Published in final edited form as:
J Eur Acad Dermatol Venereol. 2012 March ; 26(3): 336–343. doi:10.1111/j.1468-3083.2011.04071.x.

Disease severity and therapy as predictors of cardiovascular risk in psoriasis: a population-based cohort study

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Abstract

Background—Previous studies suggest an increased risk of cardiovascular disease in psoriasis, but the relative contributions of traditional risk factors and markers of disease severity are unclear. We examined the effect of psoriasis disease characteristics on cardiovascular risk after adjusting for traditional cardiovascular risk factors.

Methods—Study populations included (a) case-cohort sample of 771 patients nested within a population-based psoriasis incidence cohort, and (b) cohort of 1905 patients with incident and prevalent psoriasis patients. Both cohorts were followed up to ascertain disease and treatment characteristics, traditional cardiovascular risk factors and cardiovascular outcomes. Cox proportional hazards regression models were used to identify predictors of cardiovascular outcomes.

Results—After adjusting for traditional risk factors, increasing number of psoriasis affected body sites at disease onset (HR 1.53 per additional site, 95% CI: 1.20, 1.95) was significantly associated with an increased risk of cardiovascular outcomes. Phototherapy (HR 3.76, 95% CI: 2.45, 5.77) and systemic therapy (HR 2.17, 95% CI: 1.50, 3.13) were associated with a higher risk of cardiovascular outcomes in univariate analyses, but these relatively strong associations disappeared after adjusting for cardiovascular risk factors.

Conclusion—Increasing number of psoriasis affected body sites may be a severity indicator in psoriasis and is associated with an increased cardiovascular risk. Due to low number of patients exposed to systemic therapy, this study had limited power to examine the effect of treatment on cardiovascular risk. Strong associations with phototherapy and systemic therapy suggest that the cardiovascular risk in psoriasis is confined to patients with severe disease.

Keywords

Psoriasis; Psoriatic Arthritis; cardiovascular disease; population-based study

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Conflict of interest disclosure: This publication was made possible by Grant Number R01-AR30582 from the National Institute of Arthritis and Musculoskeletal and Skin Diseases and an unrestricted research grant from Amgen.

INTRODUCTION

Although psoriasis has been traditionally viewed as an inflammatory disorder confined to the skin, recent advances in understanding the immunopathogenesis of psoriasis has shifted the focus to consider psoriasis as a systemic inflammatory condition, similar to other inflammatory autoimmune disorders. Evidence supporting an inflammatory basis for atherosclerosis and heart failure (HF)[1–4] has stimulated research investigating the risk of heart disease in patients with systemic inflammatory conditions, such as rheumatoid arthritis and psoriasis. Although the increased risk of ischemic heart disease and heart failure is firmly established in patients with rheumatoid arthritis, controversy continues whether a similar risk exists for patients with psoriasis[5, 6]. Some published studies indicate that the increased cardiovascular risk may be confined to patients with severe skin disease[7–15]. However, in the absence of robust measurements of disease severity, such as Psoriasis Area and Severity Index (PASI), studies to date relied almost solely on systemic treatment as a proxy for disease severity. This may be problematic because the likelihood of treatment is influenced by a number of factors, not just disease severity[6]. The objective of the current study was to examine the effect of psoriasis disease characteristics on cardiovascular risk after adjusting for traditional cardiovascular risk factors in a population-based cohort of patients with psoriasis.

METHODS

This study was performed using the resources of the Rochester Epidemiology Project (REP). As described previously[16, 17], REP system links medical records generated by different health care providers over many years to specific individuals, maintains an electronic index of diagnoses and surgical interventions, and provides an ongoing census of individuals as they move in and out of the community over time. As a result, subjects can be followed through their outpatient office, urgent care, emergency department, and hospitalization contacts with all local health care providers, allowing for longitudinal follow-up over several years. All contemporary and archived medical records are easily accessible for chart review and validation of diagnoses, treatments, disease signs and symptoms.

Using this data resource, we assembled two separate cohorts of psoriasis patients covering different time periods. The first cohort was a case-cohort sample of patients nested within a population-based incidence cohort of patients with adult-onset psoriasis first diagnosed between 1/1/1970 and 1/1/2000 [18, 19]. A case-cohort design combines the advantages of cohort studies(multiple outcomes and time-dependent covariates) and case-controlanalyses (fewer subjects) and are more efficient than cohortstudies[20]. Rather than incurring the substantial time associated with collecting detailed information on a large cohort of psoriasis patients (most of whom never developed the cardiovascular outcomes of interest), the case-cohort approach allowed us to collect disease characteristics and cardiovascular risk factors only in a stratified random sample (i.e. a psoriasis sub-cohort) of our entire psoriasis incidence cohort. Briefly, we first identified a random sub-cohort of 500 psoriasis patients in a large incidence cohort of 1624 psoriasis patients first diagnosed with psoriasis between 1/1/1970 and 1/1/2000 (see figure in Appendix). We also identified 271 patients who had experienced cardiovascular events either before psoriasis incidence or between psoriasis incidence and the end of the study (1/1/2009). The sub-cohort plus all psoriasis patients with cardiovascular events (total n=771) comprised the analytic sample for the case-cohort analyses.

The second cohort (referred to as the prevalence cohort in the rest of this manuscript) comprised 660 incident and 1245 prevalent adult psoriasis (total 1905 patients), including 191 psoriatic arthritis (PSA) patients, who were Olmsted County residents and under

observation between 1/1/1998 and 12/31/2007. The time frame of the second cohort was designated to have access to all relevant medical records electronically and to include patients exposed to various systemic drugs and biologics, which were first approved for use in psoriasis or PSA in 2002.

Psoriasis and PSA diagnoses were validated through medical record review. Psoriasis diagnosis was validated by either a confirmatory diagnosis in the medical record by a dermatologist, or a physician's description of the lesions in the medical record or a skin biopsy, whenever available. Review and validation of PSA diagnoses was based on ClASsification of Psoriatic ARthritis (CASPAR) criteria[21]. Data on psoriasis disease characteristics was collected only in the case-cohort sample and included the type (plaque, guttate, erythrodermic, pustular or sebo-psoriasis) and site of psoriasis lesions (palms and/or soles, elbows and/or knees, trunk, face, scalp, axilla, groin, inframammary, intergluteal/perianal or genital) and presence of nail involvement at psoriasis incidence. Number of affected body sites was determined based on location of lesions. For example, when both elbows were affected, this was counted as one location. Treatment characteristics were ascertained in both cohorts and verified through medical record review. We collected data on start and stop dates of all courses of phototherapy with ultraviolet B (UVB), psolaren plus UVA (PUVA), and systemic drug therapy, including methotrexate (MTX), oral retinoids, azathioprine, cyclosporine, hydroxyurea, sulfasalazine, leflunomide, and biologics (i.e. etanercept, infliximab, adalimumab, golimamab, efalizumab, alefacept). If a drug was discontinued for more than one month and re-started, then, the second course was recorded as a new course of therapy with that drug.

Data collection for cardiovascular risk factors and outcomes was slightly different in the two cohorts. In the case-cohort sample, all hospitalized myocardial infarctions (MI) were verified using standard epidemiologic criteria based on the presence of cardiac pain, biomarker values, and the Minnesota coding of the electrocardiogram (ECG)[22, 23]. In the prevalence cohort, MI were defined based on physician confirmation in the setting of a hospitalized event (without review of the presence of cardiac pain, biomarker values, and the ECG). Coronary revascularization procedures were defined similarly in both cohorts and included percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass grafting (CABG). Cerebrovascular events were defined similarly in both cohorts and reviewed only in the setting of a corresponding clinical event and classified as cerebral infarction, intracerebral hemorrhage or subarachnoid hemorrhage and transient ischemic attacks. Cerebrovascular events that were found only on imaging, traumatic subdural hematoma, hemorrhage in the setting of a background pathology (such as tumor or inflammation) and isolated infarction of the retina, labyrinth or cochlea were not included. Ischemic cardiovascular events were defined as any occurrence of MI, CABG, PTCA or cerebral infarction. Heart failure (HF) was defined according to the Framingham Heart Study criteria[24] in the case-cohort sample and based on physician confirmation in the prevalence cohort. Cardiovascular deaths were identified using underlying cause of death recorded in death certificates (ICD-9 codes 390–459 or ICD-10 codes I00–I99). In the case-cohort sample, dyslipidemia[25], hypertension[26] and diabetes mellitus[27] were ascertained based on strict epidemiological criteria (details described in a separate publication[19]), whereas they were based on physician diagnosis in the prevalence cohort. We also retrieved all electronically available height, weight, blood pressure and lipid measurements. Values closest to the incidence or prevalence date (within a 2 years window) were considered as baseline values. Patients were categorized as obese if body mass index was ≥30 kg/m^2 [28]. Cigarette smoking and alcohol abuse data was available only in the case-cohort sample. Smoking was categorized as current, former, and never at psoriasis incidence. Alcohol abuse was considered to be present if a physician's diagnosis of alcoholism was recorded in patients' medical records. Personal cardiac history was ascertained similarly in both cohorts

and included presence of one or more of the following prior to cohort entry (baseline): MI, revascularization procedures, stroke, HF or clinical diagnosis of angina pectoris.

Statistical methods

Two sets of analyses were performed—In the case-cohort sample, the association between psoriasis characteristics and cardiovascular outcomes was evaluated with standard Cox proportional hazards models with modification of the standard errors based on robust variance estimates[29]. Adjustments were made for age, sex and cardiovascular risk factors. Because the underlying cardiovascular disease rate was age-dependent, patients were analyzed on an age scale. Patients were entered into the analysis at the age of psoriasis diagnosis and were included until they had an event (i.e. MI) or were censored (at death or last follow-up). By using the age time scale, the model was automatically adjusted for age effects upon the baseline rate of cardiovascular events[30,31]. Cases outside the random sub-cohort are only considered to be at risk for an event from just before the event to the event time. The impact of the sampling scheme on the standard errors of the risk estimates were accounted for using the robust sandwich estimate as in Lin and Wei[32]. In analyses of individual cardiovascular outcomes, patients with prior history of the specific cardiovascular event were excluded. Risk factor data collected throughout follow-up were included as time-dependent covariates. These time-dependent covariates allow patients to be changed from the unexposed category to the exposed category at the time of diagnosis of a particular risk factor during followup. In the analysis of disease duration, the exposure status of patients changed in yearly intervals throughout the followup period. With a subcohort of 500 psoriasis subjects and a total of 175 cardiovascular events that occurred after psoriasis onset, we had approximately 80% power to detect a hazard ratio of 1.59 for a risk factor with 30% prevalence (significance level of 0.05). Similarly, Cox proportional hazards regression models were used to estimate the influence of potential predictors of cardiovascular events in the prevalence cohort of 1905 patients (cohort included both incident and prevalent psoriasis patients). Patients with certain characteristics were compared with those without the characteristic. Age was used as the time scale for these models. Factors assessed throughout followup (i.e. PSA, phototherapy, systemic therapy) were modeled as time-dependent covariates. Patients who received phototherapy or systemic drug therapy were classified as “ever exposed” and cardiovascular events following exposure were attributed to the exposed category. Hazard ratios (HRs) for systemic drug use and phototherapy were calculated, after adjusting for age, sex and cardiovascular risk factors. Prevalent patients who had a history of phototherapy or systemic therapy prior to cohort entry were considered exposed at baseline whereas, phototherapy and systemic drug therapy that started during follow-up were included as time-dependent covariates.

RESULTS

The baseline characteristics of the two study populations are shown in table 1. The first column shows the baseline (i.e. at psoriasis incidence) characteristics of the random sub-cohort of 500 patients included in our case-cohort sample of 771 patients. The second column shows the baseline characteristics of the 1905 patients included in the prevalence cohort. In the random sub-cohort, mean age at psoriasis incidence was 42.8 years and 51% of patients were men. In the prevalence cohort, mean age (48.8 years) was slightly higher and prevalent psoriasis patients constituted 65% of the cohort. The number of patients with PSA at baseline were 12 (2.4%) and 96 (5%), respectively in the two study cohorts. Information on psoriasis type, nail involvement and number of affected body sites were available only in the random sub-cohort. At psoriasis incidence, 380 (76%) patients had plaque psoriasis, 69 (14%) patients had nail involvement and the mean number of affected sites was 1.9 (median: 2, interquartile range 1, 2, min: 1 and max: 8).

Table 1 also shows the baseline distribution of the cardiovascular risk factors in the two cohorts. In the random sub-cohort of 500 patients, missing data was less than 10% for most risk factors except for actual lipid measurements which were missing for younger psoriasis patients. Similarly, half of the patients in the prevalence cohort of 1905 patients did not have lipid measurements at cohort entry, mainly younger patients. Mean body mass index was similar in both cohorts and 25% of the patients were classified as obese with a BMI ≥30 kg/m^2. In the random sub-cohort, the prevalence of dyslipidemia, hypertension and diabetes were 42.6%, 31.8% and 5.6%, respectively. In the prevalence cohort, the prevalence of hypertension (34%) and diabetes (13%) was slightly higher, whereas the prevalence of dyslipidemia (33%) was lower than patients in the random sub-cohort. Smoking and alcohol abuse data were available only in the random sub-cohort. One third (36.5%) of the incident psoriasis subjects were current smokers and alcohol abuse was also common at 16.9%. A higher proportion (12%) of patients in the prevalence cohort had a history of cardiovascular disease than incident patients (4.6%) included in the random sub-cohort. During a mean 14.7 (±8.7) years of follow-up of the random sub-cohort of 500 patients, 103 (21%) patients received phototherapy and 44 patients (9%, including 25 who received methotrexate and 12 biologics) received systemic drug therapy. In the prevalence cohort, the proportion of patients with a history of either phototherapy or systemic therapy at baseline was limited to 21 patients who had received phototherapy and 82 patients who had received some form of systemic treatment. During a mean 6.3 (±3.5) years of follow-up of the 1905 psoriasis patients, 157 additional patients received phototherapy (total 178 phototherapy) and 191 additional patients received systemic therapy (total 273 patients who ever received systemic therapy during the entire follow-up). Of these 273 patients, 86 received methotrexate and 73 patients received biologics.

Data presented in table 2 and appendix table (univariate results for different cardiovascular outcomes) are based on the case-cohort analyses and show the risk of cardiovascular outcomes associated with various psoriasis disease characteristics. The first column in table 2 shows the univariate age- and sex-adjusted analyses and the subsequent columns show results from two different multivariate models, as outlined in the table legend. In age- and sex-adjusted univariate analyses, cardiovascular risk was slightly higher for patients with plaque psoriasis and nail involvement and this was mainly due to increased risk of HF in these patients (as shown in appendix table). Intergluteal lesions were significantly associated (HR 1.85, 95% CI: 1.03, 3.34) with a higher risk of cardiovascular events (mainly ischemic events) but presence of lesions at other body sites (scalp, trunk, elbow, knees, palms and sloes, face) were not. Patients with PSA (total 30 patients) did not appear to have had a higher risk of any of the cardiovascular outcomes examined.

In this case-cohort sample, patients who received phototherapy at any time during the disease course, and the 44 patients who received systemic therapy also did not appear to have a higher cardiovascular risk. Yet, when various cardiovascular outcomes were examined separately (appendix table), phototherapy was associated with a significantly reduced risk of cardiovascular deaths, whereas, systemic therapy was associated with a higher risk of HF but this was not significant. There was no indication that the cardiovascular risk increased by disease duration (overall p-value for duration comparisons=0.199), indicating that the risk is the same for a newly diagnosed 60-year old with psoriasis and another 60-year old who has had psoriasis for 10 years. We also performed additional analyses of ischemic events by excluding CABG and PTCA. Results remained largely unchanged except for intergluteal lesions which were no longer significant. There was also no calendar year effect on the incidence of ischemic events (p=0.07).

Analyses presented in Table 3 are based on the prevalence cohort and show the cardiovascular risk estimates by psoriasis disease status at cohort entry (incident vs

prevalent), PSA disease status, phototherapy and systemic therapy, after adjusting for age, sex and cardiovascular risk factors. Patients who had a history of cardiovascular events prior to cohort entry (n=221) were excluded from these analyses. In age- and sex-adjusted analyses, patients who received phototherapy (HR 3.76, 95% CI: 2.45, 5.77) or systemic therapy (HR 2.17, 95% CI: 1.50, 3.13) had a significantly higher risk of a cardiovascular event compared with those who did not receive phototherapy or systemic therapy. However, these relatively strong associations disappeared after adjusting for the traditional cardiovascular risk factors.

DISCUSSION

There is growing controversy as to whether cardiovascular risk is elevated in psoriasis, and if so, whether it is limited to certain subgroups of patients, such as those with moderate-to-severe disease or those who had an earlier age of onset[5, 6]. In this study, we examined the extent to which the cardiovascular risk in psoriasis is associated with disease characteristics and systemic therapy, as a potential surrogate marker of disease severity. After adjusting for traditional cardiovascular risk factors, the number of psoriasis-affected body sites and presence of intergluteal lesions remained as significant predictors of cardiovascular events. Although it is unknown whether these are valid markers of disease severity, our findings nevertheless suggest that a higher psoriasis disease severity may play a role in etiopathogenesis of cardiovascular disease in psoriasis. Furthermore, similar to other published studies, we found that patients who had received phototherapy or systemic therapy had a higher risk of cardiovascular events compared with those who did not receive these treatments. However, these relatively strong associations disappeared after adjusting for the cardiovascular risk factors suggesting that the cardiovascular risk in psoriasis is more strongly mediated with the traditional cardiovascular risk factors.

Epidemiological studies in psoriasis are challenging in many regards, due to difficulties associated with the diagnosis and classification, a waxing and waning disease course, and lack of objective clinical or laboratory criteria to assess disease severity and the need for systemic treatment[33–37]. Many of the severity measures have been limited to the clinical trial setting and their biological plausibility as measures of biological severity remains speculative[36]. Consequently, the majority of longitudinal studies examining the cardiovascular risk in psoriasis relied on systemic therapy as a surrogate for disease severity[12, 38, 39].

Studies that reported on specific disease characteristics were limited to a few small cross sectional studies[40–42]. The only longitudinal study reporting on psoriasis severity as a predictor of cardiovascular disease included a cohort of 648 PSA patients attending a tertiary clinic in Canada[43]. In that study, PSA patients with PASI scores greater than 20 had a higher risk of MI, suggesting that severe disease may be associated with a higher cardiovascular risk. Yet, it is difficult to compare their findings to psoriasis patients in general because all of the patients included in that cohort had PSA with possible severe, persistent disease necessitating regular follow-up at a specialized referral clinic. Although we were unable to ascertain PASI scores in this historical cohort study, we examined a number of disease characteristics that could be identified retrospectively through chart review. Although the number of affected body sites per se is not an established disease severity indicator in psoriasis, it nevertheless may reflect more extensive skin involvement and suggests that disease severity is an important determinant of cardiovascular risk in psoriasis. The biological plausibility of intergluteal lesions is unknown and there is a high likelihood of measurement error for documentation of intergluteal lesions in the medical records. We speculate that intergluteal lesions may be a marker of more extensive disease, as physicians would be more likely to conduct a thorough skin evaluation in patients with extensive

disease. Previous findings from our group indicated that presence of intergluteal/perianal lesions were also associated with a higher risk of PSA among psoriasis patients[44].

Determining the potential role of systemic therapy on the risk of cardiovascular disease in psoriasis is even more problematic. In one database study[45], methotrexate use was associated with a reduced risk of cardiovascular disease, but this observation had not been corroborated in other studies. In studies by Boehncke and colleagues[46, 47], continuous systemic therapy in patients with severe plaque-type psoriasis was accompanied by improvement of endothelial vasodilator function and various cardiovascular biomarkers, suggesting that better control of disease activity in psoriasis may result in cardioprotective effects. Otherwise, studies that used systemic therapy as a surrogate for disease severity found an increased risk among those exposed to various systemic agents[12, 38, 39]. Similar to some of these studies, we found a significantly higher risk of cardiovascular events among patients who were on systemic drugs or phototherapy but these significant associations disappeared after further adjustment for cardiovascular risk factors. Although our study was not designed to examine the role of therapy, our findings nevertheless suggest that cardiovascular risk factors may be a more important determinant of cardiovascular risk in psoriasis. Further studies, and possibly prospective studies, would be needed to better quantify the relative contribution of disease severity and therapy on the risk cardiovascular disease in psoriasis, by relying on valid measures of disease severity and inflammatory burden.

The strengths of the current study are the large and well-characterized cohort of psoriasis patients who were consistently followed-up for several years from disease onset, markers of disease severity derived from description of lesions in the original medical records, and the use of confirmed and adjudicated cardiovascular risk factors and cardiovascular events. However, several potential limitations are important to consider while interpreting the results. Despite the large study population and long duration of follow-up, this study had limited power to examine associations with rare exposures. The number of patients exposed to systemic drugs was low in this population and consequently, we had limited power to examine the effect of treatment on cardiovascular risk. In particular, in our case-cohort sample, patients exposed to phototherapy and systemic therapy were limited to 21% and 9% patients, respectively. Additionally, majority (32%) of the patients on systemic therapy were actually being treated for PSA and not skin disease. We similarly did not have sufficient power to examine the risk by individual categories of drugs, dose or duration of treatment, or in different age groups. Data on disease characteristics in the case-cohort sample were available only at psoriasis incidence. We similarly were not able to ascertain serial PASI scores, as they were not systematically recorded in the medical records. If certain conditions, such as nail involvement or intergluteal lesions, were not recorded in the medical records, then the data would have been missed. Indeed, the disease course in psoriasis may vary considerably from patient to patient, and serial measures would be needed to accurately characterize the disease activity and disease burden over time. Finally, the majority of patients included in our study were patients with adult-onset psoriasis, and therefore, we were unable to examine the cardiovascular risk in patients with childhood-onset psoriasis.

In summary, our findings demonstrate that the number of body sites affected by psoriasis and the presence of intergluteal lesions are independent predictors of cardiovascular disease in psoriasis patients, even after accounting for the influence of traditional cardiovascular risk factors. These findings suggest that disease severity in psoriasis may act independently to increase the risk of cardiovascular disease. Future studies should rely on more accurate disease severity measures and address whether psoriasis specific interventions, such as systemic therapy, would have an effect on the risk of cardiovascular disease in psoriasis. In the meantime, assessment and management of traditional cardiovascular risk factors are of

the utmost importance in identifying high-risk patients and potentially reducing cardiovascular risk in psoriasis patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We are grateful to Justin Carlin for programming support, and Rita Black, Diane Carlson and Deborah Olson for data collection.

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Table 1

Baseline characteristics of the random sub-cohort of 500 psoriasis patients and prevalence cohort of 1905 patients

	Random sub-cohort (n=500)	Prevalence cohort (n=1905)
Age, years, mean (±SD)	42.8 (±16.8)	48.8 (±17.5)
Men, %	255 (51%)	921 (48%)
Psoriasis characteristics at cohort entry, no (%)		
Prevalent patients	--	1245 (65%)
Psoriatic arthritis*	12 (2.4%)	96 (5%)
Plaque psoriasis	380 (76%)	
Other	105 (21%)	
Unknown	15 (3%)	
Nail involvement	69 (14%)	
Number of affected sites	1.9 (±1.1)	
Location		
Scalp	214 (46%)	
Trunk	117 (25%)	
Intergluteal perianal	47 (10%)	
Cardiovascular risk factors, no (%)		
Obesity	117 (25%)	476 (25%)
Body Mass index, kg/m2, mean (±SD)	27.2 (±6.0)	28.3 (±6.4)
≤20.0	28 (6%)	77 (5%)
20.1–24.9	161 (35%)	408 (28%)
25–29.9	160 (34%)	471 (33%)
30.0–34.9	66 (14%)	269 (19%)
≥35	51 (11%)	207 (14%)
Dyslipidemia	213 (43%)	630 (33%)
Serum cholesterol, mg/dl, mean (±SD)		
Total cholesterol	213.4 (±49)	202 (±42)
High-density lipoprotein cholesterol	47.1 (±18.2)	51 (±15)
Low-density lipoprotein cholesterol	129.5 (±35.9)	118 (±36)
Triglycerides	159 (±201.2)	166 (±109)
Hypertension	159 (32%)	642 (34%)
Blood pressure, mmHg, mean (±SD)		

	Random sub-cohort (n=500)	Prevalence cohort (n=1905)
Systolic	128.7 (±20.0)	128 (±20)
Diastolic	77.9 (±11.9)	76 (±11)
Diabetes mellitus	28 (6%)	257 (13%)
Smoking status		
Current smoker	179 (37%)	
Former/ever smoker	134 (27%)	
Never smoked	177 (36%)	
Alcohol use	83 (17%)	
History of cardiovascular disease	23 (5%)	221 (12%)
Heart failure	8 (2%)	39 (2%)
Stroke	3 (0.6%)	136 (7%)
MI or revascularization	13 (3%)	86 (5%)
History of psoriasis treatment at baseline		
Phototherapy	--	21 (1%)
Any systemic treatment		82 (4%)

* Including patients who developed PSA during follow-up, there were a total of 30 PSA patients in the random sub-cohort and total 191 in the prevalence cohort over the entire follow-up period.

Table 2

Psoriasis disease characteristics as predictors of cardiovascular events in psoriasis (estimates derived from multivariate models, adjusting for age, sex and cardiovascular risk factors)

	Hazard ratio (95% confidence intervals)		
	Age- and sex-adjusted	**Multivariate model 1**	**Multivariate model 2**
Plaque psoriasis vs others	1.55 (0.81, 2.95)	1.33 (0.72, 2.46)	0.77 (0.25, 2.38)
No. of psoriasis sites	1.12 (0.92, 1.36)	1.12 (0.93, 1.35)	1.53 (1.19, 1.96)
Nail involvement	1.49 (0.83, 2.64)	1.41 (0.79, 2.51)	1.14 (0.42, 3.14)
Intergluteal lesions	1.85 (1.03, 3.34)	1.98 (1.06, 3.71)	3.40 (1.21, 9.55)
Psoriatic arthritis*	0.71 (0.31, 1.62)	0.68 (0.31, 1.49)	NA
Phototherapy*$	1.03 (0.61, 1.74)	1.08 (0.65, 1.80)	1.06 (0.41, 2.74)
Any systemic therapy*$	0.85 (0.37, 1.96)	0.77 (0.34, 1.76)	0.24 (0.04, 1.48)

Model 1 adjusted for age, sex, smoking status, alcohol use, and time dependent variables for obesity, dyslipidemia, hypertension, diabetes mellitus.

Model 2 adjusted for age, sex and individual Framingham risk factors (total cholesterol, high-density lipoprotein cholesterol, systolic and diastolic blood pressure, smoking, and diabetes).

* time dependent variables

$ A total of 103 patients had received phototherapy. A total of 44 patients received systemic therapy (25 methotrexate).

Data presented in this table comes from the case-cohort sample.

Table 3

Predictors of cardiovascular disease* in psoriasis

	Hazard ratio (95% confidence intervals) for cardiovascular events	
	Age and sex-adjusted	**Multivariate adjusted****
Prevalent (vs incident)	1.03 (0.81, 1.31)	1.14 (0.75, 1.73)
Psoriatic arthritis$	1.28 (0.90, 1.83)	1.21 (0.68, 2.15)
Phototherapy$	3.76 (2.45, 5.77)	1.28 (0.55, 2.98)
Any systemic therapy$	2.17 (1.50, 3.13)	0.93 (0.49, 1.75)

* includes MI, revascularization procedures, cerebrovascular events, HF and cardiovascular death.

** adjusted for age, sex, obesity, dyslipidemia, hypertension, diabetes mellitus, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, blood pressure values

$ time-dependent covariates

Data presented in this table come from the prevalence cohort