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Psoriasis and Cardiovascular Comorbidities

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Review Article

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Abstract: Psoriasis is one of the most prevalent T-cell-mediated chronic inflammatory disorders affecting the skin, scalp, nails, and joints. Its pathophysiology is characterized by immune responses mediated by type 1 and type17 helper T lymphocytes and synthesis of various cytokinesthat produce inflammation of the skin and joints. In recent years, several studies demonstrated that psoriasis is associated with an increased risk of various cardiovascular diseases.This report synthesizes the current understanding of the prevalence and characteristics of cardiovascular comorbidities in patients with psoriatic disease, and the importance of screening for and treating modifiable cardiometabolic risk factors.

Keywords: cardiovascular disease; atherosclerosis; inflammatory disorders; T-cell-mediated; metabolic syndrome.

INTRODUCTION

Psoriasis is a recalcitrant disease of chronic and systemic inflammation affecting approximately 2- 3% of the world population [1-2]. The most common type is psoriasis vulgaris, which is characterized by the presence of papulosquamous plaques in the skin. Psoriasis can occur at any age, but the onset is generally between the ages of 18 and 35 years. The plaque severity and degree of affected body surface area vary throughout an individual's life. Regardless of disease severity, psoriasis is associated with significant morbidity that extends beyond the skin [3]. Indeed, in recent years, several studies demonstrated that psoriasis is associated with an increased risk of various cardiovascular diseases, including peripheral arterial disease[4], coronary artery disease, [5] atrial fibrillation, ischemic stroke, [6] deep venous thromboses, pulmonary emboli, [7] and renal insufficiency [8].

To date, the exact underlying pathways that link cardiometabolic comorbidites to psoriasis are complex and not fully understood [9]; Nevertheless, several recent observational studies provide evidence that common inflammatory pathways are likely involved in the pathophysiology of psoriasis and cardiovascular inflammation, both of which are associated with a chronic proinflammatory, proangiogenic, and prothrombotic state [10-11].

However, it is still unclear whether psoriatic inflammation primarily contributes to the development of cardiometabolic comorbidities, or whether preexisting metabolic dysfunction causes immunologic dysregulation that then leads to the development of psoriasis [12].

This report synthesizes the current understanding of the prevalence and characteristics of cardiovascular comorbidities in patients with psoriatic disease, and the importance of screening for and treating modifiable cardiometabolic risk factors.

Psoriasis and metabolic syndrome

The metabolic syndrome refers to the commonly occurring disorder comprising central obesity, atherogenic dyslipidemia, hypertension, and insulin resistance [13]. The definition of metabolic syndrome requires central obesity (BMI > 30 kg/m2) and any two of the following abnormalities: elevated plasma triglycerides reduced HDL cholesterol, elevated blood pressure and raised fasting plasma glucose [14-15]. It is associated with accelerated atherosclerosis in response to chronic inflammation and vascular

endothelial dysfunction and has long been associated with psoriatic disease [4-18].

In a study comparing 625 hospitalized psoriasis patients and 1044 non psoriasis patients, hyperlipidemia, hypertension, coronary artery disease, type 2 diabetes, and increased Body mass index are increased in psoriasis than in controls [14-19].

Langan *et al.* performed a cross-sectional study of patients with psoriasis in the United Kingdom for whom information on body surface area involvement by psoriasis was available and found a positive dose dependent relationship between objective measures of psoriasis severity and metabolic syndrome [20].

Obesity

Recent studies have shown that obesity may precede the onset of psoriasis as a risk factor [21-22]. In meta-analysis of 16 observational studies, the pooled odds ratio (OR) for obesity among patients with psoriasis was 1.66 (95% confidence interval (CI) 1.46–1.89) compared with those without psoriasis. Among studies that accounted for psoriasis severity, the pooled OR for the association between obesity and mild and severe psoriasis were 1.46 (95% CI, 1.17-1.82) and 2.23 (95% CI, 1.63- 3.05), respectively [23] and one incidence study found that psoriasis patients have a hazard ratio of 1.18 (95% CI 1.14–1.23) for new-onset obesity [24].

Hypertension

Several studies have reported an increase in the prevalence of hypertension in psoriasis patients [21]. The majority of these authors establish a relationship between the severity of psoriasis and the risk of hypertension [25-26].

In a meta-analysis of 24 observational studies, patients with psoriasis had significantly increased odds of hypertension (OR, 1.58; 95% CI, 1.42–1.76), and the prevalence was greatest in those with severe psoriasis and psoriatic arthritis [27].

Two cohort studies also observed psoriasis to be associated with an increased risk of incident hypertension [28-29]. In addition, studies of patients with hypertension suggest more severe hypertension and poorly controlled blood pressure among patients with psoriasis compared with those without psoriasis [23-30-31]. Whereas other studies have not observed a significant association between psoriasis and hypertension [21-32].

Diabetes mellitus

Several recent observational studies provide evidence that the risk of diabetes is higher in patients with psoriasis compared with a healthy control group [21].

A meta-analysis of 5 cohort studies assessing the risk of incident diabetes among patients with psoriasis found a pooled relative risk (RR) for diabetes of 1.27 (95% CI, 1.16-1.40) [33].This risk increases with the duration and severity of psoriasis and it is not related to a high body mass index alone [21].

Moreover, diabetic patients with psoriasis appear to be more likely to require pharmacologic management [34] and suffer from macro- and microvascular diabetes complications than diabetic patients without psoriasis [23-35].

Dyslipidemia

Dyslipidemia may be more prevalent among patients with than without psoriasis [23]. In a systematic review, 20 of 25 included studies demonstrated a significant correlation between psoriasis and lipid profile abnormalities including elevated triglyceride levels in 16%, high-density lipoprotein cholesterol level of less than 40 mg/dL in 12%, and unspecified hyperlipoproteinemia in 8%. However in 5 of included studies, there were no differences in lipid levels between psoriasis patients and controls [4-36].

The directionality of the association between psoriais and dyslipidemia remains unclear; some studies suggest dyslipidemia may be a risk factor for developing psoriasis [37-38].

Psoriasis and coronary artery disease

Patients with psoriatic disease are at an increased risk of coronary artery disease [5,39,40] and myocardial infarction [4,41-43]. In a prospective, population based cohort study, 130,976 patients with psoriasis was compared to 556,995 controls for myocardial infarction with a mean follow-up of 5.4 years ; The myocardial infarction incidence per 1000 person-years for control patients and patients with mild and severe psoriasis was 3.58 (95% CI, 3.52-3.65), 4.04 (95% CI, 3.88-4.21), and 5.13 (95% CI, 4.22-6.17), respectively [44].

In studies that stratified patients by age, the risk seemed to be greatest in younger patients [5]. Furthermore, data from the US Nurses' Health Study II demonstrated that women with psoriatic arthritis were significantly more likely to have a nonfatal myocardial infarction than women with psoriasis alone [43], suggesting that joint involvement may also confer greater risk [4].

Atrial fibrillation

Atrial fibrillation is also more prevalent in patients with psoriasis [6,45]. A cohort study analyze the risk of Atrial fibrillation in the patients with psoriasis; the authors showed that in the patients with mild psoriasis, the adjusted risk ratios for Atrial fibrillation were 1.50 (95% CI: 1.21–1.86) in those under 50 and 1.16 (1.08–1.24) in the patients over 50

years, respectively. And in the patients with severe psoriasis, a higher risk of Atrial fibrillation was observed with RR = 2.98 (95% CI: 1.80–4.92) in those under 50 and 1.29 (95% CI: 1.01–1.65) in the patients over 50 years, suggesting that psoriasis was associated with an increased risk of Atrial fibrillation independent of age, gender and co-morbidity [6,46].

In addition, in a cohort study of patients with nonvalvular atrial fibrillation who had not been treated with anticoagulation, those with psoriasis had significantly higher rates of thromboembolism and related mortality, which exceeded that predicted by their CHA2DSVASc score by 2.6 to 3.4 times [45].

Impact of therapies on psoriasis and cardiovascular disease

Since inflammation is the driving link between psoriasis and cardiovascular disease, it is reasonable that targeting inflammation would improve cardiovascular outcomes. Unfortunately, traditional anti-inflammatory agents [47, 48], as well as the systemic immunomodulatory [49-50], have been associated with an increased risk of dyslipidemia, homocysteinemia, hypertension, and adverse cardiovascular events [4]. Despite the effects of these medications, available data suggest that some systemic agents can be cardio protective [3]. Low-dose methotrexate has been shown to reduce the risk of major cardiovascular disease events in psoriasis patient [51]. Moreover multiple studies have shown that tumor necrosis factor-blocking agents seem to be cardio protective [52-53]. In addition supplementation with folic acid, vitamin B6, and B12, had significantly reduced vascular disease compared with untreated patients with psoriasis (relative risk, 0.73; 95% CI, 0.55-0.98) [51].

Recently, a meta-analysis of 6 studies in patients with psoriasis or psoriatic arthritis revealed a significant protective effect of all systemic medications on relative risk of cardiovascular disease [47]. Furthermore, cardiovascular medications may affect psoriasis. Statins have been suggested as a potential treatment for psoriasis because of their anti-inflammatory properties [3]. A pilot study evaluated the effectiveness of simvastatin in patients with severe psoriasis found that statins can correct lipid metabolism and reduce cutaneous lesions in psoriasis [54]. More recently, some authors reported a decreased risk of psoriasis associated with statin intake [14, 55]. Also oral statins may enhance the therapeutic effect of topical steroids against psoriasis [56]. Beta-blockers have been suggested to induce and exacerbate psoriasis [57,58]. However, in many cases, betablockers were associated with a psoriasiform reaction rather than psoriasis, and histologic testing, did not support the diagnosis of psoriasis [3]. More recently, A large population-based case–control analysis does not support that betablocker use is associated with an increased risk of psoriasis [59]. In addition, other antihypertensives have been suspected to have an association with psoriasis [60]. Angiotensin-converting enzyme inhibitors [60-62], calcium channel blockers [63], and clonidine [64] have been reported to have a possible association with psoriasis [3]. However, the results of the studies have remained controversial [9,65,66].

CONCLUSION

There is growing argument supporting an association between psoriasis and cardiovascular comorbidities. Until more evidence is available, and multidisciplinary guidelines, all patients with moderate to severe psoriasis should be considered to be at a higher risk of cardiovascular disease and managed accordingly.

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