Cardiovascular comorbidities in psoriatic arthritis: epidemiology and risk factors in two different European populations

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Abstract

Objective

Psoriatic arthritis (PsA) is a chronic inflammatory disease, frequently associated with cardiovascular (CV) comorbidities. Our aim was to compare the prevalence of CV comorbidities between two groups of PsA patients from different European countries: Belgium and Italy.

Methods

This is a cross-sectional analysis of two longitudinal cohorts in which 803 PsA patients were enrolled (463 from Belgium and 340 from Italy). All enrolled patients were ≥18 years old and fulfilled the ClASsification criteria for Psoriatic Arthritis (CASPAR criteria). For each patient, demographics, clinical assessments, smoking habits, the presence of arterial hypertension (AH), obesity (BMI ≥30), type 2 diabetes (T2D), CV diseases (acute myocardial infarction, stroke or transient ischaemic attack), dyslipidaemia (Italy only) and hypercholesterolaemia (Belgium only) were collected.

Results

The most prevalent comorbidities among Italian patients with PsA were: AH (45.1%), dyslipidaemia (38.6%) and obesity (30.8%), and among Belgian patients were: hypercholesterolaemia (30.9%), obesity (27%) and AH (26.4%). Moreover, the prevalence of T2D and CV diseases was respectively 14.2% and 7.1% among Italian patients and 7.6% and 3.5% among Belgian patients. When comparing the two groups, AH, T2D and CV diseases were significantly more prevalent in Italian PsA patients. After controlling for different confounders, Italian patients, regardless of age, sex, smoking habits, PsA duration, other CV comorbidities, therapy, disease activity and function, had a higher risk to be hypertensive (OR 2.00, p=0.007). Instead, the country in which patients lived was not a predictor for the risk of T2D and CV diseases. Obesity prevalence was not different between the two groups. The lipid profile was unfavourable in both populations (even if not comparable between the two groups, due to the different way of collection), as is often the case in PsA.

Conclusion

The prevalence of AH, T2D and CV diseases were higher in Italian patients rather than Belgians. Moreover, among patients with PsA, the risk of AH was higher in the Italian cohort compared to the Belgian cohort. These results suggest that further research is needed to evaluate potential extrinsic factors (geography and sociocultural aspects) that may contribute to CV risk.

Key words

psoriatic arthritis, comorbidities, epidemiology, cardiovascular

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Received on October 10, 2022; accepted in revised form on January 9, 2023.

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Funding: this study was supported by the New Horizon Fellowship Committee. The BEPAS cohort is supported by MSD Belgium.

Competing interests: none declared.

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory joint disease associated with chronic skin psoriasis (PsO). Both PsA and PsO are associated with high prevalence of metabolic and cardiovascular (CV) comorbidities in comparison to the general population (1, 2). Such comorbidities are clinically relevant because they could have a major impact on morbidity and mortality in PsA patients (3, 4). Increasing evidence links the presence of metabolic and CV comorbidities with more difficulties in achieving disease control (5, 6) and with a poorer response to some therapies (7). Moreover, obesity is reported to increase the risk of developing PsA (8) both in the general population (9) and in patients with PsO (10).

Different results were reported about the mortality rates in PsA. In a recent Greek paper on all-cause mortality in systemic rheumatic disease, Bournia *et al*. showed that the survival rates over 5 years in PsA patients (under treatment) are becoming comparable with those of the general population (11), assuming that the newest therapies and a better control of the disease could also improve the survival rate. However, a higher mortality risk was previously described in PsA patients compared to the general population. This particularly applies to young patients between 20 and 39 years old, that have a substantially increased standardised mortality ratio up to 3.36 (12) compared to their healthy counterparts. As heart disease tops all causes of mortality for patients with PsA and PsO, the European Alliance of Associations for Rheumatology (EULAR) recommends that CV diseases and metabolic syndrome could be considered in the daily management of patients with PsA (13). This recommendation aims to control comorbidities, particularly modifiable risk factors.

Some of the metabolic and CV comorbidities could be intrinsic to the disease and may share pathophysiological mechanisms, yet extrinsic factors such as geography and sociocultural aspects can also play an important role. Better knowledge of such extrinsic factors may lead to improved patient profiling and contribute to more comprehensive disease control. Therefore, we compared the prevalence of some CV comorbidities between two geographical and sociocultural different groups of PsA patients, divided in different cohorts from Belgium and Italy.

Materials *and methods*

Study design and patient cohorts

This study is a cross-sectional analysis of 803 patients with PsA, including the Belgian Epidemiological Psoriatic Arthritis Study (BePAS) and 2 prospective longitudinal Italian cohorts. BePAS, a multi-centre longitudinal cohort with patient inclusion from 17 Belgian rheumatology practices, collected clinical, radiographic and demographic data from 463 patients with PsA (14). Patient enrolment took place from December 2012 until December 2014. The Italian cohorts included 340 patients with PsA who were recruited in Naples (227 from University of Campania L. Vanvitelli and S. Giovanni Bosco Hospital, "Naples cohort"- protocol number 11.25-20210015240) and in Campobasso (113 from University of Molise, "Campobasso cohort"- IRB protocol number 0001-017-2021) from January 2018 until December 2019. All patients included in the analyses were ≥18 years old and had a clinical diagnosis of PsA determined by a rheumatologist. All patients fulfilled the ClASsification criteria for Psoriatic Arthritis (CASPAR criteria) (15).

Data collection

A detailed medical history, including age, sex, smoking habits, body mass index (BMI, kg/m^2) and details of the physical examination were recorded for each patient. PsA-specific assessments at enrollment included: disease duration, number of tender (on 68 joints) and swollen (on 66 joints) joints and C-reactive protein (CRP) blood levels (mg/dl). Enthesitis was assessed using the Leeds Enthesitis Index (LEI) (16) and dactylitis recorded as present, absent, or history of it. Skin assessment was recorded as presence of PsO at the time of the visit (yes/no) and the extension was quantified using Body Surface Area (BSA) as assessed by the rheumatologist. PsA disease activity was evaluated by the

Disease Activity for Psoriatic Arthritis (DAPSA) score (17) and the Minimal Disease Activity (MDA) for PsA (18). Extra-articular manifestations such as gastrointestinal involvement (Crohn's disease and ulcerative colitis) or ocular involvement (past or present uveitis) were also recorded. Patient Global Assessment (PtGA) on visual analogue scale (VAS) (1–10 cm), pain assessment (VAS, 1–10 cm), Physician's Global Assessment (PhGA) of disease activity (VAS, 1–10 cm), and Health Assessment Questionnaire-Disability Index (HAQ-DI) (0-3) were also collected. Information on current and former drug treatment of PsA [non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), biological and targeted synthetic DMARDs] was collected.

In addition, the following CV comorbidities were collected: (1) arterial hypertension (AH), defined by the use of antihypertensive drugs or diagnosis by a medical specialist; (2) overweight and obesity, respectively defined as a BMI ≥25 and <30 kg/m^2, and a BMI ≥30 kg/m^2; (3) type 2 diabetes (T2D), defined by the use of anti-diabetic drugs or insulin intake, or based on a diagnosis by a medical specialist; (4) acute myocardial infarction (AMI), defined as acute ischaemic heart disease with a diagnosis made by a medical specialist; (5) stroke or transient ischaemic attack (TIA), defined as permanent or transient cerebrovascular disorder (ischaemic or haemorrhagic) diagnosed by a medical specialist; (6) hypercholesterolaemia (recorded only in Belgian patients), defined as blood total cholesterol ≥200 mg/dL, or Low Density Lipoprotein Cholesterol ≥160 mg/dL, or High Density Lipoprotein Cholesterol <40 mg/dL for men and <50 mg/dL for women; (7) dyslipidaemia (recorded only in Italian patients), defined as hypercholesterolaemia, as defined above, and/or a blood triglycerides levels >200 mg/dL. Due to the different way, in which the lipid profile data were collected between the two groups (Belgian and Italian), these results are only reported to show their prevalence, without using them for other analysis. All blood test

Table I. Comparison of demographic characteristics, smoking habits, physical characteristics, PsA assessment, therapy, CV risk factors and diseases, divided by country.

	Italian PsA patients n=340	Belgian PsA patients n=463	*p*-value
Sex (M), n. (%)	182 (53.5)	264 (57)	0.32
Age, mean (SD)	55.4 (±12.3)	52.7 (±12.3)	0.002
Smokers, n. (%)			
Never smoke	168/322 (52.2)	208/457 (45.5)	0.03
Current smoke	77/322 (23.9)	101/457 (22.1)	
Past smoke	77/322 (23.9)	148/457 (32.4)	
Weight (kg), median (IQR)	78 (66-89)	80 (67-90)	0.07
Height (m), median (IQR)	1.68 (1.61-1.75)	1.70 (1.64-1.77)	<0.001
BMI (kg/h^2), median (IQR)	27 (23-31)	27 (23-30)	0.62
PsA Assessment			
Disease duration (years), mean (SD)	11.2 (8.42)	8.5 (9.25)	<0.001
Tender joints/68, median (IQR)	2 (0-4.5)	1 (0-5)	0.57
Swollen joints/66, median (IQR)	0 (0-0)	0 (0-2)	<0.001
CRP (mg/dl), median (IQR)	0.2 (0.1-0.5)	0.2 (0.1-0.7)	0.73
LEI, median (IQR)	0 (0-0)	0 (0-0)	0.95
Dactylitis, n. (%)			
Never	246/328 (75)	241/454 (53.1)	<0.001
Past	62/328 (18.9)	155/454 (34.1)	
Present	20/328 (6.1)	58/454 (12.8)	
Psoriasis, n. (%)			
No	188/326 (57.7)	154 (33.3)	<0.001
Yes	138/326 (42.3)	309 (66.7)	
BSA, median (IQR)	0 (0-2)	1 (0-3)	<0.001
PtGA, median (IQR)	3 (1-5)	3.4 (1.7-5.1)	0.13
Pain on VAS, median (IQR)	3 (1-5)	3.5 (1-6)	0.06
PhGA, median (IQR)	0.5 (0-2)	1.9 (0.7-3.5)	<0.001
Crohn disease, n. (%)	4/337 (1.2)	4/460 (0.9)	0.66
Ulcerative colitis, n. (%)	0/337 (0)	3/460 (0.7)	0.08
Uveitis Present or Past, n. (%)	7/337 (2)	24/455 (5.3)	0.001
DAPSA, median (IQR)	8.4 (4-15.3)	10.16 (5.15-18.85)	0.01
MDA 5/7 n. (%)	153/305 (50.2)	139/330 (42.1)	0.042
MDA 7/7, n. (%)	58/305 (19.0)	45/330 (13.6)	0.066
HAQ-DI, median (IQR)	0.5 (0.125-1.125)	0.625 (0.125-1.125)	0.75
Therapy			
NSAIDs, n. (%)	58/335 (17.3)	216/455 (47.5)	<0.001
Corticosteroids, n. (%)	24/336 (7.1)	146/463 (31.5)	<0.001
Oral	20/336 (5.9)	56/463 (12.1)	0.003
Intra-articular	0/336 (0)	21/463 (4.5)	<0.001
Topical	4/336 (1.2)	71/463 (15.3)	<0.001
csDMARDs, n. (%)	157/336 (46.7)	421/462 (91.1)	<0.001
Methotrexate, n. (%)	109/336 (32.4)	386/462 (83.5)	<0.001
Anti-TNF-α, n. (%)	175/336 (52.1)	228/463 (49.2)	0.428
Combo therapy csDMARDs + anti TNF-α, n. (%)	83/336 (24.7)	218/462 (47.2)	<0.001
Anti-IL 17	54/336 (16.1)	-	
Anti-IL-12/23	36/336 (10.7)	-	
Apremilast	14/336 (4.2)	-	
CV risk factors and CV diseases			
Arterial hypertension, n. (%)	152/337 (45.1)	121/459 (26.4)	<0.001
Obesity (BMI ≥30), n. (%)	96/312 (30.8)	117/433 (27)	0.264
Type 2 diabetes, n. (%)	48/337 (14.2)	35/460 (7.6)	0.002
Cardiovascular disease	24/337 (7.1)	16/460 (3.5)	0.030
- Acute myocardial infarction, n. (%)	16/337 (4.7)	8/460 (1.7)	0.014
- Stroke or transient ischaemic attack, n. (%)	8/337 (2.4)	8/460 (1.7)	0.528
Hypercholesterolaemia n. (%)	-	140/453 (30.9)	-
Dyslipidaemia n. (%)	130/337 (38.6)	-	-

CV: cardiovascular; Sex (M): male sex; SD: standard deviation; n. : number; %: percentage; kg: kilograms, m: meters; kg/h^2: kilograms/height^2; IQR: interquartile range; CRP (mg/dl): C-reactive protein (milligrams/deciliters); LEI: Leeds Enthesitis Index; BSA: body surface area; PtGA: Patient Global Assessment; VAS: Visual Analogue Scale; DAPSA: Disease Activity for PSoriatic Arthritis; MDA: Minimal Disease Activity; HAQ-DI: Health Assessment Questionnaire-Disability Index; NSAIDs: non-steroidal anti-inflammatory drugs; csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; TNF-α: anti-tumour necrosis factor alpha; IL: interleukin.

data were obtained no more than three months before the visit. AMI and stroke or TIA were separately described when considering prevalence, but they were each considered as a unique category labelled "CV diseases" for all other analyses.

Statistical analysis

Statistical analysis was performed using SPSS software (v. 27). All demographic and clinical characteristics were summarised using descriptive statistics. Normally distributed variables were reported by mean ± standard deviation (SD), and non-normally distributed variables by median and inter-quartile range (IQR). Normal distribution of variables was assessed graphically and supported by the Kolmogorov-Smirnov Test. Categorical data are shown as number (n) and the percentage (%). Comparison of the Belgian cohort with the Italian cohort of PsA patients was analyses using the χ^2 test for independence of the categorical variables, and the Student t-test or Mann-Whitney U-test (with confidence interval (CI) 95% as effect size measure) for the continuous variables, according to the data distribution.

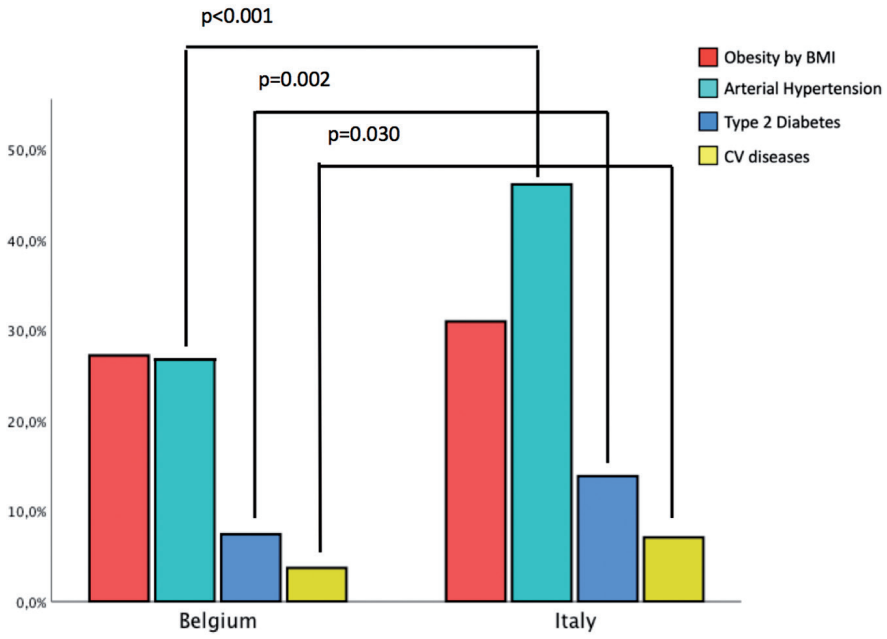

Fig. 1. Distribution between Belgium and Italy of obesity, arterial hypertension, type 2 diabetes and CV diseases (acute myocardial infarction and/or transient ischaemic attack/stroke), among the PsA studied population.
BMI: Body Mass Index; CV: cardiovascular.

Multivariate and univariate regression models were applied to evaluate the predictive factors of AH, obesity, T2D and CV diseases, focusing on the possible association between the country in which patients lived (Belgium *vs.* Italy) and these comorbidities. Multicollinearity between independent factors was evaluated by the Pearson correlation coefficient, by tolerance and by

Table II. Univariate and multivariate logistic regression analyses: association between age, sex, disease duration, country in which patients live, smoking habits and therapy with arterial hypertension, obesity, type 2 diabetes, CV diseases.
All the independent variables were used in the multivariate analysis, in each model, but only the variables with a significant association are shown.

	Univariate			Multivariate		
Dependent variable: Arterial hypertension						
	OR	CI (95%)	*p*-value	OR	CI (95%)	*p*-value
Age (years)	**1.08**	**1.07-1.10**	**<0.001**	**1.07**	**1.05-1.10**	**<0.001**
Sex (F)	0.77	0.57-1.05	0.96			
Disease duration (years)	**1.04**	**1.02-1.05**	**<0.001**			
Country (Italy)	**2.29**	**1.70-3.09**	**<0.001**	**2.00**	**1.21-3.32**	**0.007**
Smoke						
Never	-	-	0.079			
Past	**1.45**	**1.03-2.05**	**0.034**			
Current	1.01	0.69-1.48	0.966			
NSAIDs intake	**0.46**	**0.33-0.65**	**<0.001**			
Any steroids	0.84	0.58-1.23	0.381			
csDMARDs intake	**0.67**	**0.49-0.93**	**0.016**			
Anti-TNF-α intake	1.27	0.95-1.70	0.111			
BMI						
Normal-weight	-	-	<0.001	**- 2.12**	**- 1.20-3.53**	**<0.001**
Overweight	**2.55**	**1.70-3.83**	**<0.001**	**5.18**	**2.96-9.07**	**0.008**
Obesity	**5.39**	**3.52-8.24**	**<0.001**			**<0.001**
Type 2 diabetes	**4.46**	**2.75-7.23**	**<0.001**	**2.49**	**1.31-4.76**	**0.005**
CV diseases	**6.09**	**2.92-12.71**	**<0.001**	**3.63**	**1.33-9.92**	**0.012**
MDA 5/7	1.24	0.89-1.73	0.196			
HAQ-DI	**1.40**	**1.11-1.76**	**0.004**			
Details of the model				χ^2 (16, n=577) =188.739, p<0.001, R^2 = 0.279, PAC = 75.4 %		

	Univariate			Multivariate		
Dependent variable: Obesity						
	OR	CI (95%)	*p*-value	OR	CI (95%)	*p*-value
Age (years)	**1.02**	**1.01-1.03**	**0.002**			
Sex (F)	1.07	0.78-1.48	0.648			
Disease duration (years)	1.01	0.99-1.03	0.240			
Country (Italy)	1.20	0.87-1.65	0.264			
Smoke						
Never	-	- 0.75-1.58	0.586			
Past	1.09	0.57-1.30	0.646			
Current	0.86		0.475			
NSAIDs intake	0.79	0.56-1.12	0.189			
Any steroids	0.85	0.57-1.28	0.445			
csDMARDs intake	0.86	0.60-1.23	0.413			
Anti-TNF-α intake	1.09	0.79-1.50	0.587			
Arterial hypertension	**3.36**	**2.41-4.69**	**<0.001**	**3.62**	**2.32-5.63**	**<0.001**
Type 2 diabetes	**1.76**	**1.07-2.88**	**0.024**			
CV diseases	1.30	0.65-2.60	0.446			
MDA 5/7	**0.61**	**0.42-0.87**	**0.006**			
HAQ-DI	**1.65**	**1.29-2.10**	**<0.001**			
Details of the model				χ^2 (16, n=577) = 56.180, p<0.001, R^2 = 0 .093, PAC = 72.6 %		
Dependent variable: Type 2 diabetes						
	OR	CI (95%)	*p*-value	OR	CI (95%)	*p*-value
Age (years)	**1.06**	**1.04-1.07**	**<0.001**	**1.04**	**1.01-1.07**	**0.003**
Sex (F)	**0.60**	**0.37-0.97**	**0.036**			
Disease duration (years)	**1.05**	**1.02-1.07**	**<0.001**			
Country (Italy)	**2.02**	**1.28-3.20**	**0.003**			
Smoke						
Never	- 1.15	- 0.68-1.95	0.857			
Past	1.00	0.55-1.81	0.600			
Current			0.989			
NSAIDs intake	**0.32**	**0.18-0.60**	**<0.001**			
Any steroids	0.61	0.31-1.17	0.138			
csDMARDs intake	0.66	0.39-1.02	0.064			
Anti-TNF-α intake	1.12	0.71-1.77	0.612			
BMI						
Normal-weight	-	-	0.001	**- 3.31**	**- 1.34-8.19**	**0.033**
Overweight	**3.20**	**1.55-6.62**	**0.002**	**2.76**	**1.08-7.06**	**0.009**
Obesity	**3.85**	**1.83-8.07**	**<0.001**			**0.033**
Arterial hypertension	**4.46**	**2.75-7.22**	**<0.001**	**2.75**	**1.43-5.22**	**0.002**
CV diseases	**3.74**	**1.79-7.83**	**<0.001**			
MDA 5/7	1.06	0.64-1.74	0.823			
HAQ-DI	**1.68**	**1.21-2.34**	**0.002**			
Details of the model				χ^2 (16, n=577) = 71.196, p<0.001, R^2 = 0.116, PAC = 89.3 %		
Dependent variable: CV diseases						
	OR	CI (95%)	*p*-value	OR	CI (95%)	*p*-value
Age (years)	**1.07**	**1.04-1.10**	**<0.001**			
Sex (F)	0.76	0.39-1.48	0.425			
Disease duration (years)	1.02	0.99-1.05	0.178			
Country (Italy)	**2.03**	**1.05-3.91**	**0.034**			
Smoke						
Never	-	- 0.94-4.10	0.200			
Past	1.96	0.59-3.25	0.073			
Current	1.38		0.460			
NSAIDs intake	0.55	0.26-1.18	0.128			
Any steroids	0.46	0.16-1.32	0.148			
csDMARDs intake	**0.45**	**0.23-0.87**	**0.018**			
Anti-TNF-α intake	1.04	0.54-1.98	0.908			
BMI						
Normal-weight	-	- 1.38-10.0	0.034			
Overweight	3.72	2.85-0.99-8.25	**0.009**			
Obesity	2.85		0.052			
Arterial hypertension	**6.09**	**2.92-12.71**	**<0.001**	**3.46**	**1.27-9.45**	**0.015**
Type 2 diabetes	**3.74**	**1.78-7.83**	**<0.001**			
MDA 5/7	0.90	0.43-1.88	0.774			
HAQ-DI	2.03	1.28-3.21	0.002	**2.77**	**1.35-5.69**	**0.005**
Details of the model				χ^2 (16, n=577) = 45.84, p<0.001 R^2 = 0.076; PAC = 95.3 %		

OR: odds ratio; CI 95%: confidence interval 95%; Sex (F): female sex; NSAIDs: non-steroidal anti-inflammatory drugs; csDMARDS: conventional synthetic disease-modified anti-rheumatic drugs; TNF-α: tumour necrosis factor alpha, BMI: Body Mass Index; MDA: Minimal Disease Activity; HAQ-DI: Health Assessment Questionnaire-Disability Index; PAC: percentage accuracy in classification.

VIF: factors with a Pearson correlation coefficient more than 0.7, or tolerance <0.1 or VIF ≥10, were not included in the multivariate model. Goodness of fit of every regression model was estimated using the Omnibus Tests of Model Coefficients and Cox & Snell R^2. The Percentage Accuracy in Classification (PAC) was used to indicate how well the model was able to predict the correct category for each case. Odds ratios (OR) were used as a measure of association and a statistical significance was defined as a 2-tailed *p*-value ≥0.05.

Results

Demographic and disease characteristics of the PsA patients in the different cohorts

In total, 803 patients were included in the study: 463 Belgian (BE) and 340 Italian (IT) patients with PsA. Italian patients tended to be older (mean difference: 2.7 years, CI 95% (-4,40, -0.95)) and have a longer disease duration (years) than Belgian patients (mean difference: 2.7 years, CI 95% (-3.97, -1.46)).

Sex distribution and BMI were not different between the countries (Table I).

Clinically, Belgian patients tended to have more swollen joints, a higher prevalence of PsO at the time of visit, more dactylitis and more present or history of uveitis (Table I). Number of tender joints, PtGA, patients' pain, LEI, CRP and gastrointestinal involvement were not different between the two groups. The median DAPSA was in the low disease activity range (<14) for both groups, but Italian patients tended to have lower disease activity and achieved the MDA 5/7 status more easily. The use of NSAIDs, corticosteroids, csDMARDs and methotrexate was higher in the Belgian cohort, but there was no difference in anti-tumour necrosis factor-alpha (anti-TNFα) use (Table I). Other biological and targeted DMARDs were uniquely used in the Italian patients as these drugs were not yet available when the data for the Belgian patients were collected.

CV comorbidities and geographical differences

AH was more frequent in the Italian cohort (Table I and Fig. 1). Moreover, as shown in the multivariate analysis, there was an association between AH and the country in which patients lived: Italian patients seem to have an increased risk for AH compared to Belgian patients. This result was found both in the univariate and in the multivariate analysis (when adjusted for other confounding factors, including NSAIDs, corticosteroids, csDMARDs and bDMARDs) (Table II). Moreover, as expected, age was an independent factor associated with AH. Other comorbidities, including overweight, obesity, T2D and CV diseases, were also independently associated with AH; the combination of these factors explains almost 28% of the risk of arterial hypertension in this cohort of patients with a moderate accuracy (PAC 75.4%).

Prevalence of obesity was similar in both cohorts (Table I and Fig. 1). In the univariate and multivariate analysis obesity was associated with AH (Table II). Moreover, the achievement of MDA 5/7 was negatively associated with obesity, although this association was not observed in the multivariate model.

T2D was more prevalent in the Italian cohort than the Belgian cohort (Table I and Fig. 1); however, in the multivariate analysis, after adjusting for other confounding factors, such as obesity, CV diseases, AH, the use of NSAIDs, corticosteroids, csDMARDs and bDMARDs there was not a statistically significant association between T2D and the country in which patients lived (Table II). Moreover, the factors that showed an association with T2D, independently of the country where patients lived were: age, BMI and AH. The combination of these factors explains about 11% of the risk of T2D in this cohort of patients, with high accuracy (PAC 89%).

AMI was also more prevalent in Italian patients than in Belgian patients with PsA (Table I). When considering "CV diseases" as a unique category, including AMI and stroke or TIA, Italian patients also had a higher prevalence. Moreover, in the multivariate analysis, CV diseases were associated with AH and worse function via the HAQ-DI, but no association was found with DAPSA and MDA (Table II). After adjusting for confounding factors (including NSAIDs, corticosteroids, csDMARDs and bDMARDs), there was no association between the country in which patients lived and CV diseases. Cardiovascular diseases were independent of sex in both PsA cohorts (Table II).

Discussion

In addition to classical musculoskeletal and skin manifestations, people with PsA also present with high numbers of CV and metabolic comorbidities (19), a factor that could contribute to the increasing morbidity and mortality, even if in a recent population-based study the survival rates over 5 years of the PsA patients were comparable with the general population (11)

We studied relationships between comorbidities and proposed risk factors in PsA cohorts from two different European countries, thus allowing us to also document differences between the two populations. For PsO and PsA, epidemiological differences between different countries and also within the same geographical area were reported (20). We found that, AH, T2D CV diseases (AMI, stroke, TIA) were more prevalent amongst patients with PsA located in Italy compared to Belgium. When these factors were studied in a multivariate regression model the association between arterial hypertension and living in Italy (rather than Belgium) was confirmed. One of the risk factors for AH is being overweight. In the present study prevalence of obesity and mean BMI were similar between Italian and Belgian patients and these do not explain the observed difference in prevalence of AH.

The high prevalence of obesity in both cohorts remains a concern and is slightly higher than the mean European prevalence (21). Obesity is recognised as an important risk factor for developing PsO and PsA (22, 23) and in a recent mendelian-randomisation study (24), it also seems to be responsible for the transition from skin to joint disease. Beyond this, obesity worsens PsA disease activity and it reduces the treatment response to TNF inhibitors (5, 24). On the other hand, weight loss

may be associated with positive effects on all disease domains (25). Unlike some other CV comorbidities, obesity is a modifiable risk factor, therefore it is potentially a treatment target within the PsA population. Moreover, in our PsA group, independent of country, obesity was associated with AH and T2D. All of this implies that BMI should be assessed as a part of the management of PsA.

Beyond CV comorbidities, Belgian patients with PsA tended to have more swollen joints, more dactylitis, more severe psoriasis at the time of the visit, more past or present uveitis, reflecting a higher disease activity but they were younger and had a shorter disease duration than the Italian patients. Belgian patients tended to have higher disease activity (DAPSA) and less remission (MDA). These data suggest that there might be country-specific differences in disease impact, which is in line with data from ASAS-PerSpA study (26).

Yet, other confounders or cohort-specific selection bias may also explain the observed differences, such as level of physical activity or specific diet.

This study has several limitations and consequently the country related differences must be interpreted with caution. Data for the Belgian cohort were collected in an earlier time window during which the availability of biologics was more limited than it is today. This may explain why Belgian patients tended to use more NSAIDs, corticosteroids and csDMARDs, and less biological therapies distinct from anti-TNF. Moreover, the data on the lipid profile of these two populations are not comparable, because they were collected as hypercholesterolaemia for Belgian patients and as dyslipidaemia for Italian patients.

In conclusion, this study suggests that geographical differences may influence the PsA clinical profile, in particular the presence of CV comorbidities. Different geographic-related and cultural factors such as genetic background, lifestyle, eating habits may further explain the observed differences. Further research is needed to evaluate potential extrinsic factors (geography and sociocultural aspects) that may contribute to CV risk.

Key messages

- Arterial hypertension is more prevalent in patients with PsA from Italy compared with patients from Belgium. Moreover, the risk to be hypertensive is 2 times higher for Italian patients rather than Belgians, independently from other confounding factors.
- Prevalence of T2D and CV diseases is higher in Italian patients, however, when these data were adjusted for other confounding factors the probability to be affected by T2D and CV diseases was not associated with the country in which patients lived.
- The prevalence of obesity was similar in the two groups.
- Belgian patients with PsA showed higher disease activity (DAPSA) and higher csDMARD, corticoidsteroid and NSAIDs utilisation.

Acknowledgements

The authors wish to thank Maura Raimondi and Luca Riccio from the Dipartimento di Medicina di Precisione, Sezione di Rheumatologia, Università degli Studi della Campania L. Vanvitelli, Naples, Italy, and Hermine Leroi from MSD Belgium, for their valuable contribution to this work.

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