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A Review of the Epidemiology of Cardiovascular Comorbidities in Psoriasis

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Abstract Several epidemiologic studies suggest that there is an association between psoriasis and cardiovascular comorbidities, possibly due to overall systemic inflammation. Psoriasis is an independent risk factor for cardiovascular disease and mortality that is also associated with many of the traditional cardiovascular risk factors. This article summarizes important studies that demonstrate an association between psoriasis with smoking and alcohol intake, as well as increased risk of psoriasis patients for atrial fibrillation, atherosclerosis, coronary artery calcification, type 2 diabetes, dyslipidemia, hypertension, metabolic syndrome, obesity, peripheral vascular disease, myocardial infarction, stroke, and cardiac death.

Keywords Atherosclerosis · Cardiovascular disease · Cardiovascular risk factors · Inflammation · Psoriasis · Methotrexate · Tumor necrosis factor-α inhibitor · Myocardial infarction

Introduction

Psoriasis is a common, chronic, T-lymphocyte–mediated inflammatory dermatosis. It affects nearly 2% to 3% of the world's population in all geographic regions, with slight variation in prevalence depending on ethnicity; approximately 7.5 million people in the United States are affected [1–3].

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To date, the majority of comorbidity research in dermatology has been conducted in psoriasis [4]. Recent epidemiologic data point toward an association between psoriasis and increased prevalence of cardiovascular (CV) disease, including atrial fibrillation, atherosclerosis, coronary artery calcification, diabetes type 2, dyslipidemia, hypertension, metabolic syndrome, obesity, peripheral vascular disease, myocardial infarction, stroke, and cardiac death. Psoriasis is also associated with smoking and alcohol intake. In light of these facts, the observed increase in cardiovascular disease (CVD) and mortality among psoriasis patients is compounded by the cumulative effect of traditional risk factors for CV disease. This review summarizes important epidemiologic findings with a focus on the past 3 years that provide new data in regards to an association between psoriasis and CVD in a way that is relevant to clinicians practicing in the community. We searched Pubmed using the terms "psoriasis" and "atrial fibrillation, atherosclerosis, coronary artery calcification, diabetes type 2, dyslipidemia, hypertension, metabolic syndrome, obesity, peripheral vascular disease, myocardial infarction, stroke, cardiovascular disease, or cardiovascular mortality," and included retrospective cohort studies, case-control studies, meta-analyses, cross-sectional studies, and all prospective studies but did not include case reports. We did not include articles that discussed the affect of psoriasis therapy on cardiovascular risk factors or events, which are beyond the scope of this article. With these search parameters, we were able to find 50 articles.

Atrial Fibrillation

Among the many complications of CVDs, atrial fibrillation (AF) is the most common cardiac arrhythmia that puts

patients at a significantly increased risk of stroke, as high as seven times that of the general population. Ahlehoff et al. [5] have shown that psoriasis is associated with increased risk of AF, as patients with mild psoriasis had a higher risk of AF with adjusted rate ratios of 1.50 (95% CI, 1.21–1.86) and 1.16 (95% CI, 1.08–1.24) in patients aged <50 years and ≥50 years, respectively. Patients with severe psoriasis had a higher risk of AF, with rate ratios of 2.98 (95% CI, 1.80–4.34) in patients aged <50 years and 1.29 (95% CI, 1.01–1.65) in patients ≥50 years. On the other hand, in a retrospective analysis study that examined coronary heart disease (CHD) and stroke risk in a total of 1,591 psoriasis patients (1,082 moderate psoriasis patients with psoriasis area and severity index [PASI] scores ≥10 and ≤20, and 509 severe psoriasis patients with >20 PASI scores), a total of seven AF incidents were observed in the moderate group and none were observed in the severe group. [6].

Atherosclerosis

Atherosclerosis is the underlying major cause of myocardial infarction (MI), ischemic stroke, and peripheral arterial disease (PAD). Besides the traditional major cardiac risk factors, a large body of literature suggests that chronic systemic inflammatory conditions that promote elevation of C-reactive protein, interleukin-6, or psychosocial stress may contribute to the eventual formation of atherosclerosis [7]. Psoriasis is a chronic systemic inflammatory disease that may promote the formation of atherosclerosis, much as the association between atherosclerosis and systemic lupus erythematosus and rheumatoid arthritis [8, 9], by promoting proinflammatory states.

Shapiro et al. [10] have shown the age-adjusted proportion of atherosclerosis was significantly higher in psoriasis patients compared to the control group with an odds ratio (OR) of 1.28 (95% CI, 1.04–1.59) [10]. A study by Prodanovich et al. [11•] has also shown that patients with psoriasis have increased prevalence of ischemic heart disease (IHD), with an OR of 1.78 (95% CI, 1.51–2.11) compared to controls, as well as increased cerebrovascular and peripheral vascular diseases, with ORs of 1.70 (95% CI, 1.33–2.17) and 1.98 (95% CI, 1.38–2.82), respectively. Also, in a study that investigated a possible association between psoriasis and prevalent use of CV medications such as antihypertensives, anticoagulant and antiplatelet agents, digoxin, nitrates, lipid-lowering drugs, and antidiabetic drugs, psoriasis patients used significantly more of these drugs compared to the matched control group [12]. In another study that examined the incidence of risk factors for MI and other vascular diseases in patients with psoriasis, patients with psoriasis had higher risk of incident PAD, with a hazard ratio (HR) of 1.29 (95% CI, 1.13–1.47) [13].

Coronary Artery Calcification

The ability to detect and quantify coronary artery calcium deposition using currently available imaging studies has created significant advancement in diagnostic capability for coronary artery disease (CAD). In a study that examined the prevalence and degree of coronary artery calcification (CAC) using non-contrast, row spiral computed tomography in patients with psoriasis, CAC was more prevalent in patients with psoriasis when compared to the controls: calcification was present in 59.4% of patients with psoriasis compared with only 28.1% in the control population, with an OR of 2.11 (P=0.015) [14]. Also, the severity of CAC was more pronounced in psoriasis group, with a score of 3.7 versus a score of 0.0 in the control group according to the Agatston CAC scoring system.

Diabetes Mellitus Type 2

Diabetes mellitus type 2 is a metabolic disorder that is characterized by unregulated blood glucose level in the context of insulin resistance and relative insulin deficiency. It is a component of metabolic syndrome and is a known risk factor for CVDs. Long-term untreated diabetes type 2 can increase the risk of MI, stroke, PAD, diabetic retinopathy, as well as kidney failure. There is abundant and accumulating evidence on the classification of psoriasis as a systemic disease that exhibits a host of co-morbidities, including insulin resistance and type 2 diabetes. Boehncke et al. [15] have suggested that patients with psoriasis without overt diabetes mellitus often exhibit evidence of insulin resistance, supporting the concept of insulin resistance, which is reduced uptake of glucose by metabolically active cells upon exposure to insulin. The study contributes insulin resistance to a chronic systemic inflammatory state and the elevated proinflammatory cytokines secondary to it.

Work by Gelfand et al. [16] has elucidated existence of a strong association between diabetes mellitus (independent of obesity) and severe psoriasis, as patients with psoriasis were more likely to have diabetes as compared with that of controls. Also, in a Shapiro et al.'s [10] study that analyzed the association between psoriasis, diabetes, and atherosclerosis, the age-adjusted proportion of diabetes was significantly higher in psoriasis patients compared with the control group (OR 1.27; 95% CI, 1.1–1.48). Specifically, extensive use of very potent topical steroids as well as use of systemic therapy for psoriasis was associated with a significantly higher proportion of diabetes, which suggests that the proportion of diabetes in psoriasis patients may be associated with psoriasis severity. Also, in a study that examined a potential association between psoriasis and CV risk factors in one particular ethnic group, there was higher prevalence

of metabolic syndrome, CVDs, hypertension, and hyperlipidemia in patients with psoriasis compared to the controls [17•].

In a recent study that analyzed psoriasis and the risk of developing diabetes and hypertension in women in the United States, women with psoriasis were at increased risk of developing type 2 diabetes compared with women without psoriasis (relative risk [RR] 1.63; 95% CI, 1.25–2.21), even after adjusting for body mass index (BMI), smoking status, alcohol intake, and physical activity [18•]. This study finding has demonstrated an increased risk of diabetes in women with psoriasis, confirming the findings from previous cross-sectional studies that have suggested a positive association between psoriasis and diabetes. In a large General Practice Research Database (GPRD) study that analyzed incidence rates of new-onset diabetes between patients with psoriasis and a comparison group without psoriasis, the risk of incident diabetes was increased for patients with psoriasis versus the control group, and the risk increased with psoriasis duration and severity and was not dependent on high BMI alone [19]. Specifically, of the total of 65,449 patients in the study population, 1,061 incident cases of diabetes were identified. Fifty-nine percent of these had a history of psoriasis, rendering an incidence rate ratio of 1.36 (95% CI, 1.20–1.53). Also, the adjusted OR for patients with ≥2 years disease duration and >2 prescriptions per year for oral psoriasis treatment was found to be 2.56 (95% CI, 1.11–5.92). In another study that analyzed the incidence of risk factors for MI and other vascular diseases in patients with psoriasis, the incidence of having diabetes was increased among patients with psoriasis compared to the controls, with a hazard ratio (HR) of 1.33 (95% CI, 1.25–1.42) [13].

Dyslipidemia

Dyslipidemia is a component of metabolic syndrome that may contribute to the progression of atherosclerosis and further CAD. In a study that examined an association between dyslipidemia and oxidative stress in mild and in severe psoriasis patients, elevated low-density lipoprotein (LDL) cholesterol was prevalent in psoriasis patients, and the degree of elevation correlated with the severity of psoriasis [20]. Also, there were elevated levels of serum triglycerides, very low-density lipoprotein cholesterol, lipoprotein (a), and apolipoprotein B in psoriasis patients compared to the control group. In the GPRD study by Gelfand et al. [16] that examined the risk of MI in patients with psoriasis, hyperlipidemia was observed in both mild and severe psoriasis groups. Hyperlipidemia was also more frequent among patients with psoriasis in general compared to non-psoriatic patients, with an HR of 1.17 (95% CI: 1.11–1.230) [18].

In a study conducted by Koebnick et al. [21••] that examined the association of psoriasis and elevated blood lipids in overweight and obese children, mean total cholesterol, LDL cholesterol, triglycerides, and alanine aminotransferase (ALT) were significantly higher in children with psoriasis compared with children without psoriasis after adjusting for BMI. Among the overweight to extremely obese adolescents, children with psoriasis had significantly higher mean total cholesterol (P=0.020), LDL cholesterol (P=0.007), triglycerides (P=0.014), and ALT (P=0.016) compared to those without psoriasis. Mean high-density lipoprotein (HDL) cholesterol was not significantly different between the two groups.

Hypertension

In recent years, many population studies have examined hypertension frequency in psoriasis patients. Hypertension was found to be two times more common in patients with psoriasis than in the general population [22, 23]. In Gelfand et al.'s GPRD study [16], hypertension was present in 20% of patients with severe psoriasis, 15% of patients with mild psoriasis, and 12% of controls.

Quereshi et al. [18•] have shown that the patients with psoriasis were at increased risk for development of hypertension, with a RR of 1.17 (95% CI, 1.06–1.30) when compared to the control group. In another retrospective case-control study, psoriasis patients with hypertension were found to have more severe hypertension and required more medications to control blood pressure when compared to the control group [24]. These study results reinforce an important need for dermatologists to routinely screen patients with psoriasis for hypertension.

Metabolic Syndrome

Metabolic syndrome is a name for a group of risk factors that occur together and increase the risk for CAD, stroke, and diabetes mellitus type 2. In a study conducted by Love et al. [25], patients with psoriasis had increased prevalence of the metabolic syndrome. The univariate and multivariate ORs for patients with psoriasis and the metabolic syndrome were 2.16 (95% CI, 1.16–4.03) and 1.96 (95% CI, 1.01–3.77), respectively. Abdominal obesity and disturbances in lipid profiles were the most important factors leading to the increased prevalence of the metabolic syndrome in psoriasis patients. In another study that analyzed the levels of triglyceride, LDL cholesterol, HDL cholesterol, and erythrocyte sedimentation rate (ESR) in psoriasis patients, the levels of ESR, LDL, and triglyceride were all elevated, whereas HDL cholesterol level was low in psoriasis group compared to the

control population [26]. Also, psoriasis patients manifested significant lipid abnormalities, including notably higher very low-density lipoprotein and HDL fractions, which suggest that lipid abnormalities in psoriasis may be genetically acquired [27]. In Gelfand et al.'s GPRD study [16], patients with both mild and severe psoriasis were found to have increased prevalence of diabetes mellitus, hyperlipidemia, and hypertension compared to the controls. Also, a study showed a significant correlation between the PASI score and insulin secretion in patients with moderate-to-severe plaque-type psoriasis. The PASI score was significantly correlated with serum resistin levels, a cytokine known to be increased in insulin resistance, which shows that patients with psoriasis without overt diabetes mellitus exhibit insulin resistance [28].

Obesity

Obesity, more specifically abdominal obesity, is a component of metabolic syndrome that increases the risk of developing CVD. Obesity, defined as BMI ≥30 kg/m^2, was found to be more common in patients with psoriasis, occurring up to two times more frequently than in the general population [29]. Interestingly, obesity appeared to be the consequence of psoriasis, not a risk factor for the onset of disease, as overweight and obesity often occurs after the onset of psoriasis. Also, obesity did not have an impact on the response to therapies, including methotrexate, psoralen-UV-A, and topical corticosteroids, in patients with plaque psoriasis as compared to non-obese psoriasis patients. Also, obesity was found to be more prevalent in patients with psoriasis, with an OR of 1.79 (95% CI, 1.55–2.05) when compared to the control group, as well as being more frequent in patients with more severe psoriasis compared to mild psoriasis, with an OR of 1.47 (95% CI, 1.32–1.63) [16]. In a study by Kaye et al. [13], the incidence of being obese was more prevalent in patients with psoriasis compared to the control cohort, with an HR of 1.21 (95% CI, 1.14–1.23).

Overweight and obesity were found to be associated with higher odds of psorasis in children [21••]. The ORs for psoriasis increased with an increase in body weight: the OR for psoriasis was 0.68, 1.00, 1.31, 1.39, and 1.78 (1.49–2.14; *P* value <0.001) for underweight (BMI-for-age <5th percentile), normal weight (BMI-for-age ≥5th and <85th percentile), overweight (BMI-for-age ≥85th percentile or a BMI ≥25 kg/m^2 and BMI-for-age <95th percentile or a BMI <30 kg/m^2), moderately obese (BMI-for-age ≥95th percentile or a BMI ≥30 kg/m^2 and BMI-for-age <1.2×95th percentile or a BMI <35 kg/m^2), and extremely obese children (BMI-for-age ≥1.2×95th percentile or a BMI ≥35 kg/m^2), respectively.

In the Nurses' Health Study II, which prospectively examined the relationships between BMI, weight change, waist circumference, hip circumference, waist-hip-ratio, and incident psoriasis in 78,626 women over 14-year period by information on weight, height, and weight at the age of 18 years collected on biennial mailed questionnaires, there was a graded positive association between BMI measured at multiple time points and the risk of incident psoriasis [30]. Compared to a BMI ≥21.0 to 22.9, the multivariate RRs of psoriasis were 1.40 (95% CI, 1.13–1.73) for a BMI of ≥25.0 to 29.9, 1.48 (95% CI, 1.15–1.91) for a BMI of ≥30.0 to 34.9, and 2.69 (95% CI, 2.12–3.40) for a BMI of ≥35.0 (*P* for trend <0.001). Also, weight gain from the age of 18 years, higher waist circumference, hip circumference, and waist-to-hip ratio were all associated with a higher risk of incident psoriasis (all *P* values for trend <0.001). Also, in a study that analyzed the association of psoriasis and smoking habit, BMI, and stressful life events, the frequency of psoriasis varied significantly in relation to BMI: ORs for plaque psoriasis were 1.6 (95% CI, 1.2–2.2) and 2.2 (1.5–3.4) for BMI groups 26 to 29 and ≥30, respectively, when compared to BMI <26 [31].

Smoking

It is well documented that smoking is widespread among patients with psoriasis. In a recent study, patients with psoriasis were more likely to be smokers when compared to patients without psoriasis [29]. An interesting finding of this study is that smoking appears to have a role in the onset of psoriasis, as the majority (78%) of the study participants indicated that they began smoking before the onset of disease, whereas obesity appears to start after the onset of psoriasis. In another study that examined smoking habits in US women, the risk of having psoriasis was 37% higher among past smokers and 78% higher among current smokers when compared to women who never smoked [32]. In another study that analyzed both alcohol and tobacco-related causes of death among patients with psoriasis, patients with psoriasis who smoked were found to have increased standardized mortality ratio (SMR) for smoking-related causes of death such as pancreatic cancer, lung cancer, and CHD when compared to nonsmoking patients with psoriasis [33]. Also, the risk of psoriasis was higher in former and current smokers than in never-smokers: OR for former smokers was 1.9 (95% CI, 1.3–2.7), OR for current smokers was 1.6 (95% CI, 1.2–2.2), 1.7 (95% CI, 1.1–2.5), 1.7 (95% CI, 1.0–3.2) for 1 to 10 cigarettes per day current smokers, 11 to 20 cigarettes per day current smokers, and ≥21 cigarettes per day current smokers, respectively [31]. This study shows that a dose response with smoking and risk of psoriasis has not been well established to date. Regardless of whether there is a positive relationship between dose response with smoking and risk of psoriasis, these study findings along with other well-established hazardous health

effects of smoking provide evidence for the need for smoking cessation in those with psoriasis.

Alcohol Intake

There has been much focus on the association between alcohol consumption and psoriasis. In a study that examined an association between alcohol consumption and the risk for psoriasis in US women, the women with history of non-light beer intake other than light beer, white wine, red wine, or liquor, were at increased risk of developing psoriasis compared to women who did not drink alcohol [34•]. Women who drank at least 5 non-light beers per week (one drink was defined as 12.8 g of alcohol) were 1.8 times more likely to develop psoriasis compared with women who abstained from alcohol. On the other hand, lower intake of non-light beer and intake of other types of alcohol beverages did not influence the risk of developing psoriasis. Poikolainen et al. [33] have shown that the excess mortality rate for all causes of death directly related to alcohol in both men and women was higher in patients with psoriasis compared to the control group, with SMR of 4.46 (95% CI, 3.60–5.45) and 5.60 (95% CI, 2.98–8.65), respectively. However, this study did not directly measure alcohol intake in the cohort group, and thus the observed association cannot be explained as a consequence of alcohol intake history.

Myocardial Infarction

Among the many CVDs, MI is one of the complications of long-term untreated atherosclerosis of coronary arteries. Many studies in the past have suggested that psoriasis is associated with a higher prevalence of CVDs, including MI [16]. Gelfand et al.'s [16] cohort study reported an increased rate of MI in patients with psoriasis compared with a psoriasis-free population. For a 30-year-old patient with mild or severe psoriasis, the RR of having an MI was 1.29 (95% CI, 1.14–1.46) and 3.10 (95% CI, 1.98–4.86), respectively. For a 60-year-old patient with mild or severe psoriasis, the RR of having an MI was 1.08 (95% CI, 1.03–1.64) and 1.36 (95% CI, 1.13–1.64), respectively. MI was observed to be more prevalent in patients with psoriasis in central China. Even after adjusting for systemic therapies and CV risk factors such as obesity, diabetes, hypertension, hyperlipidemia, smoking, age, and sex, the ORs for having an MI were 1.72 (95% CI, 1.29–2.30) and 2.01 (95% CI, 1.45–2.79) in mild and severe psoriasis group, respectively, when compared to the controls [35•]. Also, severe psoriasis (receiving a psoriasis diagnosis and systemic therapy) was found to be a risk factor for major adverse cardiac events, defined as occurrence of nonfatal MI, nonfatal stroke, or death due to etiology [36•]. The incidence of major adverse cardiac events per 1,000 person-years was 16.4 (95% CI, 14.3–18.9) and 11.6 (95% CI, 10.7–12.6) in patients with psoriasis and patients without psoriasis, respectively. Even after adjusting for traditional CV risk factors (age, sex, hyperlipidemia, hypertension, smoking, and diabetes), severe psoriasis was found to be a risk factor for major cardiac events, with an HR of 1.53 (95% CI, 1.26–1.85). This study also estimated that the 10-year risk of major adverse cardiac events to be approximately 6.2%. In addition, prognosis following first-time MI in patients with psoriasis was found to be significantly impaired in another study. The incidence rates per 1,000 patient-years for all-cause mortality were 119.4 (95% CI, 117.2–138.3) and 138.3 (95% CI, 114.0–167.7) for patients without and with psoriasis, respectively, and the adjusted HR associated with psoriasis was 1.18 (95% CI, 0.97–1.43) [37].

In a large population-based study that examined the incidence or risk of acute MI developing after the diagnosis of psoriasis in Asian populations using a nationwide Taiwanese population-based claims database, the hazard of acute MI was 2.10 times greater (95% CI, 1.27–3.43; $P=0.004$) in patients with psoriasis compared with controls even after adjusting for possible confounders [38•].

In a prospective study that analyzed the prevalence of CVD morbidities in patients with psoriatic arthritis (PsA), there were more observed events for MI, angina, and hypertension in the PsA group compared with the general population, The standardized prevalence ratios (SPRs) for MI (2.57; 95% CI, 1.73–3.80), angina (1.97; 95% CI, 1.24–3.12), and hypertension (1.90; 95% CI, 1.59–2.27) were statistically significant, whereas the SPRs for congestive heart failure (1.19; 95% CI, 0.50–2.86) and cerebrovascular accident (0.91; 95% CI, 0.34–2.43) were not [39•]. Also, in the same study that showed increased observed findings of diabetes in patients with psoriasis, psoriatic patients had higher risks of incident MI, with a HR of 1.21 (95% CI, 1.10–1.48) [18•].

On the other hand, there are a few studies that propose that psoriasis is not an independent risk factor for CVD, including MI. Stern et al. [40] recently proposed that even after adjusting for confounding and bias, psoriasis is unlikely to be a clinically relevant risk factor for MI. His reasoning was based on applying five criteria advocated by the US Preventative Task Force for evaluating new risk factors for heart disease [41]. For example, one of the five criteria for evaluating a risk factor for CVD should be easily and reliably measured. Stern et al. [39] comment that severe psoriasis lacks a good measurement basis to accurately classify an affected person's severity of psoriasis for purposes of CVD risk stratification. In another PUVA follow-up cohort study by Stern et al. [42], very severe psoriasis was associated with increased noncardiovascular mortality such as liver disease, with a SMR of 1.1 (95% CI, 2.76–5.70) and

causes of death other than cancer or CVD, with a multivariate HR of 1.56 (95% CI, 1.14–2.13). However, psoriasis was found to be not a significant independent risk factor for CVD, as the number of deaths due to CVD was nearly identical as compared with the general population (SMR= 1.02; 95% CI, 0.9–1.6) [42].

Gelfand et al. [43•] have recently made a comment regarding the PUVA follow-up study, saying the study results are in contrast to a large and growing body of literature that indicate patients with more severe psoriasis have a clinically significant increased risk of mortality in general and CVD in particular. Gelfand et al. [43•] point out that the discrepancy between the mortality experience in the PUVA follow-up study and studies of psoriasis patients identified using population-based methods can be explained by the difference in the basic principles of epidemiologic study design. For example, to minimize bias in a study, modern epidemiologic studies rely on "population-based" designs. In contrast to a typical population-based study, the PUVA follow-up study was not based on this model, as subjects were derived from a clinical trial of a novel therapeutic intervention (selection bias). Also, the PUVA study carries an information bias, as there were different approaches used to ascertain the cause of death: the mortality experience in psoriasis patients was determined on the basis of telephone interviews with patients, clinicians, or patients' relatives or extraction from death certificates and reviewed by the authors if there was ambiguity (15% of cases), whereas death rates for the US population were derived from routine data sources. Also, they comment that the study failed to show any association between severe psoriasis and obesity or between obesity and CV mortality in the setting of extensive literature supporting these associations [43•].

Wakkee et al. [44] have found interesting results in their study that analyzed the risk of ischemic heart disease (IHD) hospitalizations and acute MI in patients with psoriasis and a matched reference cohort. The age- and gender-adjusted HR for IHD was comparable between the two cohorts: 1.10 (95% CI, 0.99–1.23). After adjusting for potential confounders such as earlier use of antihypertensive, antidiabetic, and lipid-lowering medications, the HR for IHD decreased further to 1.05 (95% CI, 0.95–1.17). The age- and gender-adjusted HR for acute MI was 0.99 (95% CI, 0.84–1.17) and the adjusted HR for IHD was 0.94 (95% CI, 0.80–1.11). These study findings suggest the cause-and-effect association between psoriasis and IHD or acute MI is still unclear and needs further investigation. In a study by Schmitt et al. [45] that explored the association between psoriasis, psychiatric morbidities (depression, stress-related disorders, behavioral disorders, and schizophrenic disorders), cardiovascular risk factors (diabetes, hypertension, obesity, and dyslipidemia), and cardiovascular events (MI, stroke), unlike relatively significant associations found between psoriasis and psychiatric morbidities and cardiovascular risk factors, MI, and stroke were found to be not strongly associated with psoriasis: the OR for MI was 1.14 (95% CI, 0.81–1.62) and OR for stroke was 0.97 (95% CI, 0.61–1.54) [45].

Stroke

Stroke is a major cause of morbidity and mortality. It can be classified into two major categories: ischemic and hemorrhagic. About 87% of total stroke incidences are caused by ischemia and the remaining by hemorrhage. A recent study by Gelfand et al. [46••] has demonstrated that psoriasis, particularly severe cases, is an independent risk factor for stroke. The unadjusted overall risk of stroke per 1,000 person-years was slightly lower in mild psoriasis patients (3.7; 95% CI, 3.5–3.8) compared to controls (4.05; 95% CI, 4.0–4.1). The unadjusted overall risk of stroke per 1,000 person-years was higher in severe psoriasis patients (6.1; 95% CI, 4.8–7.6) than in controls (4.4; 95% CI, 3.8–5.0). Interestingly, when the major risk factors for stroke (age, sex, diabetes, history of stroke or transient ischemia attack, hyperlipidemia, hypertension, smoking) were adjusted, both mild and severe psoriasis were independent risk factors for stroke, with HRs of 1.06 (95% CI,1.0–1.1) and 1.43 (95% CI, 1.1–1.9), respectively.

In a study that attempted to estimate the 10-year risks of CHD and stroke in patients with moderate to severe psoriasis and to compare risks between patients and the general population, the estimated 10-year risks of developing stroke using the prediction point-system method of D'Agostino et al. [47] developed on the basis of Framingham Heart Study estimations, was 11.8% greater in patients with moderate to severe psoriasis compared with the general population [6]. Also, the 10-year stroke risk stratified by psoriasis severity increased with PASI scores: in patients with PASI scores ≥10 and ≤20, 75.5% had low risk of stroke, 16.3% had intermediate risk of stroke, and 8.2% had high risk of stroke. In patients with PASI scores >20, 69.3% had low risk of stroke, 19.8% had intermediate risk of stroke, and 10.9% had high risk of stroke. Ahlehoff et al. [5] also have shown that patients with psoriasis were at increased risk of disease severity-dependent ischemic stroke, with RRs of 1.97 (95% CI, 1.66–2.34) and 2.80 (95% CI, 1.81–4.34) in patients aged <50 years with mild and severe psoriasis, and RRs of 1.13 (95% CI, 1.04–1.21) and 1.34 (95% CI, 1.04–1.71) in patients aged ≥50 years with mild and severe psoriasis, respectively.

Cardiac Death

It has been reported that patients with severe psoriasis have a 3- to 4-year average decrease in their life expectancy,

comparable with the estimated reduction in the longevity of patients with hypertension [48]. This shortened lifespan is likely due in part to increased prevalence of CAD, which is the most common cause of death in patients with psoriasis. In an epidemiologic nationwide Danish study, psoriasis was found to be associated with increased risk of adverse CV events and all-cause mortality, as the event rates and rate ratios of all-cause mortality, CV death, MI, coronary revascularization, stroke, and a composite of MI, stroke, and CV death were all increased in patients with psoriasis compared with matched controls [21••]. The overall rate ratios for the composite endpoint were 1.2 (95% CI, 1.14–1.25) and 1.58 (95% CI, 1.36–1.82) for mild and severe psoriasis, respectively. The corresponding rate ratios for CV death were 1.14 (95% CI, 1.06–1.22) and 1.57 (95% CI, 1.27–1.94). This study finding supports the concept that psoriasis is a clinically significant independent risk factor for CV comorbidities, including cardiac death.

In a recent GPRD study by Mehta et al. [49••], severe psoriasis was found to be a significant independent risk factor for CV mortality even after adjusting for traditional CV risk factors. The unadjusted overall risk of mortality due to CVD per 1,000 person-years in patients with severe psoriasis was 8.75 (95% CI, 7.18–10.56) and 6.19 (95% CI, 5.51–6.93) in unexposed patients. After adjusting for the major CV risk factors, severe psoriasis was found to be a significant independent risk factor for CVD mortality, with an HR of 1.57 (95% CI, 1.26–1.96). In another GPRD study by Abuabara et al. [50•], severe psoriasis was found to be associated with an increased risk of mortality from CVD, with an HR of 1.57 (95% CI, 1.26–1.96) and other diseases including malignancies (HR 1.41; 95% CI, 1.07–1.86), chronic lower respiratory disease (HR 2.08; 95% CI, 1.36–9.72), infection (HR 1.65; 95% CI, 1.26–2.18), kidney disease (HR 4.37; 95% CI, 2.24–8.53), and unknown causes (HR 1.44; 95% CI, 1.09–1.88). The absolute and excess risk of death was highest for CVD, with values of 61.9 and 3.5 deaths annually per 1,000 patients, respectively, in the study.

Conclusions

The association between CVD and psoriasis is an area of research in its infancy and largely limited to retrospective data analysis of patient data sets. Evolving number of epidemiologic data indicate that there may exist an association between psoriasis, especially severe psoriasis, with increased prevalence of many types of CVD. In part, this increase may be explained by the higher prevalence of traditional CV risk factors among patients with psoriasis as compared with matched control groups. Several studies point that the increased frequency of CVD and mortality found in patients with psoriasis could be due to a mere cumulative effect of higher prevalence of CV risk factors in psoriasis patients. Nevertheless, inflammation appears to serve as a common link between psoriasis and CV comorbidities, as both entities share similar pathogenic mechanisms of disease process. We believe patients with psoriasis, especially in moderate to severe disease, should be educated about their potential increased risk for developing CVD and undergo appropriate medical evaluations and treatment of modifiable risk factors.

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