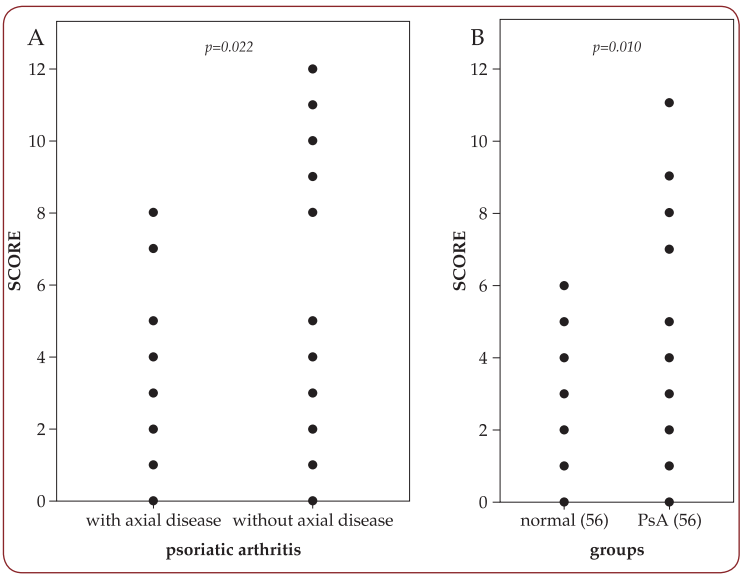


**FIGURE 1A.** Distribution of SCORE values among PsA subgroups with axial disease (n = 46; average 2.9%) and without axial disease (n = 57; average 1.7%; p = 0.022). **B.** Distribution of SCORE values in the normal female group (n = 56; average 1.79%) compared to 56 PsA female patients (average 3.02%; p = 0.010).

| variable | present | absent | p | variable | value |
|---|---|---|---|---|---|
| males | 44 (42.7%) | 59 (57.3%) | 0.167 | age (years) | 52.3 (12.7; 23 - 80) |
| smokers | 24 (23.3%) | 79 (76.7%) | < 0.001 | age onset (years) | 45.8 (14.1; 17 - 80) |
| periph. dis. | 99 (96.1%) | 4 (3.90%) | < 0.001 | dis. duration (mo) | 53 (1 - 360) |
| axial dis. | 46 (44.7%) | 57 (55.3%) | 0.324 | BMI (kg/m2) | 27.9 (5.6; 15.1 - 44.5) |
| PAD | 42 (40.8%) | 61 (59.2%) | 0.076 | TC (mg/dL) | 198 (102 - 305) |
| NSAID | 68 (66.1%) | 35 (33.9%) | 0.001 | TG (mg/dL) | 114 (37 - 677) |
| GCs | 21 (20.4%) | 81 (79.6%) | < 0.001 | FPG (mg/dL) | 106.1 (40.6; 66 - 428) |
| DMARD | 78 (75.7%) | 25 (24.3%) | < 0.001 | ESR (mm/1h) | 37.2 (2 - 124) |
| biologics | 20 (19.4%) | 83 (80.6%) | < 0.001 | CRP (mg/L) | 9.43 (0.14 - 139.4) |
| type II DM | 12 (11.6%) | 92 (89.3%) | < 0.001 | SBP (mmHg) | 130.6 (12; 110 - 150) |
| AHT | 44 (42.7%) | 59 (57.3%) | 0.167 | SCORE (%) | 1 (0 - 12) |
| IHD | 23 (22.3%) | 80 (77.7%) | < 0.001 | | |
| obesity | 36 (34.9%) | 67 (65.1%) | 0.003 | | |
| dyslipidemia* | 35 (33.9%) | 68 (66.1%) | < 0.001 | | |
| statins | 32 (31.1%) | 71 (68.9%) | < 0.001 | | |

**TABLE 1.** PsA group's general characteristics (n = 103).

* 32 patients (31.1%) were on statins; 12 patients (11.7%) were on fibrates

PsA – psoriatic arthritis; PAD – peripheral (periph.) and axial disease (dis.); NSAID – non-steroidal anti-inflammatory drugs; GCs - glucocorticoids; DMARD – disease modifying anti-rheumatic drugs; biologics – TNFα blockers; DM – diabetes mellitus; AHT – arterial hypertension; IHD – ischemic heart disease; BMI – body mass index; TC – total cholesterol; TG – triglycerides; FPG – fasting plasma glucose; ESR – erythrocyte sedimentation rate; CRP - C-reactive protein; SBP – systolic blood pressure.

| | SCORE | | | SCORE | |
|---|---|---|---|---|---|
| variable | rho | p | variable | rho | p |
| age | 0.815 | < 0.001 | BMI | 0.239 | 0.015 |
| age at onset | 0.766 | < 0.001 | TC | 0.118 | 0.235 |
| disease duration | - 0.137 | 0.168 | TG | 0.223 | 0.023 |
| ESR | 0.148 | 0.136 | FPG | 0.432 | < 0.001 |
| CRP | 0.163 | 0.100 | SBP | 0.141 | 0.154 |

**TABLE 2.** Spearman correlations of SCORE with continuous variables in the PsA groups (n = 103).

PsA – psoriatic arthritis; BMI – body mass index; TC – total cholesterol; TG – triglycerides; FPG – fasting plasma glucose; ESR – erythrocyte sedimentation rate; CRP – C-reactive protein; SBP – systolic blood pressure

| | subgroup | | p |
|---|---|---|---|
| SCORE value | males (n = 44): 3.5% | females (n = 59) 1.3% | < 0.001 |
| | with periph. dis. (n = 99): 1.0% | without periph. dis. (n = 4): 3.0% | 0.146 |
| | with axial dis. (n = 46): 2.9% | without axial dis. (n = 57): 1.7% | 0.022 |
| | with PAD (n = 42): 2.8% | without PAD (n = 61): 1.9% | 0.080 |
| | with NSAID (n = 68): 2.5% | without NSAID (n = 35): 2.2% | 0.551 |
| | with GCs (n = 21): 1.5% | without GCs (n = 81): 2.5% | 0.041 |
| | with DMARD (n = 78): 2.2% | without DMARD (n = 25): 2.6% | 0.551 |
| | with biologics (n = 20): 1.4% | without biologics (n = 83): 2.5% | 0.065 |
| | smokers (n = 24): 3.7% | nonsmokers (n = 79): 1.9% | 0.021 |
| | with AHT (n = 44): 3.6% | without AHT (n = 59): 1.4% | < 0.001 |
| | with IHD (n = 23): 3.7% | without IHT (n = 80): 1.8% | < 0.001 |
| | with DM (n = 11): 4.0% | without DM (n = 92): 2.1% | 0.064 |
| | obese (n = 36): 2.5% | non-obese (n = 67): 2.2% | 0.416 |
| | with dyslipidemia (n = 35): 2.6% | without dyslipidemia (n = 68): 2.1% | 0.154 |

**TABLE 3.** Spearman correlations of SCORE with continuous variables in the PsA groups (n = 103).

& SCORE percentages represent the mean of the certain PsA subgroup

PsA – psoriatic arthritis; PAD – peripheral (periph.) and axial disease (dis.); NSAID – non-steroidal anti-inflammatory drugs; GCs – glucocorticoids; DMARD – disease modifying anti-rheumatic drugs; biologics – TNFα blockers; DM – diabetes mellitus; AHT – arterial hypertension; IHD – ischemic heart disease.

The SEPHAR study data offer an adequate comparison regarding the cardiovascular risk and its factors, since this study was carried out on a representative sample of the normal Romanian population. Thus, the average cardiovascular risk of the SEPHAR sample, estimated using the same high risk SCORE charts, was 3.5% (range: 0-35%) (28), higher than the average of our 103 PsA patients. This difference probably originates from the type of patients included in the two studies: most of the SEPHAR subjects were not on record for cardiovascular risk factors and thus they did not benefit from medical strategies aimed to reduce their risk, while our PsA patients, due to the nature of their chronic disease, were regularly reevaluated by their physicians and were receiving adequate medical therapies (blood pressure and lipid lowering drugs, aspirin etc.) and lifestyle modification advice. The prevalence of AHT (42.7%) and smoking (23.3%) in our PsA group did not differ significantly from the respective frequencies in the SEPHAR sample (44.9%; 906/2017; p=0.661; respectively 27%; 545/2017; p=0.407) (28,29). Compared to the data from the PRESENT study (another epidemiologic study conducted on a representative sample for the normal Romanian population) (30), our PsA group had significantly lower prevalence of type II DM (11.6% compared to 20%; 159/796; p=0.043) and dyslipidemia (33.9% compared to 47%; 374/796; p=0.013), and a significantly higher prevalence of IHD (22.3% compared to 13%; 104/796; p=0.011), with no significant differences in obesity prevalence (34.9% compared to 33%; 263/796; p=0.698). The differences regarding the prevalence of DM and dyslipidemia can be explained by the fact that PRESENT investigators recorded these diagnoses anamnestically, while our study, besides anamnesis (which includes questions regarding drug therapies) was designed to objectively measure of FPG and lipid profile.

It is interesting to note that SCORE correlated in our PsA group with two elements of the metabolic syndrome (FPG, BMI) (31,32), which indicates a common physiopathological process responsible for metabolic and cardiovascular modifications. The fact that SCORE was significantly higher in men, smokers, patients with AHT and IHD from our sample strengthens this assertion.

Regarding the differences of SCORE between PsA subgroups, two aspects deserve discussion. The first aspect refers to the unusual behavior of the PsA subgroup which was on GCs at the time of inclusion in the study. The expected therapeutic effect of GCs in PsA is their anti-inflammatory function, but our GCs-treated PsA patients had significantly higher ESR than those not treated with GCs. Some of the most important side effects of GCs are the metabolic modifications (dyslipidemia, obesity), but our GCs-treated PsA patients had a significantly lower average BMI and dyslipidemia prevalence than those not receiving GCs. Although they did not differ from any other point of view, GCs-treated PsA patients had a significantly lower SCORE than those not receiving

GCs. These observations point out either a cardio-protective role of GCs either the preference of rheumatologist to prescribe GC to patients with a better cardiovascular risk factor profile and active disease. Testing these hypotheses requires a prospective study design, which must record the duration and dose of GCs therapy. The fact that anti-TNFα treated patients had a significantly longer disease duration reflects the algorithm by which patients end up receiving biologic drugs, in the sense that their disease activity has to be insufficiently controlled by DMARD therapy first. In spite of this difference, knowing that a longer disease duration is associated with a more adverse cardiovascular profile, our PsA treated with biologics tended to have a lower SCORE, which is in accordance with the general view on cardiovascular risk reduction potential of biologics.

The second aspect refers to the cardiovascular risk of PsA with axial involvement, which was significantly higher in our group compared with non-axial disease. There are many studies which demonstrate on one hand that PsA patients have a higher cardiovascular risk than the general population and on the other hand that spondylarthritis is associated with such an elevated risk (33,34), but to our knowledge, no other author reported a higher cardiovascular risk in PsA with axial involvement.

The limits of the study include: its cross-sectional design, which did not allow following the patients and recording their cardiovascular events/diagnoses; the relatively small sample size, which did not produce normally distributed variables; the lack of normal age-matched male subjects (cardiovascular risk profiles in men and women evolve quite differently so, even in the availability of a normal male group, the statistical analysis would have been more appropriately done for each sex subgroup independently); the absence of such variables as cholesterol fractions (HDL, LDL) and abdominal circumference, which would have allowed the diagnosis of the metabolic syndrome. ❑

| variable | PsA (n = 56) | normal (n = 56) | p |
|---|---|---|---|
| female | 56 (100%) | 56 (100%) | 0.000 |
| smokers | 17 (30.3%) | 13 (23.2%) | 0.393 |
| type II DM | 9 (16.1%) | 10 (17.8%) | 0.801 |
| AHT | 27 (48.2%) | 39 (69.6%) | 0.021 |
| IHD | 17 (30.6%) | 17 (30.6%) | 1,000 |
| dyslipidemia | 21 (37.05%) | 34 (60.7%) | 0.014 |
| obesity | 22 (39.3%) | 17 (30.6%) | 0.321 |
| age (years) | 56.89 (9.41) | 56.95 (9.27) | 0.968 |
| BMI (kg/m2) | 28.9 (5.9) | 29.7 (5.2) | 0.383 |
| TC (mg/dL) | 207 (125-302) | 211 (132-333) | 0.481 |
| TG (mg/dL) | 125.5 (54-667) | 110 (43-843) | 0.076 |
| FPG (mg/dL) | 99 (79-428) | 104 (80-210) | 0.238 |
| ESR (mm/dL) | 32.5 (2-112) | 21 (5-133) | 0.013 |
| CRP (mg/L) | 9.78 (1.3-139) | 4 (0.1-155) | < 0.001 |

**TABLE 4.** The comparison between a subgroup of PsA women and an age-matched normal women group.

* SCORE difference remains significant after controlling with any of the listed variables

PsA – psoriatic arthritis; DM – diabetes mellitus; AHT – arterial hypertension; IHD – ischemic heart disease; BMI – body mass index; TC – total cholesterol; TG – triglycerides; FPG – fasting plasma glucose; ESR – erythrocyte sedimentation rate; CRP – C-reactive protein

## CONCLUSIONS

Cardiovascular risk of PsA patients estimated on SCORE charts correlates with metabolic clinical and laboratory features (BMI, triglycerides, FPG) and is associated with classical cardiovascular risk factors (male gender, smoking, IHD, AHT). These cardiovascular risk factors have a strong tendency to aggregate in the same patient. The axial involvement in PsA is associated with a higher cardiovascular risk when compared to non-axial PsA. Women with PsA have a higher cardiovascular risk than normal women, which sustains the opinion that PsA may be considered an independent cardiovascular risk factor. The cardiovascular risk of PsA patients receiving classical DMARDs was similar with that of PsA patients without this treatment, but it was significantly lower in PsA patients on GCs when compared to those without GCs. Prospective studies are needed to asses the true value of disease modifying therapy in PsA regarding cardiovascular risk reduction.

*Conflicts of interests: none declared.*

*Financial support: none declared.*

*Acknowledgments: The authors would like to thank the rheumatologists of "Sfanta Maria" Clinical Hospital of Bucharest for providing patients.*

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