Metabolic Disorders in Patients with Psoriasis and Psoriatic Arthritis

Lotus Mallbris, MD, PhD, Christopher T. Ritchlin, MD, and Mona Ståhle, MD, PhD

Corresponding author
Lotus Mallbris, MD, PhD
Department of Medicine, Dermatology Unit,
Karolinska Institutet, 171 76, Stockholm, Sweden.
E-mail: lotus.mallbris@ki.se

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Psoriasis is one of the common complex disorders in Western world, affecting 2% to 3% of the population. Recent studies indicate that psoriasis is associated with an increased risk of comorbidity and mortality compared to the general population. It appears that patients with psoriasis have a higher prevalence of metabolic disorders such as diabetes, hypertension, obesity, and hyperlipidemia, as well as a higher frequency of cigarette smoking. These concomitant diseases can complicate the treatment of psoriasis. Even though the etiology of these associations is elusive, physicians should be aware of them and take active steps to reduce the risk profiles of patients with psoriasis and psoriatic arthritis, in order to lessen mortality and comorbidity.

Introduction

Psoriasis (Ps) is a common immune-mediated, inflammatory disease, affecting 2% to 3% of the Caucasian population [1]. Although the skin is the primary target organ, it is estimated that up to 40% of Ps patients develop psoriatic arthritis (PsA) over time [2].

The etiology and pathogenesis underlying Ps and PsA remain elusive. However, overwhelming evidence exists for a strong genetic contribution to the disease. To date, no definitive candidate Ps gene has been identified, but several loci for genetic susceptibility to the disease (PSORS1-10) have been reported [3]. The main locus is located in the major histocompatibility complex (MHC) region on chromosome 6p21, and recent data point to the HLA-Cw*0602 as the susceptibility allele, particularly in early-onset Ps [4] and in a certain phenotype [5]. Ps is considered as a genetically and clinically heterogeneous disease.

Apart from PsA, which may be considered the most common comorbidity, Ps is associated with several other disorders, such as cardiovascular disease (CVD), obesity, and diabetes [6,7]. Comorbidity profiles may differ among distinct subphenotypes of Ps, which may complicate the preventive measures.

Metabolic Syndrome

Definition

CVD and diabetes are the major causes of mortality in the Western industrialized countries. In 2001, ischemic coronary heart disease, stroke, and other forms of cardiovascular disorders were the leading causes of death in countries of all economic profiles, and collectively, they accounted for more than 20% of all deaths worldwide [8]. Diabetes was estimated to be the fifth leading cause of death globally [8].

The classification of risk factors for diabetes and/or CVD has gained substantial interest, and several factors have been identified as major contributors. Established atherogenic lifestyle risk factors include physical inactivity, cigarette smoking, and increased body mass index (BMI). In addition, other modifiable factors such as hypertension, impaired glucose metabolism, and high serum cholesterol concentration also play a role [9]. The metabolic syndrome is a cluster of these associated disorders, affected by lifestyle, genetic predisposition, and environment. Several definitions of the metabolic syndrome exist, but all definitions retain the syndrome's essential components: central obesity, atherogenic dyslipidemia, hypertension, and glucose intolerance or impaired fasting glucose or insulin resistance (IR) (Table 1). Thus, the metabolic syndrome represents a clinical crossroad as being a risk factor for type II diabetes and premature CVD. Furthermore, the syndrome is associated with an increased risk for a number of adult cancers and fatty liver disease.

The potential role of C-reactive protein in CVD

Extensive evidence now strongly supports that chronic inflammation, a characteristic feature of Ps, may play a key role in many, if not all, stages of CVD [10]. Elevated levels of C-reactive protein (CRP), an acute phase protein

Table 1. Various definitions of the metabolic syndrome

	WHO	NCEP-ATP III	EGIR	IDF
Criteria	One of the following: -diabetes -impaired fasting glucose -impaired glucose tolerance -insulin resistance and 2 or more of the factors below	3 or more of the factors below	Insulin resistance-hyperinsulinemia, and 2 or more of the factors below	Central obesity (measured as ethnicity-specific waist circumference or BMI > 30 kg/m^2), and 2 or more of the factors below
Fasting plasma glucose (mg/dL)	Not included	≥ 110	≥ 110	≥ 100 or previously diagnosed type 2 diabetes
Microalbuminuria (μg/min)	≥ 20, or albumin-to-creatinine ration ≥ 30 mg/g	Not included	Not included	Not included
Central obesity	*Waist-to-hip ratio* Male: > 0.90 Female: > 0.85 or BMI > 30 kg/m^2	*Waist circumference* Male: > 102 cm Female: > 88 cm	*Waist circumference* Male: > 94 cm Female: > 80 cm	See criteria 1
Hypertension (mm Hg)	Systolic ≥ 140 Diastolic ≥ 90	Systolic ≥ 130 Diastolic ≥ 85	Systolic ≥ 140 Diastolic ≥ 90	Systolic ≥ 130 Diastolic ≥ 85, or on anti-hypertensive treatment
Triglycerides (mg/dL)	≥ 150	≥ 150	≥ 177	≥ 150, or specific treatment for TG abnormality
HDL-c (mg/dL)	Male: < 35 Female: < 39	Male: < 40 Female: < 50	< 45	Male: < 40 Female: < 50, or specific treatment for HDL-c abnormality

BMI—body mass index; EGIR—European Group for the Study of Insulin Resistance; HDL-c—high-density lipoprotein cholesterol; IDF—International Diabetes Federation; NCEP-ATP III—National Cholesterol Education Program Adult Treatment Panel III; TG—triglycerides; WHO—World Health Organization. Data from [56], [57], [58], and [59].

and a hallmark of inflammation, is an emerging risk factor for CVD, and accumulated data point to increased CRP concentration as a predictor for long-term risk for cardiovascular events [11]. Experimental studies further suggest that CRP is not merely a marker of CVD but also an active player in the development and progression of atherosclerosis, the major underlying cause of CVD [11]. Also, clinical studies have reported that CRP is an independent predictor of atherothrombosis, hypertension, and myocardial infarction, even after adjusting for other confounding factors such as age, smoking, obesity, diabetes, and hypercholesterolemia [12,13].

Ps is an inflammatory disease, and several studies have demonstrated an increased level of CRP in patients with Ps [14,15]. Elevated CRP levels have also been reported in PsA, and they are highest in patients with radiographic evidence of joint destruction [16]. Elevated serum CRP levels correlated with increased serum concentrations of interleukin (IL)-6 and the S-100 pro-inflammatory molecules myeloid-related protein (MRP)8, MRP14, and the heterodimer MRP8/MRP14 [17–19]. Moreover, serum CRP concentration correlated with synovial lining layer expression of all three S-100 molecules, and they were highly expressed in perivascular structures. These findings suggest two potential mechanisms to explain the linkage of CRP with endothelial inflammation: 1) upregulation of IL-6, a cytokine with established proatherogenic actions; or 2) altered expression of vascular proinflammatory molecules that contribute to the formation of atherosclerotic plaques [20].

Features of Metabolic Syndrome in Patients with Ps and PsA

Obesity in patients with Ps and PsA

The prevalence of obesity (defined as BMI ≥ 30) and overweight (BMI ≥ 25 and < 30) has increased at an alarming rate over the past two decades. In the United States, more than 60% of adults are overweight or obese [21]. Although the true prevalence of obesity in patients with Ps remains to be established, multiple studies have consistently shown an association between increased BMI and Ps, suggesting that patients with Ps are more frequently overweight or obese than the general population [6,22••,23•] (Table 2).

A large population-based survey from Scandinavia [6] was among the first reports that showed that women with Ps, as a group, had a higher prevalence of obesity ($P < 0.001$) [6]. In a case control study involving 560 patients with recently diagnosed (< 2 years) Ps compared with 690 control individuals who had been recently diagnosed with other dermatological diseases, Naldi et al. [23•] identified obesity as an independent, modifiable risk factor associated with Ps, accounting for 16% of all Ps cases at onset [23•]. Herron et al. [22••] found more than a twofold higher prevalence of obesity in Ps patients enrolled in the Utah Psoriasis Initiative (UPI) compared to that of Utah's general population (34% vs. 18%; $P < 0.001$). Notably, BMI increased after the diagnosis of Ps in most patients, suggesting that obesity is a consequence rather than a risk factor for the onset of Ps [22••]. Interestingly, the authors also demonstrated a positive correlation between obesity and severity of Ps [22••], supporting the notion that a vegetarian diet and weight loss may improve chronic inflammatory Ps [24•]. In contrast to the study by Naldi et al. [23•] but in line with the findings of Herron et al. [22••], a recent case-control study involving 200 Ps patients at disease onset (< 1 year) noted no difference between BMI in Ps patients at disease onset and matched controls [25••]. Regarding the time from disease onset until the initiation of these studies, this study began a year later after disease onset than the study performed by Naldi et al. [23•]. Therefore, it is conceivable that the metabolic condition differs in the early stage of the disease, and that psoriasis indeed precedes the increased BMI.

Cytokines such as tumor necrosis factor (TNF)-α, which may play an important role in the pathophysiology of Ps, also have a central role in obesity pathogenesis [24•]. In addition, the satiety hormone leptin has been shown to elicit a number of immunoregulatory effects, including the promotion of T-cell proliferation and the stimulation of TNF-α production in the adipose tissue. Thus, leptin might act as a link between Ps immunopathology and nutritional status in patients [24•].

Ps is a chronic condition, and its clinical symptoms and sometimes cumbersome therapies can have profound impact on quality of life. Thus, the disease may negatively affect patient's body image. Poor diet and/or a lack of physical activity, perhaps due to underlying depression, may significantly contribute to obesity in a subset of Ps patients. Furthermore, in light of the importance of genetic factors in Ps, it would be most interesting to investigate the prevalence of obesity in family members of Ps patients.

The relationship between obesity and PsA was recently analyzed by Reddy et al. [26]. Bone density was compared in rheumatoid arthritis (RA) and PsA subjects enrolled in the Consortium of Rheumatology Researchers of North America (CORRONA) database. Bone density was higher in PsA patients compared with RA patients, but these differences were not evident when adjusted for weight. Indeed, the PsA patients were on average 17 pounds heavier than those with RA despite similar demographic features and disease duration. These findings suggest that overweight and most likely obesity is more prevalent in PsA than RA despite the fact that inflammatory arthritis is the dominant clinical feature in both disorders.

Taken together, the data suggest an association between obesity, Ps, and PsA. Preliminary studies indicate that psoriasis occurs before obesity, but longitudinal perspective studies are needed. The pathomechanisms are likely complex. Whether obesity constitutes a real risk for disease onset [23•] or is a consequence of Ps [22••] is unclear.

Atherogenic dyslipidemia in patients with Ps and PsA

Over the past 50 years, a possible association between dyslipidemia and Ps has been discussed, and multiple studies have been performed (Table 3). However, these inconsistent studies often involve highly heterogeneous populations and/or have not accounted for duration of psoriasis or previous treatments. Elevated serum/plasma concentrations of triglycerides (TG), very low-density lipoprotein (VLDL), and low-density lipoprotein (LDL), as well as low serum concentration of high-density lipoprotein cholesterol (HDL-c) are recognized risk factors for CVD [9]. Overall, the majority of studies have reported an atherogenic lipid profile associated with Ps. The reported profiles are characterized by significantly increased concentrations of total TG, total cholesterol, cholesterol in VLDL, and LDL-particles, as well as decreased concentrations of cholesterol in HDL-particles. In contrast to the others, two studies showed a decreased level of HDL-c concentration. These studies involve either children with Ps or patients at the onset of the disease. The etiology of this finding remains unclear, but the authors speculate that age at onset and duration of Ps might influence the lipoprotein phenotype, and thereby, these profiles eventually may look similar to those reported by others [25••,27].

Patients with Ps who require systemic treatment are particularly at risk for developing hyperlipidemia due to the side effect of certain antipsoriasis medications [28]. Cigarette smoking, increased BMI, and systemic inflammation have also been incriminated as possible factors.

Apart from the lipid abnormalities included in the metabolic syndrome, Ps patients seem to have an atherogenic lipoprotein composition already at the onset of disease with significantly higher cholesterol concentration in the VLDL fractions [25••]. The abnormal lipoprotein profile appears to be independent of established confounding factors (eg, age, sex, BMI, smoking, blood pressure, physical activity, and alcohol consumption), which suggests that dyslipoproteinemia in Ps might be genetically determined rather than acquired [25••].

Fasting lipids, lipoproteins, and their subfractions were analyzed in age-matched controls and 50 PsA patients with relatively mild psoriasis [29]. Both HDL

Table 2. Case-control studies performed in the last 15 years reporting prevalence of obesity and smoking in patients with psoriasis

Study	Design	Setting	Study size	Obesity	Cigarette smoking
Naldi et al. [45]	Case control	20 Italian dermatology centers, 1987-1992	Adult Ps at onset: n = 215 Controls: n = 267	Not considered	OR (current vs never-smokers) OR: 2.1; CI 1.1–4.0
Poikolainen et al. [44]	Case control	Outpatients at 3 Finnish dermatology hospitals	Adult females Ps: n = 55 Controls: n = 108	Not considered	OR (high intensity vs never-smokers) OR: 3.3; CI 1.4–7.9
Naldi et al. [23•]	Case control	20 Italian dermatology centers, 1987-1997	Adult Ps at onset: n = 560 Controls: n = 690	OR (BMI > 30 vs < 26) OR: 1.9; CI 1.2–2.8	OR (ex- vs never-smokers) OR: 2.2; CI 1.5–3.2 OR (current vs never-smokers) OR: 1.6; CI 1.2–2.2
Herron et al. [22••]	Cross-sectional, case control	UPI prospective cohort	Adult Ps: n = 557 Controls Utah: n = 480 Controls NPF: n = 17,378	OR (UPI vs Utah) OR: 2.39; CI 1.98–2.90 OR (UPI vs NPF) OR: 1.77; CI 1.48–2.12	OR (UPI vs Utah) OR: 4.02; CI 3.31–4.88
Fortes et al. [46]	Hospital-based, cross-sectional	Inpatients at an Italian dermatology hospital, 2000-2002	Adult Ps: n = 818	Not considered	OR (high vs low-intensity smokers) OR: 2.2; CI 1.2-4.1

BMI—body mass index (kg/m^2); CI—95% confidence interval; OR—odds ratio; Ps—psoriasis; Ps at onset— onset < 2 years; UPI—Utah Psoriasis Initiative.

Table 3. Case-control studies performed in the last 20 years reporting an abnormal lipid profile in patients with psoriasis

Study	Study size	Cholesterol				TG				Lp(a)	Apo A I	Apo B
		Total	VLDL	LDL	HDL	Total	VLDL	LDL	HDL			
Vahlquist et al. [60]	Male Ps: n = 20 Controls: n = 36	ND	Up; $P < 0.05$	ND	ND	Up; $P < 0.001$	Up; $P < 0.001$	Up; $P < 0.001$	ND		ND	ND
Ferretti et al. [27]	Prepubertal Ps: n = 15 Controls: n = 15	Up; $P < 0.02$			Up; $P < 0.02$							
Seishima et al. [53]	Male Ps: n = 38 Controls: n = 40	ND			ND	Up; $P < 0.005$					Down; $P < 0.01$	Up; $P < 0.001$
Uyanik et al. [61]	Adult Ps: n = 72 Controls: n = 30			ND	ND	Up; $P < 0.01$				Up; $P < 0.01$	ND	ND
Vanizor Kural et al. [14]	Adult Ps: n = 35 Controls: n = 35	Up; $P < 0.01$		Up; $P < 0.02$	Down; $P < 0.001$	Up; $P < 0.01$	ND	ND	ND		ND	ND
Piskin et al. [62]	Male Ps: n = 100 Controls: n = 100	Up; $P < 0.001$	Up; $P < 0.05$	Up; $P < 0.001$	Down; $P < 0.05$	Up; $P < 0.05$						
Rocha-Pereira et al. [15]	Adult Ps: n = 88 Controls: n = 40	Up; $P < 0.01$	Up; $P < 0.01$	Up; $P < 0.01$	Up; $P < 0.001$	Up; $P < 0.001$				Up; $P < 0.001$	Up; $P < 0.01$	Up; $P < 0.001$
Mallbris et al. [25••]	Adult Ps at onset*: n = 200 Controls: n = 285	Up; $P < 0.01$	Up; $P < 0.05$	ND	Up; $P < 0.001$	ND	ND	ND	ND	ND	Up; $P < 0.001$	ND

*Onset < 12 months.
Up indicates a significant increase in the level in patients, and down indicates significant decrease in the level in patients. Apo A I—apolipoprotein AI; Apo B—apolipoprotein B; HDL—high-density lipoprotein; LDL—low-density lipoprotein; Lp(a)—lipoprotein a; ND—no significant difference; Ps—psoriasis; TG—triglycerides; VLDL—very low-density lipoprotein.

and total cholesterol were reduced, although the most dense subfraction (LDL3) was significantly higher in the PsA patients. This shift in LDL composition is associated with a higher atherosclerotic risk profile. Similar findings were reported in an earlier study of 40 PsA patients by Lazarevic et al. [30].

For the time being, the management of lipids and lipoprotein alterations in Ps and PsA patients should follow existing guidelines for screening. Nevertheless, the possibility that Ps might predispose these individuals to an atherogenic lipid profile should be considered.

Hypertension in patients with Ps and PsA

Although it is widely assumed that hypertension is associated with Ps, solid clinical data linking Ps with incident hypertension are scarce. In 1970s, Preece [31] reported an association between hypertension and Ps. Since then, only a limited number of epidemiological studies have compared blood pressure in Ps patients and controls.

In a hospital-based case-control study, Ena et al. [32] observed a significantly higher prevalence of essential hypertension in 100 Ps patients compared with matched hospitalized nonpsoriatic patients. In a cohort study, Lindegard [6] showed an overall excess frequency of hypertension ($P < 0.001$) among 372 patients with Ps compared to that of patients hospitalized other reasons. Although these studies confirmed a positive association between hypertension and Ps, it is noteworthy that the studies have not considered several potentially confounding factors, including previous systemic treatments that can cause hypertension (eg, cyclosporine) [28]. However, no evidence exists that Ps patients are more susceptible to the nephrotoxicity of cyclosporine than other patients.

In a recent study of 200 patients whose Ps onset within 1 year, Mallbris et al. [25••] found no differences between hypertension in patients with mild Ps and that of matched controls (systolic blood pressure > 149 mm Hg: 18% Ps vs 16.5% controls; diastolic blood pressure ≥ 90 mm Hg: 15.5% Ps vs 11% controls) [25••]. Though this finding clearly contrasts the concept that hypertension is associated with Ps, it is consistent with recent findings that suggest that hypertension is linked to the level of systemic inflammation [12]. Therefore, perhaps patients with mild disease at onset have no increased prevalence of hypertension, but others with severe disease activity are prone to develop hypertension over time as a consequence of chronic inflammation. Other potential mechanisms for development of hypertension (eg, concomitant obesity and cigarette smoking) may also contribute to increased prevalence of hypertension in patients with Ps. The association between hypertension and PsA has not been formally examined except in patients on cyclosporine who had a higher prevalence of elevated blood pressure compared to patients not taking this agent [33].

Insulin resistance in patients with Ps and PsA

Insulin resistance (IR), a form of impaired glucose metabolism, is associated with several life-threatening comorbidities such as obesity, hyperlipidemia, hypertension, CVD, and type II diabetes [34]. The prevalence of IR in Ps patients has been evaluated in a few studies, but the findings are inconsistent [35–38]. The studies are hampered by their small size and/or informal design. Some have selection bias, as they have included patients with history of impaired glucose tolerance in the study [36], and some have not taken cigarette smoking, a known confounder, into account. In 1977, Jucci et al. [35] demonstrated a positive correlation between Ps and IR, and they hypothesized that Ps patients are prone to increased risk for diabetes [35]. Since then, several epidemiological studies have reported a higher prevalence of type II diabetes in Ps patients than in the general population [6,7].

In a case control study, Brenelli et al. [36] confirmed the increased IR in 10 Ps patients compared with 11 control individuals. The authors proposed that the IR observed in Ps might be linked not only to impaired glucose metabolism, but also to the altered extra-renal potassium homeostasis. However, the study involved a limited number of Ps patients without taking the history of impaired glucose tolerance into account. In contrast, a cross-sectional study by Reynoso-von Drateln et al. [37], reported no difference in IR among Ps patients (n = 22), and sex-, age-, and BMI-matched, non-psoriatic control individuals (n = 22). More importantly, the authors found a significant positive correlation between the duration of Ps and insulin sensitivity [37].

In a similar study, involving 70 Ps patients (BMI < 30) and 40 healthy controls matched for sex, age, and BMI, Ucak et al. [38] measured glucose and insulin plasma concentrations at baseline and following a 75-g glucose load. IR was assessed using the plasma glucose and insulin concentrations. The study established that Ps patients were more likely to demonstrate IR than healthy controls (homeostasis model assessment [HOMA]-IR: 2.95 ± 1.90 μU/mg vs 1.96 ± 0.38 μU/mg, $P < 0.001$). Interestingly, no correlation between duration of Ps or disease severity and IR was found [38]. However, most of the Ps patients had mild disease activity, which might explain the lack of correlation between Ps severity and IR in this study [38].

Notably, cigarette smoking and central obesity are both considered to associate to IR [39,40]. Though all of the studies mentioned earlier considered and adjusted for BMI, some have no information on the smoking habits of Ps patients. Obviously, high prevalence of smoking habits among Ps patients may act as a confounder and further contribute to increased IR. Thus, smoking habits should be taken into account in future analyses. Still, given the findings of IR in Ps patient populations and the fact that obesity is more prevalent in Ps patients, it should be considered that at least a subgroup of Ps patients are at risk for IR and thereby for the development of type II diabetes.

Other Risk Factors

Cigarette smoking in patients with Ps and PsA

The most solid association between cigarette smoking and Ps has been shown in palmo-plantar pustulosis (PPP) psoriasis [41]. Although psoriasis vulgaris and PPP initially were considered closely related, recent research suggests that the two conditions should be considered distinct disorders [42]. Nevertheless, several epidemiological studies have associated current and prior smoking to the onset or/and exacerbation of Ps (Table 2), even though the association is not as strong as in patients with PPP [22••,23•,43–46]. In 1992, Mills et al. [43] performed a case-control study investigating smoking habits in 108 patients with Ps and matched controls. They demonstrated a significant association between Ps and current smoking habits (odds ratio [OR]: 2.7; 95% CI: 1.44–5.42). The authors observed an overall increased risk for Ps among those with smoking habits prior to disease onset (OR: 3.6; 95% CI: 1.5–9.8). Furthermore, the excess risk was more pronounced among the high-intensity smokers (> 20 cigarettes/day) (OR: 5.3; 95% CI: 2.1–13.0) [43]. Since that study, several other investigators have been able to confirm the association between smoking habits and Ps (Table 2). Naldi et al. [23•,45] have conducted different case-control studies that support a dose-response relationship for an association between smoking and Ps, especially in women. Furthermore, they have proposed that smoking is a risk factor for onset of Ps.

In a hospital-based cross-sectional study, involving 818 patients with Ps, Fortes et al. [46] provided further evidence for the dose-response hypothesis and for the notion that the negative impact of cigarette smoking on Ps is greater in women. In line with this finding, Herron et al. [22••], in a cross-sectional study of 557 patients with Ps compared with Utah's general population, reported cigarette smoking to correlate with disease severity. The association between smoking and PsA has not been studied [47]. In contrast, a recent landmark study in RA demonstrated that smoking in the presence of HLA-DR shared epitope alleles might trigger immune reactions to citrullinated proteins [48]. The results of this study are consistent with a gene–environment interaction that is specific to RA, in light of the lack of association of PsA with the shared epitope alleles and the low prevalence of anti-citrillunated antibodies in patients with psoriatic joint disease. Nevertheless, the association of smoking with Ps onset and severity is intriguing and suggests that gene–environmental mechanisms may be involved albeit via a different pathway than identified in RA.

It should also be emphasized in this context that patients with Ps have been reported to have an increased mortality related to smoking [49]. Accordingly, and in light of these findings, the higher prevalence of smoking seen in Ps patients can promote disease onset, contribute to disease severity, and ultimately increase mortality risk. Different mechanisms that could link nicotine to Ps, including the enhancement of proinflammatory cytokines [50] and altered morphology and functionality of leukocytes, have been discussed [51].

Cardiovascular disease in patients with Ps and PsA

Ps is associated with an increased risk for CVD [6,52]. Although the pathogenesis of increased CVD in patients with Ps is poorly understood, several possible biological factors may explain such a link. First, psoriasis appears to be associated with traditional risk factors for CVD, including increased BMI [22••,23•], hypertension [31,32], hyperlipidemia [25••,53,54], type 2 diabetes [6,7], and cigarette smoking [22••,23•,45,46]. Second, recent evidence strongly suggests that chronic inflammation, a characteristic feature of Ps, may play a role in the initiation and progression of atherosclerosis [10]. Elevated levels of high-sensitive–CRP (hs-CRP), a nonspecific marker of inflammation, are one of the emerging risk factors for CVD. The accumulated data have shown that increased hs-CRP levels can predict long-term risk for cardiovascular events [11], and several studies have demonstrated an increased level of hs-CRP in Ps [14,15]. Finally, there is evidence that established treatments for psoriasis such as retinoids and cyclosporin may induce hyperlipidemia, which can promote future CVD [28]. The risk of cardiovascular disease in PsA patients is not well understood although data from a large PsA clinic in Toronto indicated that mortality in these patients was significantly higher than in the general population, and the leading cause of death was circulatory disorders [55].

Comprehensive Care of Patients with Ps and PsA

Accumulating evidence suggests risk life factors contribute to the onset and course of psoriasis. Obviously, these findings open avenues for additional intervention and a more global therapeutic approach. Ps and PsA patients should be counseled regarding comorbidities. Targeting preventive measurements such as lifestyle modification (eg, smoking cessation, decreasing alcohol intake, dietary changes, increasing physical activity), along with treatment of hypertension, dyslipidemia, and diabetes would be highly relevant.

Conclusions

Ps patients have an increased prevalence of obesity and metabolic syndrome compared to that of matched controls. It seems that Ps precedes the obesity and other features of metabolic syndrome in patients. Although the underlying mechanisms for increased metabolic syndrome in Ps patients are not well established, a link between inflammation and metabolic syndrome seems likely. PsA patients are heavier than RA patients and they experience increased mortality rates compared to age-matched

controls. Additional studies are required, however, to determine if Ps patients with arthritis are also at increased risk for diabetes, metabolic syndrome, and hypertension. Certainly physicians, including general practitioners, rheumatologists, and dermatologists should be aware of these associations and take active steps to reduce the cardiovascular risk profiles of Ps and PsA patients in order to lessen mortality and improve quality of life.

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This study is of great importance for investigators interested in clinical psoriasis research. It is a comprehensive study of the impact of obesity and smoking on psoriasis. The authors provide evidence indicating that smoking may have a role in the disease onset, while obesity seems to be a consequence of psoriasis. The findings encourage physicians to highlight the importance of diet, exercise, and smoking cessation to patients with psoriasis.

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