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Cardiovascular Risk and Psoriasis: Beyond the Traditional Risk Factors

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ABSTRACT

Psoriasis is an autoimmune disease resulting in plaques of the skin. Similar to atherosclerosis, inflammation is integral to the initiation and propagation of plaque development. Mounting evidence has emerged demonstrating that psoriasis not only is associated with increased prevalence of cardiovascular risk factors, but also is an independent risk factor for the development of cardiovascular disease. Systemic therapies for moderate to severe psoriasis can increase the cardiovascular risk. Despite the evidence that psoriasis is an independent risk factor for cardiovascular disease, current guidelines only address managing traditional risk factors. An interdisciplinary approach is needed to find the necessary steps beyond classic risk reduction and detection of early cardiovascular disease in patients with psoriasis, as well as to develop a cardiovascular disease preventive regimen.

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Psoriasis is an autoimmune disease resulting in plaques of the skin. Although traditionally thought to be isolated to the skin, psoriasis is now recognized as a systemic inflammatory condition.[1] Increased awareness of the cardiovascular disease risk associated with psoriasis has emerged recently. Guidelines for cardiovascular disease prevention in the population with psoriasis remain limited to addressing traditional risk factors.[2] We review the evidence supporting psoriasis as an independent risk factor for cardiovascular disease, the impact of various treatments on both psoriasis and cardiovascular disease, and the need for future advancements to reduce the cardiovascular risk in the population with psoriasis.

PSORIASIS AND TRADITIONAL CARDIOVASCULAR RISK FACTORS

Psoriasis is a chronic, relapsing inflammatory disease of the skin affecting 2% to 3% of the global adult population.[3] Psoriasis can occur at any age, but the onset is usually between the ages of 18 and 35 years. A bimodal onset has been suggested with an initial peak at ages 16 to 22 years and a second peak at age 57 to 60 years.[4,5] The most common type of psoriasis, accounting for 90% of cases, is psoriasis vulgaris, which is characterized by the presence of papulosquamous plaques of various size and number. 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. People with psoriasis have impaired quality of life and psychologic burden.[6,7] In addition, psoriasis has been associated with other conditions, including diabetes, metabolic syndrome, arthritis, inflammatory bowel disease, and malignancy.[1,8-12] More recently, attention has been drawn to the relationship of psoriasis with cardiovascular disease.

Psoriasis has been associated with an increased incidence of traditional cardiovascular risk factors. Neimann et al[8] conducted a large cross-sectional study comparing the prevalence of cardiovascular risk factors in 127,706 patients with mild psoriasis and 3854 patients with severe psoriasis with controls. After adjusting for age and sex, patients with severe psoriasis were more likely than controls to be smokers and to have more diabetes, hypertension, hyperlipidemia, and obesity. Other studies also have shown the

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increased prevalence of cardiovascular risk factors in patients with psoriasis (Table 1). A recent meta-analysis by Armstrong et al,[13] which included 309,469 patients with psoriasis, found an increased risk for hypertension among patients with psoriasis compared with controls.

PSORIASIS AND CARDIOVASCULAR RISK: BEYOND TRADITIONAL RISK FACTORS

Twenty-five years ago, McDonald and Calabresi[11] performed the first study showing that patients with psoriasis had more vascular occlusive events than patients without psoriasis. Subsequently, multiple observational studies suggested that atherosclerosis is more prevalent in patients with psoriasis (Table 2). However, these studies focused on hospitalized patients and did not control for associated cardiovascular risk factors.

In a prospective, population-based cohort study, Gelfand et al[12] analyzed 130,976 patients with psoriasis and 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% confidence interval [CI], 3.52-3.65), 4.04 (95% CI, 3.88-4.21), and 5.13 (95% CI, 4.22-6.17), respectively. The findings of Gelfand et al[12] have been further confirmed by other studies (Table 2). A cross-sectional study of 2 US healthcare databases showed that there was a higher prevalence of cardiovascular atherosclerotic disease and congestive heart failure in patients with psoriasis compared with controls.[14] In a retrospective analysis of patients who underwent coronary angiography, patients with psoriasis were more likely than patients without psoriasis to have coronary artery disease (84.3% vs 75.5%, $P = .005$).[15] Other studies confirmed that patients with psoriasis have an increased risk of peripheral vascular and cerebrovascular disease compared with the general population.[16-18]

CLINICAL SIGNIFICANCE

- Psoriasis not only is associated with increased prevalence of cardiovascular risk factors, but also is an independent risk factor for the development of cardiovascular disease.
- Current guidelines focus only on traditional risk factors and ignore the disease "psoriasis" per se as an independent risk factor.
- An interdisciplinary approach is needed to find the necessary steps beyond classic risk reduction and detection of early cardiovascular disease in patients with psoriasis, as well as to develop a cardiovascular disease preventive regimen.

PSORIASIS AND ATHEROSCLEROSIS: A COMMON PATHWAY

Understanding why psoriasis is a risk factor for atherosclerosis requires a basic understanding of their shared pathogenic features (Figure 1). T-helper 1 cells of the adaptive cellular immune system are integral in plaque development and inflammation propagation for both psoriasis and atherosclerosis.[19] In atherosclerosis, T-helper 1 cells are activated when bound to antigens, such as oxidized low-density lipoprotein cholesterol, heat-shock protein 60, and pathogenic organisms.[20] The antigens triggering T-helper 1 cell activation in psoriasis are unknown, although it has been suggested that T-helper 1 cells that recognize streptococcus may cross-react with a keratin epitope.[21]

The activated T-helper 1 cells release proinflammatory cytokines, including interferon-γ, tumor necrosis factor-α, and interleukin-2.[22,23] This leads to activation of macrophages, keratinocytes, and vascular cells, all of which release additional cytokines. Downstream molecules of the cytokine cascade, including interleukin-6 and subsequent acute phase reactants, are produced both locally and systemically. The cytokines also result in the upregulation of vascular adhesion molecules, resulting in recruitment of more leukocytes.

In addition to the role of T-helper 1 cells, proinflammatory effects of T-helper 17 cells and anti-inflammatory effects of T-regulatory cells contribute to both pathologies.[24] T-regulatory cells modulate the inflammatory process by secreting anti-inflammatory cytokines, such as interleukin-10 and transforming growth factor-β. Both psoriasis and atherosclerosis have reduced numbers and activity of T-regulatory cells and resultant hyperactivity of T-helper 1/T-helper 17 cells.[25,26] Therefore, psoriasis and atherosclerosis result in plaques in the skin and arteries, respectively, that are a focus of both local and systemic immune activity.

MANAGING CARDIOVASCULAR RISK IN PATIENTS WITH PSORIASIS

Current guidelines for assessing cardiovascular risk in patients with psoriasis are based on traditional risk factors. However, patients with psoriasis are not being routinely screened in clinical practice, leaving the traditional cardiac risk factors underdiagnosed and undertreated.[27,28] Moreover, psoriasis is an independent risk factor for cardiovascular disease, making management of traditional risk factors alone insufficient.

IMPACT OF PSORIASIS THERAPIES ON CARDIOVASCULAR DISEASE

Systemic psoriasis therapies that modulate the immune system may alter cardiovascular risk. Patients with mild psoriasis can be managed with topical therapies, such as vitamin D analogues, retinoids, corticosteroids, and tar. However, treatment of moderate to severe psoriasis usually