Published in final edited form as:
Int J Dermatol. 2013 January ; 52(1): 32–40. doi:10.1111/j.1365-4632.2011.05430.x.

Risk and predictors of cardiovascular disease in psoriasis: a population-based study

Hilal Maradit-Kremers, MD[1], **Ross A. Dierkhising, MS**[1], **Cynthia S. Crowson, MS**[1], **Murat Icen**[1], **Floranne C. Ernste, MD**[2], and **Marian T. McEvoy, MD**[3]

[1]Department of Health Sciences Research, College of Medicine, Mayo Clinic, Rochester Minnesota

[2]Department of Internal Medicine, Division of Rheumatology, College of Medicine, Mayo Clinic, Rochester Minnesota

[3]Department of Dermatology, College of Medicine, Mayo Clinic, Rochester Minnesota

Abstract

BACKGROUND—Emerging evidence suggests that severe psoriasis is associated with increased risk of cardiovascular disease. The goal of this study was to examine the risk and predictors of clinical cardiovascular events in psoriasis.

METHODS—We performed a historical cohort and a nested case-cohort study. using the population-based resources in Olmsted County, Minnesota. Study population included a population-based incidence cohort of patients with psoriasis first diagnosed between 1/1/1970 and 1/1/2000 and 2678 age- and sex-matched non-psoriasis subjects. Cardiovascular events including hospitalized myocardial infarction, coronary revascularization procedures, stroke, heart failure and cardiovascular death.

RESULTS—Psoriasis was associated with an increased risk of myocardial infarction (MI) based on diagnostic codes (hazard ratio 1.26; 95% confidence intervals: 1.01, 1.58), but not when the analyses were restricted to validated MI (hazard ratio 1.18; 95% confidence intervals: 0.80, 1.74). Psoriasis was not associated with an increased risk of heart failure or cardiovascular death. Traditional cardiovascular risk factors were significantly associated with cardiovascular risk in psoriasis. Each 1% increase in Framingham risk score at psoriasis incidence corresponded to 5-10% increase in risk of cardiovascular events.

CONCLUSION—In this large incidence cohort of patients with psoriasis representing the full disease severity spectrum, psoriasis was not associated with an increased cardiovascular risk.

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease affecting 1-2% of the adult general population[1]. Several published studies[2-10], although not all[11-15], report an increased risk of cardiovascular disease in psoriasis. So far, the methodological reasons for these discrepant findings and underlying mechanisms are poorly understood[16-18]. The confounding role of traditional cardiovascular risk factors is particularly relevant because smoking and obesity are risk factors for psoriasis[19, 20] and patients with psoriasis typically have a higher prevalence of smoking, alcohol consumption, obesity, low physical activity, adverse lipid profile, and hypertension compared to their non-psoriatic peers[3, 4, 21-24]. It remains to be

Corresponding author: Hilal Maradit Kremers, MD MSc Mayo Clinic, Department of Health Sciences Research 200 First St. SW, Rochester, MN 55905 telephone: 1 507 266 3169, fax: 1 507 284 1516 maradit@mayo.edu.

determined whether the excess risk of heart disease in psoriasis is independent of traditional risk factors and is instead, mediated through biological mechanisms related to increased inflammatory activity in psoriasis, and whether the risk can be modified with immune modulating therapy. The aim of the present study was to examine the risk of clinical cardiovascular events in a population-based incidence cohort of patients with psoriasis compared with age- and sex-matched non-psoriasis subjects, and to determine whether psoriasis is a risk factor for cardiovascular disease after accounting for traditional cardiovascular risk factors.

MATERIALS & METHODS

This study was designed as a retrospective, longitudinal cohort and nested case-cohort study using the data resources of the Rochester Epidemiology Project[25]. The overall study population comprised an incidence cohort of patients with adult-onset psoriasis first diagnosed between 1/1/1970 and 1/1/2000. Two sets of analyses were performed, with slightly different study populations. Comparison of the risk of MI relied on Olmsted County MI surveillance data which were available for the time period starting 1/1/1979 until 12/31/2005. Therefore, our original psoriasis incidence cohort was restricted to 1344 psoriasis patients first diagnosed between 1/1/1979 and 12/31/1999 and follow-up was truncated at 12/31/2005 for the MI analyses. For each incident psoriasis subject, 2 non-psoriasis subjects (total 2678) were identified after matching on birth year (±3 years), sex and length of medical history prior to cohort entry (±5 years) . Each non-psoriasis subject was assigned an index date corresponding to the incidence date of the matched psoriasis subject. Both cohorts were followed up longitudinally over time to identify incident cardiovascular events and cardiovascular deaths. Second, we created a case cohort sample to examine the determinants of cardiovascular disease in psoriasis. Case-cohort sampling was performed in our 1/1/1970 - 1/1/2000 incidence cohort. A sub-cohort of 500 psoriasis patients was randomly selected. We also identified 271 patients in the psoriasis cohort who had experienced cardiovascular events either before psoriasis incidence or between cohort entry (i.e. psoriasis incidence date) and 1/1/2009 (end of the study). The sub-cohort plus all psoriasis patients with cardiovascular events (total n=771) comprised the analytic sample for the case-cohort analyses.

The entire medical records of each psoriasis patient were reviewed longitudinally by trained nurse abstractors, beginning with the subjects' records at age 18 years and continuing until the death, migration from Olmsted County, or end of the study. Data were collected on all cardiovascular events and risk factors throughout the followup period and published guidelines were used for classification (detailed definitions of cardiovascular events are provided in Appendix). Framingham risk score was calculated at psoriasis incidence (baseline) based on the newly published Framingham score[27]. Each psoriasis subject was assigned a point score based on sex, age, categorical values of total cholesterol, high-density lipoprotein cholesterol, blood pressure, smoking, and diabetes. For subjects with missing lipid values (in earlier years of the study), Framingham risk score was calculated using an imputed risk score which assigned 0 points for lipids.

Statistical Analyses

Statistical analyses were performed in 2 phases. First, we examined the risk of MI, HF and cardiovascular death in patients with psoriasis compared with age- and sex-matched non-psoriasis subjects. Data from the ongoing MI surveillance study in Olmsted County were used to identify hospitalized MI[28, 29]. The association between history of MI and HF and psoriasis disease status was examined using logistic regression. Odds ratios (ORs) were calculated to determine the associations between the presence of MI, HF and psoriasis status after adjusting for age, sex, and calendar year. Cox proportional hazards regression models

were used to estimate the risk of MI, HF and cardiovascular death in the psoriasis and non-psoriasis cohorts. Age was used as the time scale for these models and the analyses were stratified by sex. The data on subjects who died of non-cardiovascular causes prior to MI or HF, and the data on those who were still alive at last followup were censored. Hazard ratios (HRs) were computed, after adjusting for age and sex and calendar year. Subjects with a history of MI or HF prior to the incidence/index date were excluded from these analyses. The earliest recorded date of MI or HF was considered the event date.

The second set of analyses was performed in the case-cohort sample. The association between psoriasis and incident cardiovascular events was evaluated with standard Cox proportional-hazards models with modification of the standard errors based on robust variance estimates[30]. Patients from the sub-cohort were included from baseline until failure or censoring, whereas cases (i.e. psoriasis patients with cardiovascular events) outside the cohort were included just before their event. 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 scale, the model was automatically adjusted for age effects upon the baseline rate of cardiovascular events[31, 32]. Cases outside the random sub-cohort were 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[33]. In analyses of individual cardiovascular outcomes, patients with prior history of the specific cardiovascular event were excluded.

RESULTS

The study population for the analyses of the risk of cardiovascular disease comprised 1344 incident psoriasis patients and a matched comparison group of 2678 non-psoriasis subjects. Mean age of the 1344 psoriasis patients was 43.6 years and 691 (51%) were male. The 1:2 matched non- psoriasis group comprised 2678 subjects with a mean age of 43.6 years and 1375 (51%) were male. The length of medical history prior to incidence/index date was similar in both cohorts (p=0.91) with a mean of 22.7 years (SD 14.6 years) for psoriasis patients and 22.6 years (SD 14.7 years) for the non-psoriasis subjects.

Table 1 shows the prevalence of MI and HF that occurred in the psoriasis and non-psoriasis groups prior to their incidence/index date. Forty-six out of the 1344 psoriasis patients (3.4%) and 76 out of the 2678 non-psoriasis subjects (2.8%) had a diagnostic code consistent with MI prior to psoriasis onset corresponding to an odds ratio (OR) of 1.24 (95% CI: 0.84, 1.85). Only 16 (1.2%) MI in psoriasis patients and 22 (0.8%) in non-psoriasis subjects were validated MI based on cardiac pain, enzymes and ECG. After adjusting for age, sex and calendar year, these differences corresponded to an OR of 1.47 (95% CI 0.76, 2.86) for validated MI and was not significant. Table 1 also shows the findings for HF. A total of 30 (2.2%) psoriasis patients and 44 (1.6%) non-psoriasis subjects had a history of HF prior to incidence/index date, corresponding to an OR of 1.42 (95% CI 0.86, 2.32). We also examined whether the risk differed by psoriasis age of onset (data not shown) but the analyses were limited due to low number of events in younger age groups.

Using a historical cohort design, we then examined the risk of MI, HF and cardiovascular death over time following psoriasis onset (Table 2). Mean follow-up of the psoriasis cohort was 14.2 years (SD 7.6 years; total 19106 person-years) and the mean follow-up of the non-psoriasis cohort was 13.6 years (SD 7.8 years; 36426 person-years). During follow-up, 124 psoriasis patients and 205 non-psoriasis subjects received diagnostic codes consistent with

MI, corresponding to a hazards ratio of 1.26 (95% CI: 1.01, 1.58) and the difference was statistically significant. However, only 40 MI in the psoriasis cohort and 69 MI in the non-psoriasis cohort could be validated based on pain, enzymes and ECG findings. When only these validated MI were considered, the resultant hazards ratio was 1.18 (95% CI: 0.80, 1.74) and was no longer statistically significant (p=0.40). Similarly, 115 psoriasis and 221 non-psoriasis subjects developed HF during follow-up, corresponding to a hazards ratio of 1.06 (95% CI: 0.85, 1.33). The underlying cause of death was cardiovascular disease in a total of 77 psoriasis and 153 non-psoriasis subjects and the risk of dying from cardiovascular disease was not significantly different in the psoriasis and non-psoriasis cohorts.

We then used a case-cohort design to examine the impact of traditional cardiovascular risk factors on cardiovascular risk in our case-cohort sample of 771 psoriasis patients. The impact of cardiovascular risk factors was examined both at baseline (Table 3) and during follow-up (Table 4) as time-dependent covariates. The results have been adjusted for sex (as a covariate) and age (due to the use of an age time scale). Cardiovascular outcomes were classified into 4 groups as any cardiovascular event, ischemic events (MI, CABG, PTCA, ischemic stroke), HF and cardiovascular death. For each cardiovascular outcome, patients with events prior to the psoriasis date were excluded.

In age and sex-adjusted univariate analyses shown in Table 3, many of the traditional cardiovascular risk factors were significantly associated with the risk of cardiovascular disease and these significant univariate associations persisted when we considered these risk factors in time-dependent analyses, as shown in Table 4. There was some indication that male psoriasis patients had a higher risk of ischemic events (HR 1.78, 95% CI: 1.14, 2.77) and cardiovascular death (HR 1.82, 95% CI: 1.04, 3.18). Although we found a strong association with alcohol abuse and the risk of cardiovascular events (risk of any cardiovascular event, HR 1.68, 95% CI: 1.00, 2.81), smoking was not significantly associated with cardiovascular risk in this cohort. Each 1 kg/m^2 increase in BMI was associated with a 5% increased risk of any cardiovascular event (HR 1.05, 95% CI: 1.01, 1.08) and 8% increased risk of HF (HR 1.08, 95% CI: 1.04, 1.13). Similarly, we observed a graded increase in risk of any cardiovascular event and HF with increasing BMI categories. BMI results persisted when we included obesity as a time-dependent variable (Table 4) by taking into account all 225 psoriasis patients who fulfilled criteria for obesity over the entire study period. Having a BMI of ≥ 30 kg/m^2, either at psoriasis onset or anytime during the disease course, was associated with a 68% increased risk of any cardiovascular event (HR 1.68, 95% CI: 1.11, 2.54) and more than doubling of the risk of HF (HR 2.25, 95% CI 1.33, 3.81).

With dyslipidemia, significant associations were found for any cardiovascular event and ischemic events both for patients who had dyslipidemia at baseline (Table 3) and who fulfilled criteria for dyslipidemia during follow-up (Table 4). As continuous variables, the only baseline lipid measurement significantly associated with cardiovascular events was triglycerides (associated with ischemic events), but the number of patients with lipid measurements at baseline was limited to 270 patients. Similarly, presence of hypertension at psoriasis incidence was associated with a 71% increased risk of cardiovascular events (HR 1.71, 95% CI: 1.11, 2.65) and almost doubling of the risk considering patients who developed hypertension during follow-up (HR 1.97, 95% CI: 1.20, 3.22). Diabetes was the strongest cardiovascular risk factor with more than double the risk of cardiovascular events if present at baseline (HR 2.71, 95% CI: 1.44, 5.11) or anytime during follow-up (HR 2.26, 95% CI: 1.43, 3.58).

We observed a graded and significant increase in cardiovascular risk with the Framingham risk score, in particular for overall, ischemic events and HF but not as strong for cardiovascular deaths.

DISCUSSION

In a series of historical cohort and case-cohort analyses, we examined the risk and determinants of ischemic cardiovascular events (i.e. MI, revascularization procedures, stroke), HF and cardiovascular death in patients with psoriasis. Patients with psoriasis had a higher risk of MI when analyses were conducted using MI diagnostic codes, but the resultant risk was no longer significant when the analyses were restricted to validated hospitalized MI. Similarly, patients with psoriasis did not have an increased risk of HF or cardiovascular death compared with age- and sex-matched non-psoriasis subjects. Among psoriasis patients, many of the traditional risk factors were significantly associated with cardiovascular risk, including dyslipidemia, obesity, hypertension, diabetes mellitus and alcohol abuse. Similarly, each 1% increase in Framingham risk score corresponded to 5-10% increase in risk of cardiovascular events.

Given the increasing number of studies on the risk of heart disease in psoriasis, it is important to assess how this study differs from the others reported so far. First, in contrast to other clinic-based[2, 34], medical record based[7, 12] or administrative database[6, 35] studies, this is a population-based study as defined in the classic epidemiologic literature. The underlying data source for our study covers more than 98% of all medical care provided to the local population in Olmsted County. The local health care providers span the spectrum from primary outpatient care through tertiary and critical hospital care including all medical and surgical specialties[36]. The population-based nature of the study offers at least 3 distinct advantages: First, the psoriasis population reflects the complete disease spectrum, irrespective of the provider, disease course or disease severity. Therefore, this population is distinctly different from, for example the Photochemotherapy (PUVA) Cohort[11] or patients included in treatment trials[37] that both include patients with more severe disease. In an unpublished analysis from our group[38], patients with multiple affected body sites and those who had received phototherapy and systemic therapy had a significantly higher risk of cardiovascular disease, suggesting that cardiovascular risk in psoriasis may be confined to patients with severe disease. Second, our study cohort is limited to incident (i.e. new-onset) psoriasis patients, as compared to the majority of other studies that included both incident and prevalent (established disease) patients, in part due to limited medical history available to investigators at the time of their investigation. Risk estimates derived from inception cohorts can differ from those derived from non-inception cohorts with higher estimates in the latter[39]. We had access to an impressive 22 years of medical history prior to the onset of psoriasis and were able to not only create an incidence cohort, but also distinguish cardiovascular events that preceded psoriasis. Third, in contrast to previous studies, validation and unbiased measurement was an important component of this study. As reported previously by our group, electronic identification of psoriasis patients by diagnostic codes alone may lead to misclassification bias[40]. We accessed and reviewed the entire inpatient and outpatient medical records of all subjects, and diagnoses were validated not only for psoriasis but also for all cardiovascular events, including, for example, review of the original ECGs and clinical signs and symptoms of HF, for 22 years prior to and 14 years following the psoriasis onset. We examined the complete spectrum of cardiovascular events, including revascularization procedures, strokes and HF and applied rigorous and validated diagnostic criteria to ascertain cardiovascular events and risk factors. Our MI and HF criteria are identical to the case definitions used in community surveillance studies in the United States[41]. As far as we are aware, none of the previous studies used the same stringent classification criteria to ascertain cardiovascular risk factors and outcomes.

Despite the fact that we had access to full original inpatient and patient medical records of all subjects with codes for MI, we could confirm only a third, based on the presence of cardiac pain, biomarker values and ECG, as compared to 79% in the General Practice Research Database in a recently reported small validation study[42]. This is possibly due to differences in definition of validated MI. Validated MI in our study included definite and probable MI, according to the standard epidemiologic classification criteria[43, 44] and therefore, more strict that previous studies. Although measurement bias is minimized in our study, it is difficult to evaluate the extent and direction of measurement bias in other published studies in comparison to ours. Furthermore, we ascertained the cardiovascular risk factors and outcomes over many years of followup (average 14 years after cohort entry), and used them as time-dependent variables to fully account for the risk factors that developed during the course of psoriasis. We had access to more than 2 decades of medical history prior to psoriasis onset and therefore, able to examine whether cardiovascular risk precedes psoriasis and also, exclude patients if needed, in analyses of the risk of incident cardiovascular events. Extent of medical history and duration of follow-up is typically limited to less than 5 years in other published studies. Hence, this study extends the findings of previous studies, and addresses various methodological limitations through the longitudinal follow-up of a well-defined psoriasis incidence cohort and a non-psoriasis cohort sampled from the same community and well-validated measurements of risk factors and outcomes.

Nevertheless, our results should be interpreted in light of some potential limitations. First and foremost, we had limited power in our cohort analyses due to relatively younger age of the cohort and the low incidence of cardiovascular events, despite a mean 14 years of follow-up. If the cardiovascular risk is confined to psoriasis patients with severe disease, as previously suggested[7, 45], the number of patients with severe disease is too small in this cohort to demonstrate the risk with sufficient power. Indeed, only 20% of the patients in this cohort received phototherapy and 8.8% received systemic therapy, and the cardiovascular event rates are low due to relatively young age of onset of psoriasis (i.e. 43 years at psoriasis incidence). We similarly did not have sufficient power to examine effect modification of age and psoriasis on cardiovascular outcomes. This cohort also does not include childhood-onset psoriasis patients who may have a higher disease burden and therefore, higher risk for cardiovascular disease. Therefore, we cannot exclude a small cardiovascular risk, although the risk is possibly less than in patients with rheumatoid arthritis[46] or lupus. Second, we did not adjust for traditional cardiovascular risk factors when comparing the risk of MI, HF, and cardiovascular death in psoriasis and non-psoriasis cohorts because validated risk factor data was not available for the non-psoriasis cohort. Nonetheless, if the prevalence of traditional cardiovascular risk factors in psoriasis is higher than the general population, and if the cardiovascular risk in psoriasis is driven mainly with increased occurrence of these risk factors[47], we would have observed an increased risk, even without adjustment for the traditional risk factors. Therefore, this limitation could not have influenced our findings. Despite this limitation, analyses of cardiovascular risk factors within the psoriasis cohort were based on validated risk factor data reducing the likelihood of measurement bias. Third, this was a retrospective study that relied on the clinical information recorded in the patients' medical records, and therefore, it was not possible to ascertain risk factors and cardiovascular outcomes prospectively at regular intervals. Also, a large proportion of the younger psoriasis patients did not have lipid measurements at around the time of their first psoriasis diagnosis. Similarly, conditions not recorded in the medical records would have been missed. This could have been a potential problem for the ascertainment of unrecognized cardiovascular events. However, ECG rates were similar in both cohorts, suggesting that differential misclassification is unlikely. Fourth, we did not adjust for psoriasis disease severity and whether the increased cardiovascular risk is confined to patients with more severe disease. The potential role of psoriasis disease characteristics and

medications on the clinical presentation and outcome of heart disease in psoriasis is the subject of our ongoing investigation.

In summary, while we cannot exclude a modest increase in risk, our comprehensive long-term follow-up of an adult-onset incidence cohort of patients with psoriasis and stringent ascertainment of cardiovascular events indicate that patients with psoriasis may not have an increased risk of MI, HF or cardiovascular death compared with age- and sex-matched non-psoriasis subjects. Traditional risk factors are significantly associated with cardiovascular risk in psoriasis patients. Further research is needed to better understand the patterns of cardiovascular risk in psoriasis, such as examining subgroups of patients with severe psoriasis who may have an increased risk of cardiovascular events, and the methodological and biological reasons for discrepant findings across studies.

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.

Funding/Support: This study was supported in part by the Rochester Epidemiology Project (R01 AG034676 from the National Institute on Aging) and an unrestricted research grant from Amgen.

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Table 1

Risk of cardiovascular events *prior* to incidence/index date

Diagnosis	Psoriasis n=1344	Non-psoriasis n=2678	Odds ratio (95% CI)*	p-value
Myocardial infarction (by codes only)	46 (3.4%)	76 (2.8%)	1.24 (0.84, 1.85)	0.28
Myocardial infarction (validated)	16 (1.2%)	22 (0.8%)	1.47 (0.76, 2.86)	0.25
Heart failure	30 (2.2%)	44 (1.6%)	1.42 (0.86, 2.32)	0.17

*adjusted for age, sex and calendar year

Table 2

Risk of cardiovascular events *following* psoriasis incidence/index date[$]

	Psoriasis cohort N events / total	Non-PSO cohort N events / total	Hazards ratio (95% CI)[*]	p-value
Myocardial infarction (by codes only)	124 / 1298	205 / 2602	1.26 (1.01, 1.58)	0.040
Myocardial infarction (validated)	40 / 1328	69 / 2656	1.18 (0.80, 1.74)	0.40
Heart failure	115 / 1314	221 / 2634	1.06 (0.85, 1.33)	0.59
Cardiovascular death	77 / 1344	153 / 2678	1.04 (0.79, 1.37)	0.76

[*] adjusted for age, sex and calendar year

[$] subjects who experienced selected cardiovascular events prior to incidence/index date excluded

Table 3

Baseline predictors of cardiovascular events in psoriasis

	Hazard ratio (95% CI) for cardiovascular outcomes**			
	Any cardiovascular event	**Ischemic events***	**Heart failure**	**Cardiovascular death**
Male sex	1.44 (0.96, 2.18)	1.78 (1.14, 2.77)	1.35 (0.79, 2.31)	1.82 (1.04 3.18)
Smoking status				
Never smoked	1	1	1	1
Current smoker	1.15 (0.69, 1.92)	1.14 (0.66, 1.95)	1.11 (0.56, 2.18)	1.71 (0.86, 3.42)
Former smoker	0.95 (0.58, 1.57)	0.93 (0.55, 1.58)	0.75 (0.38, 1.47)	0.77 (0.37, 1.59)
Alcohol use	1.68 (1.00, 2.81)	1.49 (0.87, 2.55)	2.04 (1.07, 3.89)	2.64 (1.42, 4.90)
Body mass index (per 1 kg/m^2 ↑)	1.05 (1.01, 1.08)	1.02 (0.98, 1.05)	1.08 (1.04, 1.13)	1.00 (0.94, 1.05)
< 25	1	1	1	1
25-29.9	1.56 (0.95, 2.56)	1.53 (0.91, 2.58)	1.21 (0.63, 2.34)	1.10 (0.58, 2.07)
≥ 30.0	2.03 (1.15, 3.56)	1.44 (0.80, 2.58)	2.57 (1.25, 5.30)	0.90 (0.41, 1.95)
Presence of dyslipidemia	1.60 (1.04, 2.46)	1.71 (1.06, 2.76)	1.33 (0.75, 2.35)	0.82 (0.47, 1.44)
Total cholesterol (per 10 mg/dL ↑)	1.03 (0.97, 1.09)	1.04 (0.98, 1.11)	0.99 (0.93, 1.05)	0.99 (0.93, 1.05)
LDL cholesterol (per 10 mg/dL ↑)	0.99 (0.91, 1.09)	1.01 (0.91, 1.13)	1.04 (0.91, 1.18)	1.08 (0.98, 1.19)
HDL cholesterol (per 10 mg/dL ↑)	0.86 (0.66, 1.10)	0.96 (0.74, 1.25)	0.88 (0.61, 1.29)	1.02 (0.87, 1.20)
Triglycerides (per 10 mg/dL ↑)	1.03 (0.99, 1.06)	1.02 (1.01,1.03)	1.01 (1.00, 1.02)	1.00 (0.98, 1.02)
Presence of hypertension	1.71 (1.11, 2.65)	1.20 (0.76, 1.90)	1.62 (0.91, 2.86)	1.53 (0.88, 2.66)
Systolic BP (per 10 mmHg ↑)	1.20 (1.07, 1.34)	1.11 (1.00, 1.24)	1.24 (1.09, 1.42)	1.10 (0.96, 1.26)
Diastolic BP (per 10 mmHg ↑)	1.19 (0.98, 1.45)	1.11 (0.91, 1.34)	1.11 (0.86, 1.45)	0.95 (0.74, 1.21)
Presence of diabetes mellitus	2.71 (1.44, 5.11)	3.03 (1.58, 5.78)	2.05 (0.95, 4.42)	1.62 (0.78, 3.38)
Framingham score imputed (per 1%↑)$	1.05 (1.02, 1.08)	1.04 (1.01, 1.07)	1.04 (1.00, 1.08)	1.02 (0.99, 1.06)
Framingham score actual (per 1%↑)$	1.12 (1.06, 1.18)	1.10 (1.03, 1.17)	1.11 (1.04, 1.19)	1.08 (0.98, 1.19)

* includes hospitalized myocardial infarction, ischemic strokes, coronary artery bypass grafting and percutaneous transluminal coronary angioplasty procedures.

** Age and sex-adjusted univariate estimates

$ Imputed risk score assigned 0 points to subjects with missing lipid values (in earlier years of the study). Analyses using the actual score were restricted to subjects with complete lipid values.

Table 4

Time-dependent predictors of cardiovascular events in psoriasis

	Hazard ratio (95% CI) for cardiovascular outcomes**			
	Any cardiovascular event	Ischemic events*	Heart failure	Cardiovascular death
Obesity (Body mass index ≥30 kg/m^2)	1.68 (1.11, 2.54)	1.15 (0.75, 1.75)	2.25 (1.33, 3.81)	1.37 (0.80, 2.33)
Dyslipidemia	1.70 (1.01, 2.87)	2.03 (1.10, 3.76)	1.18 (0.59, 2.38)	0.76 (0.40, 1.46)
Hypertension	1.97 (1.20, 3.22)	1.37 (0.81, 2.30)	2.04 (0.98, 4.24)	2.06 (0.90, 4.69)
Diabetes mellitus	2.26 (1.43, 3.58)	2.30 (1.45, 3.66)	2.16 (1.18, 3.95)	1.31 (0.73, 2.35)

*includes hospitalized myocardial infarction, ischemic strokes, coronary artery bypass grafting and percutaneous transluminal coronary angioplasty procedures.

**Age and sex-adjusted univariate estimates