Metabolic Syndrome in Patients with Psoriatic Disease

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ABSTRACT. Psoriasis is a common Th-1 and Th-17-mediated chronic inflammatory disease that has been associated with metabolic syndrome, a constellation of cardiovascular risk factors including obesity, hypertension, dyslipidemia, and insulin resistance. Overlapping inflammatory pathways and genetic susceptibility may be potential biologic links underlying this association. Multiple epidemiologic studies have consistently demonstrated higher prevalence of metabolic syndrome in patients with psoriasis. Dose-response relationships between more severe psoriasis and higher prevalence of metabolic syndrome components were recently established. This association has important clinical implications for the comprehensive management of psoriasis: Patients with psoriasis should be routinely screened for metabolic syndrome and treated accordingly to manage cardiometabolic risk, while clinicians should monitor potential effects on treatment efficacy and safety in patients with comorbid psoriasis and metabolic syndrome. Further research will be necessary to establish the directionality of this association and to explore the effect of treatment on these comorbid diseases. (J Rheumatol 2012;39 Suppl 89:24–28; doi:10.3899/jrheum.120237)

Key Indexing Terms:
PSORIASIS METABOLIC SYNDROME DYSLIPIDEMIA
HYPERGLYCEMIA OBESITY

Psoriasis is a common, chronic inflammatory disease that is associated with significant impairment in health-related quality of life even in mild cases, and excess cardiovascular and all-cause mortality in patients with more severe disease[1,2,3,4,5]. Based on an increasing understanding of its immune pathophysiology, psoriasis is now thought to be a systemic disease with potential health implications beyond the skin[6,7,8]. This topic is of critical importance because emerging data suggest that patients with more severe presentations of psoriatic disease have a 50% increased risk of mortality that results in about 5 lost years of life[9]. Of special interest, diseases that share a similar immune pathophysiology with psoriasis have been investigated as comorbid outcomes. For example, Th-1 and Th-17 immune pathways that drive psoriasis are also prominent disease mediators for atherosclerosis and thrombosis[10]. A variety of studies have suggested that patients with psoriasis have an increased risk of myocardial infarction, stroke, vascular inflammation, and atherosclerotic conditions independent of traditional risk factors for cardiovascular disease[6,11,12,13,14,15,16,17,18,19,20,21,22,23,24]. Similarly, metabolic syndrome, which is a clustering of cardiovascular risk factors, specifically obesity, hypertension, dyslipidemia, and insulin resistance, is associated with chronic inflammation[25,26]. In this review, we will focus on the expanding literature linking metabolic syndrome to psoriasis and highlight some of the clinical implications of this finding.

The underlying pathophysiology linking psoriasis and metabolic syndrome may involve overlapping inflammatory pathways and genetic predisposition[27,28]. Chronic Th-1 and Th-17-mediated inflammation with dysregulation of cytokines, e.g., tumor necrosis factor-α and interleukin 6, not only promotes epidermal hyperplasia in psoriasis, but may also antagonize insulin signaling, alter adipokine expression, and mediate insulin resistance and obesity[27,28]. Conversely, hyperinsulinemia in metabolic syndrome may promote psoriasis susceptibility or severity by facilitating chronic inflammation and angiogenesis[27,28]. In addition, the existence of pleiotropic genetic loci, e.g., PSORS2-4, CDKAL1, and ApoE4, has also been implicated in the shared genetic susceptibility to both psoriasis and metabolic syndrome[28]. These shared mechanisms underscore the biological plausibility for the association between psoriasis and metabolic syndrome.

In 2006, the first studies directly linking components of metabolic syndrome to psoriasis using multivariate analyses started to emerge. For example, in a population-based,

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Supported by grants from the U.S. National Institutes of Health, the National Heart, Lung, and Blood Institute R01-HL089744 (JMG) and National Institutes of Arthritis and Musculoskeletal and Skin Disease T32-AR07465 (HY). Dr. Gelfand served as consultant with Abbott, Amgen, Celgene, Centocor, Novartis, and Pfizer, receiving honoraria; had grants or has pending grants from Abbott, Amgen, Genentech, Novartis, and Pfizer; and received a donation from Amgen to the Trustees of the University of Pennsylvania to develop the Dermatology Clinical Effectiveness Research Network. Mr. Yeung has no financial disclosures to report.

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cross-sectional study in the United Kingdom, it was shown that psoriasis was associated with diabetes independent of diabetes risk factors (such as obesity) and that the association was stronger in patients with more severe disease[29]. The increased prevalence of metabolic syndrome among patients with psoriasis has been replicated in multiple countries including Italy, Israel, India, Japan, China, Tunisia, and the United States[30,31,32,33,34,35,36,37]. Additionally, an increased prevalence of metabolic syndrome has been specifically observed among patients with psoriatic arthritis (PsA), with studies suggesting that the association is specific for PsA compared to other inflammatory arthropathies such as rheumatoid arthritis (RA) and ankylosing spondylitis[38,39]. Finally, emerging data suggest that the association of psoriasis with metabolic syndrome occurs early in the course of the disease because psoriasis is associated with obesity and elevated lipids even in childhood[40]. While these prevalence studies clearly establish an association between psoriasis and metabolic syndrome, they cannot establish the directionality of the association. Several studies suggest that obesity, a primary component of metabolic syndrome, is a risk factor for future development of psoriasis with an estimated 30% of new psoriasis cases being attributable to obesity[41,42]. Alternatively, several studies indicate that patients with psoriasis are prone to the future development of key components of metabolic syndrome such as diabetes, independent of traditional risk factors[43,44].

The relationship between psoriasis, metabolic syndrome, and its individual components was further elucidated in a recent large-scaled, population-based prevalence study in the United Kingdom[45]. Using objective measures of body surface area involvement of psoriasis and direct measurements of metabolic syndrome components, the study showed that increasing psoriasis severity was associated with higher odds of metabolic syndrome (Figure 1). The relationship remained robust even in different definitions of metabolic syndrome. Of note, several components of the metabolic syndrome — namely, obesity, hypertriglyceridemia, and hyperglycemia — demonstrated dose-response associations with psoriasis severity that are independent of other components (Figure 2). These results suggest that psoriasis severity is a driving factor behind metabolic disorders so frequently seen in this patient population, or alternatively, that metabolic disorders lead to worsening severity of psoriasis.

Importantly, this broad and expanding literature linking psoriasis with metabolic syndrome has clinical applications relevant to daily practice especially as it relates to the efficacy and safety of commonly used systemic medications. For example, more aggressive liver monitoring guidelines (including the requirement of more frequent liver biopsies) are recommended for psoriasis patients with components of the metabolic syndrome (obesity, diabetes) who are taking methotrexate[46]. Of note, patients with psoriasis have been shown to have an increased frequency and severity of non-alcoholic fatty liver disease and thus caution may be indicated when using medications with liver toxicity such as methotrexate and acitretin[47]. Moreover, increasing body mass index is associated with a reduction in psoriasis treatment efficacy, especially among non-weight-based biologic therapies[48]. Finally, emerging observational data suggest that successful systemic treatment of psoriasis may be associated with improvement in metabolic risk biomarkers[49]. Randomized controlled studies evaluating hard clinical endpoints will be necessary to determine whether the improvement in metabolic function detected in observational settings translates into clinically meaningful improvements in health outcomes.

Given the association of psoriasis with metabolic syndrome and the effect it has on the patient's health and on the efficacy and safety of treatment options, it is important that patients undergo appropriate screening as part of routine medical care[50,51]. Routine United States-based recommendations for all patients (not just those with psoriasis) include a blood pressure check at each office visit in patients 21 or older, a fasting glucose test every 3 years in patients 45 or older (or younger in patients with risk factors for diabetes), and cholesterol screening every 5 years starting at age 20[52,53,54]. Additionally, because patients with psoriasis have an increased risk of cardiovascular disease, clinicians may consider setting more stringent goals for blood pressure and cholesterol levels in these patients, as has been advocated for patients with other Th-1 diseases such as RA[55,56].

CONCLUSION

A broad and evolving literature supports the notion that psoriasis is associated with metabolic syndrome. This association has clinical implications for the care of patients with psoriasis in terms of screening for metabolic syndrome, taking steps to lower cardiovascular risk, and recognizing the effect metabolic syndrome may have on the safety and efficacy of psoriasis therapeutics. Rigorous clinical trials are necessary to determine whether successful treatment of psoriasis will lower the risk of developing metabolic syndrome and its complications.

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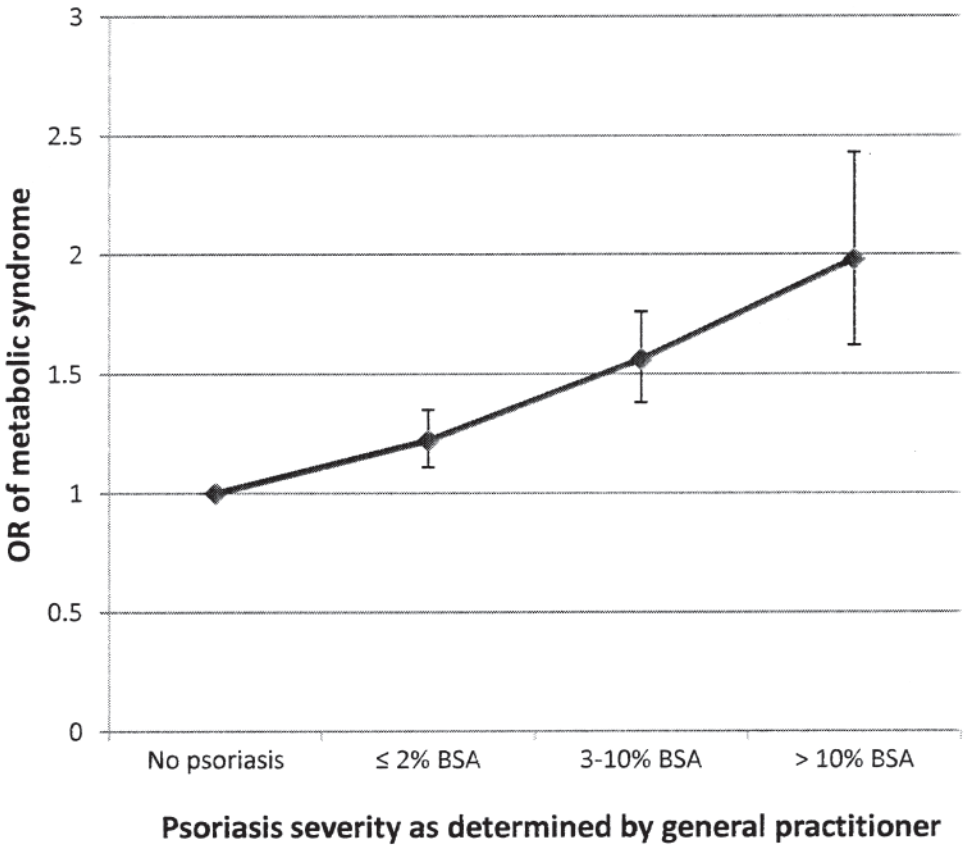

Figure 1. Increasing psoriasis severity is associated with increasing odds of metabolic syndrome. BSA: body surface area affected. Model adjusted for age and sex. From Langan, et al. J Invest Dermatol 2012;132 Pt 1: 556-62; with permission.

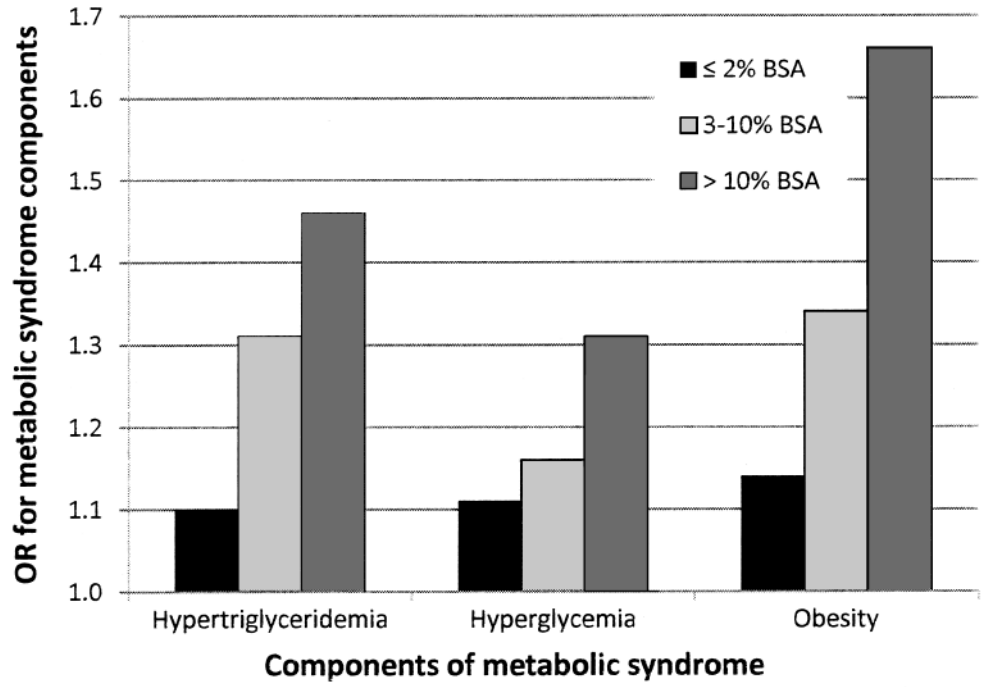

Figure 2. Increasing psoriasis severity is associated with increasing odds of metabolic syndrome components, independent of other components. BSA: body surface area affected. Model adjusted for age, sex, and other components of metabolic syndrome. From Langan, et al. J Invest Dermatol 2012;132 Pt 1: 556-62; with permission.

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