

Cardiovascular Risk Profile of Patients with Psoriasis

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Introduction

Psoriasis is a common immune-mediated, inflammatory disease, affecting 2–3 per cent of the Caucasian population (1). The disease is considered as a genetically and clinically heterogeneous condition. Apart from skin, which is the primary target organ, other organs such as joints, gut and eyes may be involved (2–5).

The most common co-morbidity is psoriatic arthritis. However, other disorders, such as obesity, diabetes and cardiovascular disease (CVD) are associated to psoriasis (6–9). Several studies indicate that patients with psoriasis have an increased risk for

cardiovascular co-morbidity and mortality compared to that of the general population (6, 10–15).

The pathogenesis of increased CVD in patients with psoriasis is poorly understood. However, there are several possible biological factors, which may explain such a link:

Firstly, psoriasis appears to be associated with traditional risk factors for CVD that are key components of the metabolic syndrome, including increased BMI (16, 17), hypertension (18, 19), hyperlipidemia (20–22), Type II diabetes (6, 7, 9) and cigarette smoking (23–25). Secondly, recent evidence strongly suggests that chronic inflammation, a characteristic feature of psoriasis, per se may play a role in the initiation and progression of atherosclerosis (26, 27). Elevated levels of high-sensitive-C reactive protein (hs-CRP), a nonspecific marker of inflammation, is one of the emerging risk factors for CVD, and accumulated data show that increased hs-CRP levels can predict long-term risk for cardiovascular events (28, 29). Psoriasis is an inflammatory disease, and several studies have demonstrated an increased level of CRP in psoriatic patients (30–32). Other chronic inflammatory disorders, such as rheumatoid arthritis and systemic lupus erythematosus are also associated with an increased cardiovascular risk compared to that of the general population.

Thirdly, there is evidence that established treatments for psoriasis such as retinoids (33) and cyclosporin (34)

may induce hyperlipidemia which can promote future CVD. Finally, patients with chronic conditions such as psoriasis may experience significant impairment of life quality both due to clinical symptoms, and sometimes also due to cumbersome therapies. Thus, the disease may negatively affect the patient's lifestyle. It is conceivable that a sedentary lifestyle, due to underlying depression, along with lack of physical activity, significantly contribute to increased cardiovascular morbidity in a subset of psoriasis patients.

Cardiovascular mortality in psoriasis

Although several previous and recent studies have demonstrated an association between cardiovascular events and psoriasis, the magnitude of the contribution of CVD towards mortality among psoriatics has not been precisely estimated. To validly assess the risk for cardiovascular death among psoriasis patients, we used Swedish nation-wide registries to follow up both inpatients and outpatients with psoriasis. Cardiovascular mortality was compared to that of the general population.

Patients hospitalized for psoriasis as the main diagnosis in dermatological wards in Sweden in 1964–1995 were identified through the Swedish Inpatient Registry. For each discharge, the registry provides the date of admission and discharge, main and contributing discharge diagnosis, surgical procedures, department and hospital, as well as the individual's national

registration number. Diagnoses are coded according to the International classification of Diseases (ICD 7-9). Since 1987, the Swedish National Inpatient Registry has nationwide coverage. In 1969, the register covered 60% of the Swedish population, in 1978 this percentage was 75%, and by the end of 1983 it was 85%. In total, 10,667 psoriatic inpatients were identified. Only individuals with no prior discharge diagnosis of CVD were included. Thus, in the end 8,991 psoriatic inpatients were analyzed.

To represent an outpatient cohort, we used the register of the members of the Swedish psoriasis association during 1987; the year the register was established. In total, 19,757 members were identified. Members of the Swedish psoriasis association represent a cross-section with a wide range of disease severity, but with most having either mild disease or disease that is controlled by outpatient treatment. An estimated 5% are

supporting members without a diagnosis of psoriasis and are included in the outpatient cohort.

In all, the cardiovascular mortality was 50% greater in patients hospitalized at least once for psoriasis compared to that of the general population (standardized mortality ratio, SMR 1.52; 95% confidence interval, CI 1.44-1.60), whereas psoriasis outpatients had no increase in risk (SMR 0.94; 95% CI: 0.89-0.99) (Table I).

There was a gradual increase in risk with increasing duration of follow-up, and with increasing number of admissions (p for trend <0.001). In general, the relative risk of death from cardiovascular disease was higher among patients who were admitted at a young age (p for trend <0.001; SMR 2.62, 95% CI: 1.91-3.49, for patients <40 yrs) (Table I). Also, the number of admission seemed to have an impact. The highest relative risk was

increased more than threefold among younger patients admitted more than three times compared to that of the patients who were admitted only once (HR 3.13, 95% CI: 1.55-6.32) (Table II). There were no differences between sexes.

Taken together, the data suggest that while psoriasis per se does not appear to increase the risk for cardiovascular death, severe disease, measured as repeated hospitalizations, and early age at first admission is associated with increased risk for mortality from cardiovascular causes. It seems that the excess risk increases with increasing duration of follow-up and increasing number of the admissions, implicating that the inflammation process may contribute to the risk for subsequent cardiovascular mortality associated with psoriasis. However, the biological mechanisms underlying this association are complex and confounding bias cannot be precluded. Longitudinal perspective studies that consider other contributed factors such as concomitant obesity, hyperlipidemia and cigarette smoking are needed.

Lipid profile in psoriasis

An atherogenic lipid profile is a risk factor for the development of CVD. In particular, increased concentration of total cholesterol (C), triglycerides (TG), very low density lipoprotein (VLDL), low density lipoprotein, (LDL) and lipoprotein (a) are each individually associated with increased prevalence of CVD morbidity and mortality in the general population. However,

Table I. Standardized Mortality Ratios (SMRs) and 95% confidence intervals (CIs) for the association between at least one hospitalization for psoriasis and cardiovascular death.

Variables	Obs ^a	Exp ^b	SMR ^c	95% CI
Total	1,529	1,007	1.52	1.44-1.60
Age at first hospital admission				
00-19	0	0,99	0.00	0.00-3.74
20-39	46	18	2.62	1.91-3.49
40-59	453	237	1.91	1.74-2.09
60+	1,030	750	1.37	1.29-1.46
Number of hospital admissions				
One time	1,529	1,007	1.52	1.44-1.60
Two times	851	501	1.70	1.58-1.81
Three times or more	610	334	1.82	1.68-1.98

^aObserved number of deaths

^bExpected number of deaths

^cThe relative risk was calculated by Standardized Mortality Ratios (SMRs) and 95% confidence interval (CIs).

Table II. Stratified analysis of the joint effect of number of admissions and age at first admission.

Variables	Number of admissions				
	1 Reference	2 HR ^a	95% CI ^b	3 or more HR ^a	95% CI ^b
Age at first hospital admission					
00-39	1.00	2.71	1.15-6.41	3.13	1.55-6.32
40-59	1.00	1.11	0.84-1.47	1.43	1.16-1.77
60+	1.00	1.18	0.99-1.42	1.35	1.17-1.57

^aHazard Ratios

^bConfidence Intervals

recent evidence suggest that the risk of CVD is more accurately predicted by looking at the assembly of lipids, and the composition and the metabolic function of the lipoproteins rather than solely the level of each variable.

Furthermore, elevated levels of CRP is one of the emerging risk factors for CVD and accumulated data points to increased CRP concentration as a predictor for long-term risk for cardiovascular events (28, 29).

Several studies have consistently shown an aberrant lipoprotein profile associate with psoriasis. However, the studies are not consistent, and they involve highly heterogeneous study populations and/or have not taken the duration of psoriasis or previous treatments into account.

To assess the blood lipid profile in patients with psoriasis at the initial stage of the disease, 200 patients derived from the Stockholm Psoriasis Cohort (SPC) were investigated, comparing plasma concentrations of lipids, lipoproteins and apolipoproteins with those of matched controls.

The SPC, which was initiated in 2001, consists of consecutive patients with recent onset (<12 months) of psoriasis in the Stockholm county. The present study includes the first 200 eligible patients. We used the Swedish Population Registry to identify a set of control subjects (n=285), selected as a stratified random sample, taking age, sex and residence area (same as when the corresponding cases obtained the diagnosis of psoriasis) into consideration. All individuals with ongoing treatment for hyperlipidemia and/or medication affecting the lipid metabolism were excluded.

Psoriasis patients manifested a significant atherogenic lipoprotein profile. Adjustment for established risk factors, such as age, sex, smoking, physical exercise, BMI, alcohol consumption and systolic blood pressure did not affect the results.

Furthermore, patients had a significantly higher hs-CRP concentration, which positively correlated with the total plasma cholesterol concentration, supporting the notion that the potentially systemic nature of the inflammatory processes underlying

ing psoriasis may be considered to promote the risk for future cardiovascular disease. However, further larger studies are needed to confirm this hypothesis.

In conclusion, although the management of psoriasis should follow existing guidelines, physicians should consider closely monitoring patients with psoriasis with a focus on risk factors for CVD, including body weight, hypertension and hyperlipidaemia, and adopt treatment regimens to control disease activity.

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