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# Higher depression rates and similar cardiovascular comorbidity in psoriatic arthritis compared with rheumatoid arthritis and diabetes mellitus

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***Abstract***

**Background:** We explore the spectrum of comorbidities in psoriatic arthritis (PsA) patients in comparison with other high comorbidity-burden diseases like rheumatoid arthritis (RA) and diabetes mellitus (DM).

**Methods:** Two hundred and fifteen PsA patients, cross-sectionally collected from two tertiary hospitals, were compared with 215 RA and 215 DM patients (age/sex-matched, similar disease duration). Cardiovascular risk factors [hypertension, current smoking, hyperlipidaemia, obesity (body mass index (BMI) ⩾30)], coronary artery disease (CAD), stroke, major adverse cardiac events (MACEs; combined CAD and stroke), depression, osteoporosis and malignancies were recorded. Odds ratios (ORs) for stroke, CAD and MACE were adjusted for age, sex, hypertension, smoking, hyperlipidaemia, BMI, glucocorticoids use and those for depression were adjusted for age, sex, disease duration, skin involvement and smoking. Within the PsA group, associations between comorbidities and demographic/clinical features were assessed.

**Results:** Depression [OR (95% confidence interval (CI)): 3.02 (1.57–5.81)], obesity [OR (95% CI): 2.83, (1.65–4.86)] and hyperlipidaemia [OR (95% CI): 1.96 (1.32–2.90)] were more prevalent in PsA compared with RA, while no differences were observed for CAD, stroke, MACE and malignancies. Depression [OR (95% CI): 4.85 (2.37–9.93)] and osteoporosis [OR (95% CI): 6.22 (1.33–29.2)] were more common in PsA than in DM. Hypertension, but not the other cardiovascular risk factors, was more frequent in DM [OR (95% CI) 0.49 (0.33–0.74)]. However, prevalence of stroke, CAD and MACE did not differ between PsA and DM. Within PsA group, depression was associated with age [OR (95% CI): 1.03 (0.99–1.06)], female sex [OR (95% CI): 3.47 (1.51–7.99)] and smoking [OR (95% CI): 2.78 (1.31–5.88)] while MACEs were associated with age [OR (95% CI): 1.08 (1.00–1.17)], male sex [OR (95% CI) for females: 0.26 (0.06–1.23) and hypertension [OR (95% CI): 6.07 (1.12–33.0)]. No differences were recorded in comorbidities between the different PsA phenotypes.

**Conclusion:** Depression was more prevalent in PsA compared with RA and DM, while cardiovascular comorbidity was comparable to both groups, supporting the need for their assessment and management.

***Keywords:*** cardiovascular disease, comorbidities, depression, diabetes mellitus, psoriatic arthritis, rheumatoid arthritis

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## Introduction

Psoriatic arthritis (PsA) is an inflammatory arthritis affecting around 0.8% of the general population.[1] It is characterized by skin involvement, arthritis, spondylitis, enthesitis, as well as manifestations from other tissues–organs. Emerging data have shown that traditional cardiovascular risk factors such as obesity[2–4] and cardiovascular events,[2–4] as well as mental-health disorders,[5–7] are more prevalent in PsA compared with healthy individuals while the prevalence of other comorbidities such as osteoporosis is comparable to that observed in the general population.[8,9] Accumulating evidence has shown that comorbidities in PsA have a significant impact on health-related quality of life[10,11] and clinical outcomes.[12,13] However, only few of the studies assessing comorbidities in PsA have examined a wide spectrum of them[14,15] or made a direct comparison with other rheumatic inflammatory disorders such as rheumatoid arthritis (RA).[4,15,16] It is increasingly recognized that the latter is accompanied by several comorbidities including cardiovascular disease.[17] Compared with PsA, some studies have shown only minor differences in the number and type of comorbidities,[4] while others have found that PsA patients have higher frequency of specific comorbidities such as hypertension, hyperlipidaemia, diabetes, ischaemic heart disease and depression.[15] Specifically for depression, results so far are conflicting.[15,16] A direct comparison with a chronic disorder of high comorbidity burden such as diabetes mellitus (DM) has not been performed hitherto.

We sought to investigate in a cross-sectional study the prevalence of major comorbidities in patients with PsA in comparison with RA and DM. Furthermore, we assessed whether comorbidities differ between the various PsA phenotypes (e.g. axial disease) and any potential associations between comorbidities and patients' clinical characteristics.

## Materials and methods

### *Patient population and study design*

Data were recorded from PsA patients meeting the CASPAR criteria, who visited the outpatients' rheumatology clinics from two different tertiary referral hospitals between December 2018 and June 2019. Patients needed to have a follow-up of at least 6 months to be included in the analysis. RA patients meeting the ACR-EULAR 2010 criteria and DM patients of type 1 and 2 followed in the diabetes outpatient clinic of our department, both age- and sex-matched (matching 1:1:1) and of similar disease duration with PsA patients, were used as control groups. PsA and RA patients with concomitant DM were excluded.

Recorded features included the following: epidemiological characteristics [age, sex, weight, height, body mass index (BMI), disease duration], ever-present enthesitis, dactylitis, involvement of distal interphalangeal joints (DIP), spine, nails, eyes and bowel, as well as laboratory features (rheumatoid factor and anti-CCP status, erythrocyte sedimentation rate, C-reactive protein), medications, clinical features [number of tender and swollen joint counts, body surface area (BSA) of skin involvement] and comorbidities: traditional cardiovascular risk factors (hypertension, hyperlipidaemia, obesity, current smoking), cardiovascular events (history of myocardial infarction/angina, stroke), osteoporosis, depression and history of malignancies, at the time of inclusion in the study. The following definitions were used: PsA-oligoarthritis pattern: $<5$ joints involved at disease diagnosis; PsA-RA-like pattern: $>4$ joints at disease diagnosis; usually symmetrical, axial disease: radiologic findings of sacroiliac joints or spine involvement, hypertension: blood pressure $>140$ mmHg over 90 mmHg in two measurements or when antihypertensive treatment was administered; hyperlipidaemia: cholesterol$>200$ mg/dl and/or low-density lipoprotein $>130$ mg/dl and/or triglycerides$>150$ mg/dl and/or receiving lipid-lowering therapy; obesity: BMI$\geq 30$; DM: use of anti-diabetic drugs, coronary artery disease (CAD): myocardial infarction or angina; major adverse cardiac event (MACE): CAD, stroke or death; osteoporosis: bone density $-2.5$ or less in dual-energy X-ray absorptiometry or requirement for anti-osteoporotic treatment; depression: treatment with antidepressants prescribed by a psychiatrist. Disease duration was defined as the time between disease diagnosis of PsA and time of enrolment to the study.

Prevalence of comorbidities was compared between PsA, RA and DM patients, after adjustment for certain variables (see Results section). Further analyses were performed within the PsA group to identify possible associations between clinically meaningful comorbidities and epidemiological chracteristics. Comparison of the comorbidites was also performed between the two major phenotypes of PsA, namely "RA-like" and "oligoarthritis" pattern as well as between PsA patients with or without axial involvement. The number of patients exhibiting only axial disease

**Table 1.** Epidemiological characteristics of patients included in the study. Comparison between psoriatic arthritis, rheumatoid arthritis and diabetes mellitus.

| | PsA *n* = 215 | RA *n* = 215 | DM *n* = 215 | PsA *versus* RA | PsA *versus* DM |
|---|---|---|---|---|---|
| Female sex, *n* (%) | 123 (57.2) | 123 (57.2) | 123 (57.2) | 1.000 | 1.000 |
| Age, years; mean (SD) | 52.6 (12.6) | 52.6 (13.7) | 52.6 (9.1) | 0.928 | 0.804 |
| Weight, kg; mean (SD) | 83.0 (16.4) *n* = 175 | 74.5 (16.6) *n* = 187 | 82.1 (22.3) | <0.0001 | 0.125 |
| Height, cm; mean (SD) | 171.6 (9.3) *n* = 175 | 168.4 (8.8) *n* = 187 | 168.3 (9.4) | 0.0007 | 0.0009 |
| BMI, mean (SD) | 28.2 (5.4) *n* = 175 | 26.2 (5.3) *n* = 187 | 29.0 (7.6) | <0.0001 | 0.839 |
| Disease duration, months; mean (SD) | 91.4 (86.2) | 89.3 (83.0) | 95.1 (74.1) | 0.868 | 0.245 |

BMI, body mass index; cm, centimetre; DM, diabetes mellitus; kg, kilogram; *n*, number; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

or DIP involvement was not sufficient for separate analyses for these subgroups.

The study was approved by the ethical boards of the participating hospitals ("Laiko" ethics committee; approval number: 967-19, and "NIMTS" ethics committee; approval number: 80-19). Written informed consent was obtained from all patients.

### *Statistics*

Two-sided Fisher's and Mann–Whitney tests were used to compare categorical and numerical characteristics, respectively. Binomial logistic regression was performed, both univariate and multivariate, having as dependent variables the examined comorbidities and correcting for relevant confounders. Results were expressed as odds ratios (ORs). Statistical significance is considered for *p*-values less than 0.05 and 0.1 in univariate and multivariate analyses, respectively. GraphPad Prism 5.00 (GraphPad Software, Inc., USA) and SPSS 24.0 (SPSS software, USA) were used.

## Results

Two hundred and fifteen PsA patients were included and compared with 215 RA patients and 215 DM patients (90 with DM type 1, 125 with DM type 2). Groups were age- and sex-matched (1:1:1) and had similar disease duration (Table 1). Clinical and laboratory characteristics as well as information about the treatment of PsA and RA patients are shown in Table 2.

### *Comparison of epidemiological characteristics and comorbidities between PsA and RA patients*

Patients with PsA had higher weight, height and BMI compared with RA patients (Table 1). Hyperlipidaemia, obesity and depression were also more frequent in PsA *versus* RA patients while current smoking was similar between the two groups. Depression remained more prevalent than RA after adjusting for age, sex, disease duration and smoking (Table 3). No differences were observed between PsA and RA in the frequency of malignancies (adjusted for age and disease duration), osteoporosis (adjusted for glucocorticoids treatment), hypertension, or CAD, stroke and MACE. For MACE, CAD and stroke, adjustments were made for age, sex, smoking, hypertension, hyperlipidaemia, BMI and glucocorticoids use (Table 3). The number of comorbidities was significantly higher in PsA compared with RA patients [median (range); 1 (0–4) *versus* 0 (0–4), $p = 0.003$, respectively].

### *Comparison of epidemiological characteristics and comorbidities between PsA and DM patients*

Patients with PsA were taller than those with DM but had comparable weight and BMI (Table 1). The prevalence of hyperlipidaemia,

**Table 2.** Clinical, laboratory and treatment characteristics of the PsA and RA patients included in the study.

| Characteristic | PsA *n* = 215 | RA *n* = 215 |
|---|---|---|
| **Type of arthritis at diagnosis** | | |
| Oligoarthritis[a], *n* (%) | 76 (35.4) | |
| RA-like, *n* (%) | 122 (56.7) | N/A |
| Axial[b] only, *n* (%) | 14 (6.5) | |
| DIP only, *n* (%) | 3 (1.4) | |
| Tender joints count, mean ± SD[c] | 1.8 ± 2.9 | 1.8 ± 3.4 |
| Swollen joints count, mean ± SD[c] | 1.1 ± 2.3 | 1.4 ± 2.9 |
| **Other features** | | |
| Body surface area[c], mild/moderate/severe[d]; *n* (%) | 174 (80.9)/39 (18.1)/2 (0.9) | |
| Axial involvement[b], *n* (%) | 73 (33.9) | |
| DIP involvement, *n* (%) | 13 (6.0) | |
| Dactylitis, *n* (%) | 42 (19.5) | NA |
| Enthesitis, *n* (%) | 47 (21.9) | |
| Nail involvement, *n* (%) | 68 (31.6) | |
| Eye manifestations, *n* (%) | 6 (2.8) | |
| Bowel manifestations, *n* (%) | 11 (5.1) | |
| **Laboratory features** | | |
| ESR, mm/h; mean (SD)[c] | 22.0 (18.9) | 22.8 (21.4) |
| CRP, mg/l; mean (SD)[c] | 4.1 (3.9) | 11.4 (4.9) |
| Positive RF, *n* (%) | N/A | 111/207 (53.6) |
| Anti-CCPs, *n* (%) | N/A | 80/155 (51.6) |
| **Treatment[e]** | **PsA *n* = 215** | **RA *n* = 215** |
| Methotrexate, *n* (%) | 112 (52.1) | 138 (64.2) |
| Sulfasalazine, *n* (%) | 6 (2.8) | 2 (0.9) |
| Cyclosporine, *n* (%) | 13 (6.0) | 1 (0.4) |
| Leflunomide, *n* (%) | 19 (8.8) | 23 (10.7) |
| Hydroxychloroquine, *n* (%) | 1 (0.5) | 41 (19.1) |
| Anti-TNF, *n* (%) | 39 (18.1) | 55 (25.6) |
| Anti-CD20, *n* (%) | 0 (0.0) | 6 (2.8) |
| Anti-IL6R, *n* (%) | 0 (0.0) | 23 (10.7) |

*(Continued)*

**Table 2.** (Continued)

| Characteristic | PsA *n* = 215 | RA *n* = 215 |
|---|---|---|
| Abatacept, *n* (%) | 2 (0.9) | 12 (5.6) |
| Anti-IL-17, *n* (%) | 15 (7.0) | 0 (0.0) |
| Anti-IL-23/-12, *n* (%) | 10 (4.7) | 0 (0.0) |
| Apremilast, *n* (%) | 13 (6.1) | 0 (0.0) |
| Current use of glucocorticoids[f], *n* (%) | 53 (24.7) | 152 (70.7) |
| Past use of glucocorticoids, *n* (%) | 61 (28.4) | 53 (24.7) |
| Past use of cDMARDs, number; median (IQR) | 1 (1–1) | 1 (1–2) |
| Past use of bDMARDs, number; median (IQR) | 1 (1–2) | 2 (1–3) |

[a]Arthritis in ⩽4 joints.
[b]Defined as presence of radiological findings (sacroiliitis or spondylitis/syndesmophytes) in X-rays or magnetic resonance imaging.
[c]At the time of inclusion to the study.
[d]Mild: <3% body surface area (BSA); moderate: 3–10% BSA; severe: >10% BSA.
[e]Treatment received at the time of inclusion to the study.
[f]Mean ± SD dose was 3.6 ± 1.3 mg/day prednisolone or equivalent.
bDMARD, biologic disease modifying anti-rheumatic drug; CCP, cyclic citrullinated peptide; cDMARD, conventional disease modifying anti-rheumatic drug; CRP, C-reactive protein; DIP, distal interphalangeal; ESR, erythrocyte sedimentation rate; IL, interleukin; IL6R, interleukin 6 receptor; IQR, interquartile range; mm/h, millimetres per hour; *n*, number; PsA, psoriatic arthritis; RA, rheumatoid arthritis; RF, rheumatoid factor; TNF, tumour necrosis factor.

smoking, obesity, stroke, CAD and MACE was comparable between PsA and DM, while hypertension was more frequent in DM patients. Adjustment for age, sex, smoking, hypertension, hyperlipidaemia and BMI did not affect the results for the cardiovascular events (stroke, CAD, MACE) (Table 3). Depression and osteoporosis were more frequent in PsA compared with DM patients. For depression and osteoporosis, adjustments for age, sex, disease duration, smoking and for glucocorticoids treatment, respectively, did not affect the results (Table 3). The number of comorbidities was comparable between PsA and DM patients [median (range); 1 (0–4) for both, $p = 0.562$].

### *Comorbidities within PsA group*

In PsA patients, univariate analyses showed that depression, which was observed in 19.5% of PsA patients, was associated with age, female sex and current smoking (Table 4). These associations remained significant in multivariable analysis after adjustments for factors that displayed statistically significant difference in the univariate analyses or were clinically meaningful, namely age, sex, smoking, disease duration, and skin involvement as assessed by BSA (Table 4).

MACEs were significantly associated with age, male sex, hypertension and hyperlipidaemia. After adjusting for these factors as well as for other relevant co-variates, including smoking and BMI, age, hypertension and male sex remained significant (Table 4). Numerical values for the features examined are presented in Supplemental material Table 1 online.

No differences in patient characteristics or in the prevalence of comorbidities were found between "RA-like" and "oligoarthritis" patterns of PsA (Supplemental Table 2) or in patients who had axial involvement compared with those without (Supplemental Table 3).

## Discussion

Comorbidities such as cardiovascular disease, metabolic syndrome and depression constitute an important aspect of PsA. As captured in the recently published EULAR recommendations, they should be taken into account in the

**Table 3.** Comparison of comorbidities between psoriatic arthritis, rheumatoid arthritis and diabetes mellitus patients.

| Comorbidity | PsA *n* = 215 | RA *n* = 215 | DM n = 215 | PsA *versus* RA | | PsA *versus* DM | |
|---|---|---|---|---|---|---|---|
| | | | | Crude OR (95% CI) | Adjusted OR (95% CI) | Crude OR (95% CI) | Adjusted OR (95% CI) |
| Smoking | 76 (35.4) | 62 (28.8) | 85 (39.5) | 1.35 (0.90–2.03) | | 0.84 (0.57–1.24) | |
| Hyperlipidaemia | 101 (47.0) | 67 (31.2) | 101 (47.0) | 1.96 (1.32–2.90) | – | 1 | – |
| Hypertension | 62 (28.8) | 51 (23.8) | 97 (45.1) | 1.30 (0.84–1.99) | – | 0.49 (0.33–0.74) | – |
| Obesity | 50 (29.4) | 24 (12.8) | 79 (36.7) | 2.83 (1.65–4.86) | | 0.72 (0.47–1.10) | |
| Coronary disease | 10 (4.7) | 10 (4.7) | 16 (7.4) | 1 (0.41–2.45) | 1.05 (0.31–3.57)[a] | 0.61 (0.27–1.37) | 0.66 (0.23–1.91)[a] |
| Stroke | 8 (3.7) | 2 (0.9) | 7 (3.3) | 4.12 (0.86–19.6) | 5.06 (0.80–32.1)[a] | 1.15 (0.41–3.22) | 1.20 (0.35–4.12)[a] |
| MACEs | 12 (5.6) | 12 (5.6) | 22 (10.2) | 1 (0.44–2.28) | 1.20 (0.40–3.63)[a] | 0.52 (0.25–1.08) | 0.42 (0.16–1.10)[a] |
| Osteoporosis | 12 (5.6) | 24 (11.2) | 2 (0.9) | 0.46 (0.21–1.03) | 0.67 (0.28–1.64)[b] | 6.22 (1.33–29.2)[b] | – |
| Depression[c] | 42 (19.5) | 15 (7.0) | 12 (5.6) | 3.24 (1.74–6.04) | 3.02 (1.57–5.81)[d] | 4.11 (2.10–8.05) | 4.85 (2.37–9.93)[d] |
| Malignancy | 12 (5.6) | 7 (3.3) | – | 1.76 (0.68–4.55) | 1.60 (0.60–4.26)[e] | – | – |

[a]Adjusted for age, sex, smoking, hypertension, hyperlipidaemia, body mass index, glucocorticoids use.
[b]Adjusted for glucocorticoids treatment; none of the DM patients was receiving steroids.
[c]6/42 (14.3%) PsA patients were already on antidepressants (mean ± SD time: 16.8 ± 10.9 months) at the time of PsA diagnosis (in five out of six, anti-depressants started after the diagnosis of psoriasis). The respective figure for RA was 2/15 (13.3%).
[d]Adjusted for age, sex, disease duration, smoking.
[e]Adjusted for age, disease duration.
CI, confidence interval; DM, diabetes mellitus; MACE, major adverse cardiovascular event; OR, odds ratio; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

**Table 4.** Associations of depression and major adverse cardiovascular events with epidemiological characteristics, within the psoriatic arthritis group.

| Factors | Depression | | | |
|---|---|---|---|---|
| | Crude OR | | Adjusted OR[a] | |
| | OR (95% CI) | *p*-value | OR (95% CI) | *p*-value |
| Age | 1.029 (1.003–1.056) | **0.029** | 1.03 (0.99–1.06) | **0.05** |
| Sex, female | 2.88 (1.34–6.23) | **0.007** | 3.47 (1.51–7.99) | **0.04** |
| BMI | 1.034 (0.97–1.10) | 0.310 | – | – |
| Obesity | 2.02 (0.94–4.35) | 0.072 | – | – |
| Smoking | 2.74 (1.38–5.46) | **0.004** | 2.78 (1.31–5.88) | **0.008** |
| Disease duration | 1.003 (0.99–1.01) | 0.080 | – | – |
| BSA, mild *versus* moderate/severe[b] | 0.99 (0.42–2.36) | 0.997 | | |
| **Factors** | **MACEs** | | | |
| | **Crude OR** | | **Adjusted OR[c]** | |
| | **OR (95% CI)** | ***p*-value** | **OR (95% CI)** | ***p*-value** |
| Age | 1.10 (1.04–1.17) | **0.001** | 1.08 (1.00–1.17) | **0.042** |
| Sex, female | 0.23 (0.06–0.87) | **0.031** | 0.26 (0.06–1.23) | **0.090** |
| BMI | 1.05 (0.95–1.15) | 0.337 | – | – |
| Obesity | 0.79 (0.20–3.04) | 0.728 | – | – |
| Smoking | 1.33 (0.41–4.34) | 0.638 | – | – |
| Disease duration | 1.002 (0.99–1.01) | 0.846 | | |
| Hypertension | 14.5 (3.0–68.4) | **0.001** | 5.12 (0.96–27.4) | **0.056** |
| Hyperlipidaemia | 6.15 (1.32–28.8) | **0.021** | – | – |
| Glucocorticoids | 1.05 (0.27–4.02) | 0.946 | | |

Statistically significant values are marked with bold numbers.
[a]Adjusted for age, sex, smoking, disease duration, body surface area (BSA) (categorized as mild *versus* moderate/severe).
[b]Mild: <3% BSA, moderate: 3–10% BSA, severe: >10% BSA.
[c]Adjusted for age, sex, smoking, hypertension, hyperlipidaemia, BMI, use of glucocorticoids.
BMI, body mass index; CI, confidence interval; MACE: major adverse cardiovascular event; OR: odds ratio.

management of PsA.[18] In this study, we examined the prevalence of multiple major comorbidities in a well-characterized PsA cohort and we made comparisons with 1:1 age- and sex-matched RA patients and DM patients.

Depression in PsA is an often neglected comorbidity among patients with PsA, with a high impact on patient quality of life.[10,11,19] In our study, depression was present in about 20% of PsA patients, which is comparable to other studies and three recently published meta-analyses in which pooled prevalence of depression in PsA was between 15% and 20%.[5–7,14,16,19–22] It has to be highlighted though that there is a wide variation in the reported prevalence of depression across different studies (ranging from 5% to 51%), possibly reflecting different methodologies and tools used for assessment of depression.[5–7,12,14–16,19–27] Interestingly, we also found a higher prevalence of depression in patients with PsA compared with RA or DM. To the best of our knowledge, only a

couple of studies so far, have directly compared the prevalence of depression between PsA and RA. In concert with our findings, Sinnathurai *et al.*,[15] examining data from 490 PsA and 3609 RA patients, found that the former had greater odds for depression [OR (95% confidence interval): 2.1 (1.7–2.6)]. In contrast, Kotsis *et al.* reported a similar percentage of depression between PsA and RA [21.7% (36.7% in PsA patients with polyarthritis) and 25.1% respectively].[16] This difference might be related to the smaller number of PsA patients ($n = 83$) included in the above study and to the different definitions used for depression. The frequency of depression in RA in our cohort (7.0%) is comparable to that observed in a recent study with the same ethnic background and the same definition for depression.[28] The association between female sex and depression in patients with PsA is in agreement with other studies,[12,29,30] while current smoking has been previously associated with higher anxiety levels but not depression.[20]

Furthermore, we found a similar prevalence of cardiovascular events in PsA compared with RA, in agreement with other investigators.[2,4,14,31,32] The risk factors for cardiovascular events in PsA remain to be further studied, although it seems that the phenomenon is multifactorial.[33] It is also possible that the mechanisms driving the increased cardiovascular risk are slightly different between RA and PsA, with the metabolic component being more pronounced in the latter.[34] Apart from the inflammatory burden of PsA,[35,36] traditional risk factors such as hypertension, hyperlipidaemia, DM and obesity contribute.[2,34,37] In accordance with other studies, we showed that obesity and hyperlipidaemia were more frequent in PsA compared with RA.[38–41] In contrast, PsA patients in our cohort did not differ from individuals with DM in terms of weight and BMI. Additionally, although patients with DM displayed a higher prevalence of hypertension, the two groups had similar prevalence of hyperlipidaemia, stroke, CAD and MACE, highlighting that cardiovascular burden in PsA is comparable to that observed in DM, a chronic metabolic disorder which is considered as cardiovascular-risk equivalent. It should be acknowledged, however, that the numbers of cardiovascular events in our study were relatively small. Therefore, the strength of these findings should be interpreted with caution. Larger studies are needed to corroborate our findings. Furthermore, our study includes both patients with DM type 1 and with type 2. Although there were differences between these two groups, the prevalence of CAD stroke, and MACE after adjustment for age/gender and BMI was comparable between patients with DM type 1 and those with DM type 2 (data not shown).

In addition, no differences were recorded in the prevalence of malignancies between PsA and RA, in agreement with other studies which enrolled a larger number of patients.[42] Of note, no differences were observed in the frequency of comorbidities between the different phenotypes of PsA. Finally, the height difference between PsA and RA or DM in our study warrants further confirmation. The clinical significance of a mean 3 cm height difference, if any, is unclear. One could speculate that this finding could be construed in light of the theory that implicates the biomechanical stress and the "synovio–entheseal" complex in the pathogenesis of PsA.[43] In this context, weight difference observed between PsA and RA in our study might be also relevant. Besides, weight and BMI have been recognized as risk factors for PsA development and are associated with adverse treatment outcomes in these patients.[39]

The strengths of our study include the assessment of a wide range of comorbidities in patients with PsA and the comparison with two age- and sex-matched groups of high comorbidity burden such as patients with RA and, for the first-time, patients with DM after adjustment for multiple potential confounders. In addition, we assessed for the first time whether there were any differences in the prevalence of comorbidities among various PsA phenotypes. We acknowledge that our study has certain limitations. First, this was a cross-sectional study and patients were not screened actively for comorbidities. However, these were longitudinally recorded in patients' medical files as part of their medical follow-up. To be mentioned, patients with a follow-up of less than 6 months were excluded. Second, some of the examined comorbidities were defined by the received treatment (e.g. anti-depressants prescribed by a psychiatrist), which makes difficult the comparison with other studies using questionnaires or self-reported outcomes. Third, due to lack of data we did not include socio-economic factors such as unemployment in our model.[15,20] For the same reason, we did not use a formal comorbidities index such

as Charlson comorbidity index.[44] Instead, we calculated the number of comorbid conditions as has been done in other studies.[45]

In summary, our results support that PsA patients have comparable cardiovascular comorbidities and higher frequency of depression compared with RA and DM. In fact, the risk for depression appears to be 3–5 times higher in PsA *versus* RA and DM, respectively. Rheumatologists should be aware of the high burden of multiple comorbidities in PsA. Assessment of these comorbidities and a strict management of modifiable risk factors outlined in the current and previous studies[2,4,20,46] is warranted to optimize outcomes for these patients.

## Conflict of interest statement

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## Supplemental material

Supplemental material for this article is available online.

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