Disease Activity and Increased Risk of Cardiovascular Death among Patients with Psoriatic Arthritis

Kristina Juneblad, Solbritt Rantapää-Dahlqvist, and Gerd-Marie Alenius

ABSTRACT. ***Objective.*** Recent studies indicate increased cardiovascular (CV) morbidity and mortality in patients with psoriatic arthritis (PsA), but results are inconsistent. This prompted our investigation of the mortality rate, cause of death, and incidence of acute CV events in patients from northern Sweden with PsA.

Methods. Patients with established PsA (464) were included. To calculate standardized mortality ratio (SMR) and standardized incidence ratio (SIR) for CV events, data were extracted from the National Causes of Death Register and the National Inpatient Care Register in Sweden, and compared with the general population. The study period was 1995–2011. To study the effect of inflammatory activity, a composite disease activity index (DAI) was used.

Results. The SMR (95% CI) for overall mortality and diseases of the circulatory system (International Classification of Diseases, 10th edition; I00-I99) was 1.22 (0.89–1.63) and 1.64 (1.02–2.52), respectively. In regression analysis, DAI was significantly associated with death (OR 1.99, 95% CI 1.41–2.80) when adjusted for age and sex ($p < 0.001$), and remained significant after stratifying patients into the 2 major causes of death: diseases of the circulatory system and malignant neoplasms. Peripheral and axial disease was associated with death (OR 4.02, 95% CI 1.84–8.84, $p < 0.001$) compared with peripheral disease only. The SIR (95% CI) for a CV event (myocardial infarction or stroke) was 0.597 (0.40–0.86); this association was only significant in men.

Conclusion. Patients with PsA had a small but significant increase in SMR for death due to diseases of the circulatory system compared with the general population. Among patients, death was associated with DAI, as well as axial involvement in combination with peripheral disease, indicating more aggressive disease phenotypes. (First Release October 1 2016; J Rheumatol 2016;43:2155–61; doi:10.3899/jrheum.160070)

Key Indexing Terms:
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An increased risk of comorbidity, particularly cardiovascular disease (CVD), has been demonstrated in patients having different rheumatic diseases, e.g., systemic lupus erythematosus (SLE)[1] and rheumatoid arthritis (RA)[2,3,4]. Corresponding data for patients with psoriatic arthritis (PsA) are more limited, but studies have indicated increased comorbidity and involvement of organ systems other than the skin and joints, e.g., renal involvement[5]. Several studies indicate that patients with psoriasis (PsO) and PsA have increased morbidity and mortality due to CVD[6,7,8,9,10,11]. In a recent study of patients with PsA, CV events were associated with traditional risk factors [hypertension (HTN), diabetes] and disease activity [erythrocyte sedimentation rate (ESR) in women; dactylitis][12]. Other studies indicate an increased level of subclinical atherosclerosis in patients with PsA compared with control subjects[13] and in patients with cutaneous PsO without arthritis[14]. Also, an increased arterial stiffness in patients with PsA, compared with control subjects, has been reported[15,16], with increased arterial stiffness associated with cumulative inflammatory burden[16]. In a recent metaanalysis, patients with PsA showed an increased carotid intima-media thickness, a higher frequency of carotid plaques, and a lower flow-mediated dilatation compared with controls[17].

An overall increased early mortality in patients with PsA has been shown, particularly in those patients with signs of a severe disease, high ESR values, and early signs of radiological changes[8,18,19,20]; however, these findings have not been confirmed in other studies[18,21,22,23].

The inconsistent results from different studies prompted a comparison of the mortality rate, cause of death, and incidence of acute CV events (CVE) in a cohort of patients

From the Department of Public Health and Clinical Medicine, and the Department of Rheumatology, University Hospital, Umeå, Sweden.

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K. Juneblad, MD, Department of Public Health and Clinical Medicine/Rheumatology, University Hospital; S. Rantapää-Dahlqvist, MD, PhD, professor, Department of Public Health and Clinical Medicine/Rheumatology, University Hospital; G.M. Alenius, MD, PhD, Department of Public Health and Clinical Medicine/Rheumatology, University Hospital.

Address correspondence to Dr. K. Juneblad, Department of Rheumatology, University Hospital, SE-901 85 Umeå, Sweden. E-mail: kristina.juneblad@vll.se

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in northern Sweden with established PsA diagnosed and investigated by experienced rheumatologists with data on the general population from the same region.

MATERIALS AND METHODS

A cohort of 464 patients with PsA (234 men, 230 women) from the county of Västerbotten, Sweden, was included in the study. All of them had been examined by a rheumatologist and diagnosed with PsA at least once between January 1, 1995, and December 31, 2005. The inclusion date was either the first visit between January 1, 1995, and December 31, 2005, or for subjects already attending the clinic, January 1, 1995. For the analysis of mortality, the followup period was until December 31, 2011, or when the patient died, while for the study of CVE, the followup period extended until December 31, 2010, or until a myocardial infarction (MI) or stroke. For 182 patients, followup at our clinic was discontinued before the end of study, either because the patient moved out of the county (n = 14) or because of clinical improvement, leaving no need for specialist care (n = 168). For individuals who were lost to followup because they left the county, the principle of last observation carried forward was applied. For individuals remaining in the county, medical data were still available in patients' medical records.

Patients' records were carefully evaluated to verify diagnosis and record disease activity and clinical progress before, during, and at the end of the study, as well as use of antirheumatic drugs. Destructive/deforming disease was defined as either typical, radiological changes, e.g., erosions, juxta-articular new bone formation, and/or irreversible deformations (e.g., ankylosis, subluxations, and/or loss of function or reduced mobility) on clinical examination. Demographic data for the patients at the end of the study or at death are presented in Table 1.

To investigate mortality and cause of death, data were extracted from the National Causes of Death Register in Sweden until the end of 2011 and compared with the general population of Västerbotten County, Sweden, and subgrouped according to diagnostic groups defined in the same register (Diseases of the circulatory system, I00-I99; Malignant neoplasms, C00-C97; and Diseases of the respiratory system, J00-J99). Only the date of death was recoverable from the register for deaths occurring during 2011, consequently details of the cause of death were extracted from the individual patients' medical records. The standardized mortality rate ratio (SMR) was also analyzed.

Table 1. Demographic data of patients with PsA. Data are n (%) unless otherwise indicated.

Age, yrs*, mean (± SD)	59.5 (13.5)
Duration PsA, yrs*, mean (± SD)	20.4 (11.1)
Duration PsO, yrs*, mean (± SD)	31.1 (16.4)
BMI*, mean (± SD)	27.7 (5.1)
Male	234 (50.4)
Destructive/deforming disease	233 (50.7)
bDMARD (ever)	57 (12.4)
sDMARD (ever)	312 (67.2)
Fulfilling CASPAR criteria	418 (90.3)
Exclusive DIP joint disease according to Moll and Wright**	3 (0.6)
Mono/oligoarthritis according to Moll and Wright**	214 (46.1)
Polyarthritis, including arthritis mutilans (n = 8), according to Moll and Wright**	197 (42.5)
Axial disease without peripheral joint involvement	33 (7.1)
Axial and peripheral joint involvement	46 (9.9)
Smoker (ever)	248 (55.0)
Smoker (current) *	69 (15.3)
Hypertension*	205 (44.5)
Hyperlipidemia*	71 (15.4)
Diabetes*	58 (12.6)

* At the end of the study (2011) or death. ** 1973 Moll and Wright criteria for PsA. PsA: psoriatic arthritis; PsO: psoriasis; BMI: body mass index; DAI: disease activity index; DMARD: disease-modifying antirheumatic drug; bDMARD: biological DMARD; sDMARD: synthetic DMARD; NSAID: nonsteroidal antiinflammatory drug; CASPAR: ClASsification for Psoriatic ARthritis (criteria); DIP: distal interphalangeal.

To investigate the incidence of a CVE, defined as stroke, MI, and/or unstable angina pectoris, according to the International Classification of Diseases (ICD), 9th edition, (acute MI = 410, 410A-X, stroke = 431,434,434A-X,436, unstable angina pectoris = 411A,B,X) and 10th edition (acute MI = 121,122, stroke = I61,I63,I64, unstable angina pectoris = I20.0) Revision Codes, data were extracted from the National Inpatient Care Register and compared with the general population of Västerbotten County, Sweden. At the time of the study, data from the National Inpatient Care Register were available from 1995 until December 31, 2010. Only a diagnosis of an MI and/or stroke was used for calculating the standardized incidence ratio (SIR), because a less specific definition of angina pectoris was used for the National Inpatient Care Register in its statistics for the general population. Therefore, patients with an unstable angina pectoris event were used only for comparison in patients with PsA with or without an event. The diagnostic codes for PsA patients were validated by studying patients' records.

Traditional CV risk factors, i.e., HTN, hyperlipidemia, diabetes, smoking, and body mass index (BMI) were recorded to evaluate any relationship with CVE or death. In addition, the study recorded the presence of PsA-specific risk factors, i.e., disease activity over time, joint destruction, disease duration, disease expression, use of nonsteroidal antiinflammatory drugs (NSAID), oral corticosteroids, synthetic disease-modifying antirheumatic drugs (sDMARD), and biological DMARD (bDMARD). The diagnoses of HTN, hyperlipidemia, and diabetes were based on current medication at the end of the study or after the subject's death.

Because data in the medical records did not allow the use of any of the standardized activity indices for PsA and/or spondyloarthritis (SpA), a disease activity index (DAI), previously used for patients with RA, was used to study the effect of inflammatory activity and risk of CVE or death[24]. The DAI was calculated as the mean of a composite index in which the number of swollen joints, ESR value, and a clinician's estimation of disease activity were extracted from the patients' records every 2 years during the course of the PsA disease, with the modification of lowering the ESR from 30 to 20.

The local ethics committee at Umeå University, Sweden, approved the study (Dnr 2010-357-31M), and all patients gave written informed consent.

Statistics. All statistical calculations were performed using PASW Statistics 18.0 program (SPSS). For calculation of SIR and SMR, the expected risk of death/CVE in the general population in Västerbotten County was used, stratified for age groups. For comparison of continuous data, unpaired t-test and regression analysis were used, and to study proportions between subgroups, the chi-squared test was used. P values ≤ 0.05 were considered significant.

RESULTS

Mortality and cause of death. Of the 464 patients with PsA, 44 (25 men, 19 women) died during the study period. The SMR (95% CI) for overall mortality was 1.22 (0.89–1.63). The dominant causes of death were diseases of the circulatory system (n = 21), followed by malignant neoplasms (n = 14). One patient died from respiratory disease and 8 from various causes. There were no sex differences (data not shown). The SMR (95% CI) for death due to disease(s) of the circulatory system (ICD-10; I00–I99) was 1.64 (1.02–2.52; Table 2).

The mean age (± SD) at death was 70.4 years (± 13.7; Table 3). The patients who died were older (70.4 ± 13.7 vs 58.4 ± 13.0, p < 0.001) and had a longer duration of skin disease (37.9 ± 19.3 vs 29.9 ± 14.9, p = 0.002), but not a

Table 2. SMR of patients with PsA compared with the general population.

Cause of Death	Women, n	Exp, n	SMR (95% CI)	Men, n	Exp, n	SMR (95% CI)	Women and Men, n	Exp, n	SMR (95% CI)
Circulatory	9	4.6	1.95 (0.91–3.75)	12	8.2	1.46 (0.75–2.55)	21	12.8	1.64 (1.02–2.52)
Neoplasms	6	6.0	1.00 (0.37–2.19)	8	6.4	1.24 (0.54–2.45)	14	12.4	1.13 (0.62–1.89)
All	19	14.7	1.29 (0.78–2.02)	25	21.4	1.17 (0.75–1.72)	44	36.1	1.22 (0.89–1.63)

SMR: standardized mortality ratio; PsA: psoriatic arthritis; Exp: expected deaths according to statistics of the general population.

Table 3. Comparison of disease characteristics at the end of the study between patients who died and those who were alive at the end of the study. Data are n (%) unless otherwise indicated.

Characteristics	Alive	Dead	p	OR (95% CI)
Age, yrs, ± SD (n)	58.4 ± 13.0 (420)	70.4 ± 13.7 (44)	< 0.001	1.08 (1.05–1.11)
Duration PsA, yrs, ± SD (n)	20.3 ± 10.9 (419)	21.4 ± 13.7 (44)	0.566	1.01 (0.98–1.04)
Duration PsO, yrs, ± SD (n)	29.9 ± 14.9 (399)	37.9 ± 19.3 (39)	0.003	1.03 (1.01–1.05)
BMI, ± SD (n)	27.7 ± 5.2 (370)	27.2 ± 4.7 (30)	0.636	0.98 (0.91–1.06)
DAI, mean ± SD (n)	3.87 ± 0.82 (411)	4.49 ± 1.13 (43)	< 0.001	1.94 (1.43–2.64)
Male	209 (50)	25 (57)	0.373	0.75 (0.40–1.41)
Smoking (ever)	224 (54)	24 (60)	0.505	1.25 (0.65–2.43)
Hypertension	181 (43)	24 (55)	0.157	1.56 (0.84–2.92)
Hyperlipidemia	66 (16)	5 (11)	0.435	0.68 (0.26–1.79)
Diabetes	49 (12)	9 (20)	0.099	1.93 (0.87–4.25)
Destructive/deforming disease	204 (49)	29 (67)	0.021	2.16 (1.11–4.21)
bDMARD (ever)	55 (13)	2 (4.5)	0.098	0.31 (0.74–1.34)
sDMARD (ever)	285 (68)	27 (61)	0.383	0.75 (0.40–1.43)
NSAID (ever)	303 (72)	24 (54)	0.014	0.46 (0.24–0.86)
Oral corticosteroid treatment (ever)	123 (29)	20 (46)	0.028	2.00 (1.07–3.76)
Fulfilling CASPAR criteria	378 (90)	40 (91)	0.882	1.08 (0.37–3.18)
Polyarthritis (according to Moll and Wright)*	173 (41)	24 (54)	0.088	1.71 (0.92–3.20)
Dactylitis (ever)	119 (41)	10 (33)	0.421	0.72 (0.33–1.60)
Nail involvement (ever)	162 (53)	16 (48)	0.640	0.84 (0.41–1.73)
Axial involvement	65 (15)	14 (32)	0.006	2.54 (1.28–5.05)
Axial and peripheral joint involvement	35 (8.3)	11 (24)	< 0.001	3.65 (1.70–7.86)

* 1973 Moll and Wright criteria for PsA. PsA: psoriatic arthritis; PsO: psoriasis; BMI: body mass index; DAI: disease activity index; DMARD: disease-modifying antirheumatic drug; bDMARD: biological DMARD; sDMARD: synthetic DMARD; NSAID: nonsteroidal antiinflammatory drug; CASPAR: ClASsification for Psoriatic ARthritis (criteria).

statistically significant longer duration of PsA, and they also had a higher mean DAI (4.49 ± 1.13 vs 3.87 ± 0.82, p < 0.001). A significantly larger number of patients who died had used oral corticosteroids (46% vs 29%, p = 0.028), while a significantly reduced number of patients had used NSAID (54% vs 72%, p = 0.014). No significant difference in death or survival was apparent in the number of patients who had been treated with sDMARD or bDMARD (Table 3). Also, a higher proportion of patients who died had destructive/deforming disease (67% vs 49%, p = 0.021) and axial involvement (32% vs 15%, p = 0.006).

All variables that achieved a significant association with death at the 5% level (PsO disease duration, DAI, destructive/deforming disease, NSAID treatment, treatment with oral steroids, and axial involvement) and sex were analyzed in a multiple logistic regression model with backward elimination. Predictors for death remaining significant were DAI (OR 1.88, 95% CI 1.30–2.72) and axial involvement (OR 0.33, 95% CI 0.15–0.74; data not shown), adjusted for age.

When axial disease involvement was further analyzed, a higher frequency of patients with a disease affecting both peripheral joints and axial involvement died (27%) compared with patients with peripheral disease only (7.2%; OR 4.02, 95% CI 1.84–8.84, p < 0.001). No such difference was seen when patients with predominantly axial disease were compared with patients with only peripheral disease (9.1% vs 7.2%, OR 1.28, 95% CI 0.37–4.48).

In regression analysis, DAI was significantly associated with death (OR 1.99, 95% CI 1.41–2.80) adjusted for age and sex (p < 0.001). The association remained significant after stratification of patients into the 2 major causes of death: diseases of the circulatory system (OR 1.86, 95% CI 1.20–2.89) and malignant neoplasms (OR 1.77, 95% CI

1.06–2.97, respectively. Stratification for age into 3 groups (< 40 yrs, 40–74 yrs, and > 75 yrs) revealed a significant difference in DAI between the group that survived and the group that died during the study, with an effect of higher DAI on death in age group 40–74 years (p = 0.001). When further stratified into 4 age groups, the association remained for the age group 55–69 years (n = 190; p = 0.005), but not in the other age groups (Figure 1). Data on patients < 40 years are not shown owing to low numbers of patients (n = 36) and only 1 death.

Analysis of CVE. During the followup period, 29 patients with PsA had an MI or stroke, with the MI being fatal in 3 cases. The SIR (95% CI) for an MI or stroke was 0.60 (0.40–0.86; Table 4). After stratification for sex, men showed a significantly lower risk of developing an MI or stroke, while no significant risk reduction was seen in women.

Patients with PsA who experienced an acute CVE were significantly older (70.7 ± 12.1 yrs vs 57.6 ± 13.3 yrs, p < 0.001; Table 5), but had a shorter disease duration (14.0 ± 13.5 yrs vs 19.9 ± 10.9 yrs, p = 0.004) compared with patients

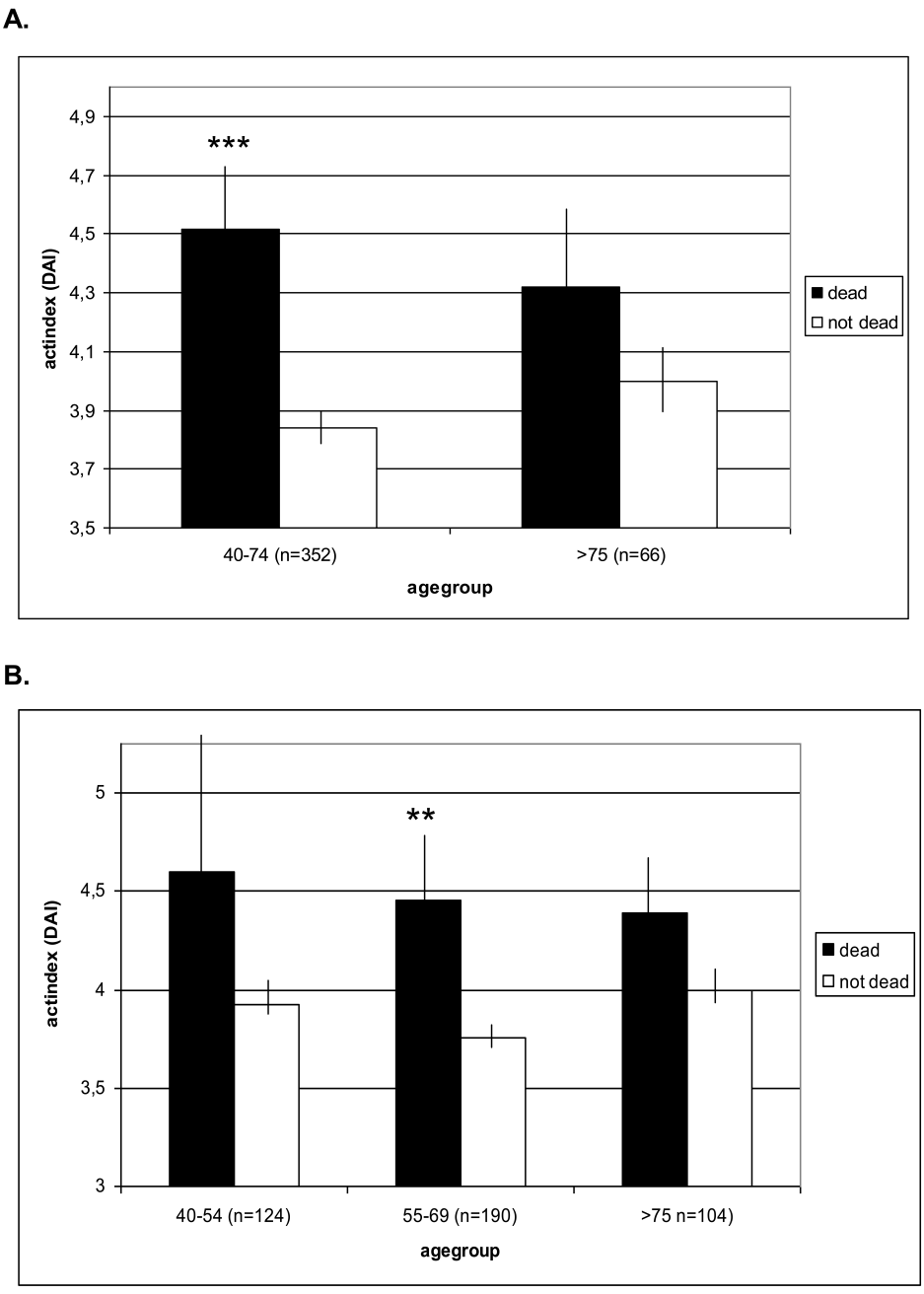

Figure 1. Disease activity index (DAI) in groups stratified by age, for patients who died and those alive at the end of the study. Ages given in years. ** p < 0.01. *** p < 0.001.

Table 4. SIR of acute cardiovascular events in patients with PsA compared with the general population.

Sex	Stroke, n	Exp, n	SIR (95% CI)	AMI, n	Exp, n	SIR (95% CI)	Stroke + AMI, n	Exp, n	SIR (95% CI)
Male	6	13.6	0.44 (0.16–0.96)	11	17.1	0.64 (0.32–1.15)	17	30.8	0.55 (0.32–0.88)
Female	8	10.0	0.80 (0.34–1.57)	4	7.7	0.52 (0.14–1.32)	12	17.8	0.68 (0.35–1.18)
All	14	23.7	0.59 (0.32–0.99)	15	24.9	0.60 (0.34–0.99)	29	48.6	0.60 (0.4–0.86)

SIR: standardized incidence ratio; PsA: psoriatic arthritis; AMI: acute myocardial infarction; Exp: expected deaths according to statistics of the general population.

Table 5. Comparison of disease characteristics at the end of the study between patients with or without event during the study. Data are n (%) unless otherwise indicated.

Characteristics	No Event	Event	p	OR (95% CI)
Age, yrs, ± SD (n)	57.6 ± 13.3 (430)	70.7 ± 12.1 (34)	< 0.001	1.08 (1.05–1.11)
Duration PsA, yrs, ± SD (n)	19.9 ± 10.9 (430)	14.0 ± 13.5 (33)	0.004	0.94 (0.90–0.98)
Duration PsO, yrs, ± SD (n)	29.5 ± 15.0 (407)	31.2 ± 21.5 (31)	0.565	1.01 (0.98–1.03)
BMI, kg/m^2, ± SD (n)	27.7 ± 5.2 (273)	27.8 ± 4.5 (27)	0.872	1.01 (0.93–1.08)
DAI, mean, ± SD (n)	3.90 ± 0.85 (420)	4.24 ± 1.02 (34)	0.030	1.47 (1.04–2.08)
Male	215 (50)	19 (56)	0.51	0.79 (0.39–1.59)
Smoking (ever)	226 (54)	22 (67)	0.16	1.70 (0.08–3.59)
Hypertension	179 (42)	26 (76)	< 0.001	4.5 (1.99–10.2)
Hyperlipidemia	61 (14)	10 (29)	0.019	2.5 (1.14–5.49)
Diabetes	49 (12)	9 (27)	0.008	2.89 (1.27–6.58)
Destructive/deforming disease	216 (51)	17 (50)	0.94	0.97 (0.48–1.96)
bDMARD (ever)	56 (13)	1 (2.9)	0.083	0.20 (0.03–1.5)
sDMARD (ever)	288 (67)	24 (71)	0.67	1.18 (0.55–2.54)
NSAID (ever)	314 (73)	13 (38)	< 0.001	0.23 (0.11–0.47)
Oral corticosteroids (ever)	128 (30)	15 (44)	0.083	1.86 (0.91–3.77)
Fulfilling CASPAR criteria	387 (90)	31 (91)	0.86	1.12 (0.33–3.83)
Polyarthritis (according to Moll and Wright)*	180 (42)	17 (50)	0.36	1.39 (0.69–2.79)
Dactylitis (ever)	119 (40)	10 (38)	0.85	0.92 (0.41–2.11)
Nail involvement (ever)	168 (53)	10 (40)	0.20	0.58 (0.25–1.34)
Axial involvement	74 (17)	5 (15)	0.70	0.83 (0.31–2.21)
Axial and peripheral joint involvement	41 (9.6)	5 (15)	0.33	1.63 (0.60–4.44)

* Moll and Wright criteria for PsA. PsA: psoriatic arthritis; PsO: psoriasis; BMI: body mass index; DAI: disease activity index; DMARD: disease-modifying antirheumatic drug; bDMARD: biological DMARD; sDMARD: synthetic DMARD; NSAID: nonsteroidal antiinflammatory drug; CASPAR: ClASsification for Psoriatic ARthritis (criteria).

not experiencing an event during the study. Among patients with PsA who had an event during the study, significantly fewer had been treated with an NSAID (38% vs 73%, p < 0.001). Also, a significantly higher proportion of patients with an event had HTN (76% vs 42%, p < 0.001), hyperlipidemia (29% vs 14%, p = 0.019), and/or diabetes (27% vs 12%, p = 0.008). No other association was recorded between any traditional risk factors, i.e., BMI, smoking, PsA disease expression, or pharmacological treatment, and an acute CVE.

All variables significantly associated with a CVE at the 5% level (HTN, diabetes, hyperlipidemia, PsA disease duration, DAI, NSAID treatment) and sex were analyzed in a multiple logistic regression model with backward elimination. Predictors for a CVE remaining significant were shorter PsA disease duration and less NSAID treatment, adjusted for age.

DISCUSSION

In our study of a cohort of patients with PsA from the county of Västerbotten in northern Sweden, patients had a statistically significant increased risk of death from disease(s) of the circulatory system compared with the general population. These results are consistent with those from a large population study from Denmark in which rate-ratios for overall mortality and cardiovascular mortality (ICD-10; I00–I99) were 1.74 (95% CI 1.32–2.30) and 1.84 (95% CI 1.11–3.06), respectively, for patients with PsA compared to controls[8]. Our finding that the SMR for all-cause mortality (1.22) was not significantly different from the general population is not consistent with a study by Wong, *et al*, who reported an SMR for overall mortality of 1.6[19]. Our finding is more in agreement with a more recent study from Ali, *et al*[25]. In that study, survival was improved, with different mortality rates in different time periods, showing 1.21 (95% CI 0.86–1.69) for the period 1996–2004[25]. A large population-based study from the United Kingdom reported that patients with PsA did not have significantly increased all-cause mortality compared with matched controls from the

general population[23]. Further, in a metaanalysis from 2013, an association with CVD and CV mortality was demonstrated using hospital-based and insurance database studies, but not in population-based studies[11], indicating differences due to the composition of study populations that could, in part, explain the differences between studies.

Concerning CVE, our study indicated a reduced risk of an MI/stroke in patients with PsA compared with the general population that, after sex stratification, was seen only in male patients with PsA. Among patients with PsA, no association between CVE and sex was found, but the strongest association was found with shorter PsA disease duration and less use of NSAID adjusted for age. The association with traditional CV risk factors (HTN, hyperlipidemia, and diabetes) was nonsignificant in multiple regression analysis.

Few earlier studies have analyzed CVE in patients with PsA. In a UK population-based study of patients with PsA, the major adverse CVE (stroke, MI, or CV death) were only significantly increased in patients with PsA not prescribed DMARD[23]. In our study there was no significant difference in the number of events among the patients irrespective of treatment with sDMARD or bDMARD, although the use of NSAID was less common in those patients who had died and in patients with a CVE. Similar results, with an inverse relationship between mortality and use of NSAID, have previously been shown in patients with ankylosing spondylitis[26].

Because previous studies on inflammatory joint diseases, e.g., PsA, RA, and SLE, implicate inflammation as part of the increased risk of CVE, and recent data indicate inflammation to be part of the pathogenesis of atherosclerosis[27], the effect of the disease burden on the risk of a CVE or death was examined. Unfortunately, the data in the medical records did not allow the use of any of the standardized activity indices for PsA and/or SpA (e.g., the 28-joint Disease Activity Score, Disease Activity in Psoriatic Arthritis, minimal disease activity, Arithmetic Mean of the Desirability Function, Psoriatic Arthritis Disease Activity Score, Bath Ankylosing Spondylitis Disease Activity Index, or any other activity index for axial activity). Instead we used a composite index, DAI, previously used for RA[24]. The DAI reflects both clinical activity for peripheral disease and laboratory activity, and also accounts for this activity over time. A high DAI possibly reflects a more aggressive disease or lack of effective treatment. Disadvantages of the DAI are that it has not previously been evaluated for PsA and does not discriminate between patients with a prolonged burden of disease and those with shorter disease duration. The association between DAI and death among patients with PsA in our study supports other studies indicating that disease activity has an effect on the risk of death[8,18,19,20].

In addition to DAI, axial disease was associated with death, while no such association was found with a CVE. The association was evident in patients with both axial and peripheral disease involvement. It was not possible to further analyze this association in our present study, but it is tempting to speculate that involvement of both spine and joints results in a higher disease burden and increased risk of death. It would be interesting to evaluate this in future studies.

A limitation of our study is that laboratory data on cholesterol, triglycerides, and blood glucose, or data concerning a metabolic disease, for example, were not available from the patients' records. It is also possible that the PsA population studied was not representative of the whole spectrum of the disease, because patients with mild disease would not be referred to specialist care. Unfortunately, the nature of the statistical database of the National Inpatient Care Register used in the study does not allow analysis of the diagnosis of unstable angina, or angina pectoris in relation to intervention, thus reducing the sensitivity of the number of events in SIR analysis. A strength of our study is that all diagnoses were established by experienced rheumatologists and validated by careful study of the patient records. Also, the population in northern Sweden is genetically homogeneous and patients are compared with controls from the general population of the same geographical area.

Though most data indicate increased CV mortality and comorbidity in patients with PsA, the results are conflicting, and heterogeneity among studies makes interpretation of data difficult[11]. Also, it is not clear whether the increased risk in patients with PsA is conferred by traditional risk factors or PsA-specific risk factors, e.g., related to inflammation. Our relatively large study, on well-characterized patients with PsA, showed increased mortality rates due to CV diseases compared with the general population. Further, among patients with PsA, an association between death and disease activity measured with DAI indicates an involvement of inflammation. The study adds to the research field of PsA and strengthens previous observations.

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