

Review

Evaluation and treatment of metabolic syndrome and cardiovascular disease in adult patients with psoriasis

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Introduction

Cardiovascular disease (CVD) and metabolic syndrome are associated with an approximately twofold increased risk in patients with psoriasis compared to the general population.¹ Recent studies have demonstrated a direct relationship between the severity of psoriasis and risk of developing CVD, major adverse cardiovascular events (MACE), and metabolic syndrome.² There is currently a debate about whether the severity of psoriasis is directly associated with the frequently evidenced reduction in coronary flow reserve.^{3,4} Osto et al. suggested that even in mild presentations of psoriasis, the sustained inflammatory state may contribute to microvascular dysfunction.^{3,4} This concept is reinforced by Flammer and Ruschitzka's theory of "two plaques for one syndrome," as a reference to the similarity of the proinflammatory cytokines

Abstract

Psoriasis is strongly associated with cardiovascular disease (CVD) and metabolic syndrome, with patients having an approximately twofold increased risk of each compared to the general population. This increased risk is based on shared underlying genetic and cytokine profiles, as well as similar environmental risks. Many screening guidelines do not address the development of CVD and metabolic syndrome in these predisposed patients. These deficits are evidenced by the exclusion of psoriasis as a risk factor in validated 10-year CVD risk calculators for adult patients with chronic inflammatory diseases, as well as insufficient screening guidelines for insulin resistance in patients with psoriasis. This manuscript aims to discuss and propose allopathic and lifestyle recommendations for the screening and management of the aforementioned comorbidities in adult patients with psoriasis.

leading to psoriatic plaques and atherosclerotic plaques.⁵ Both diseases display a common pattern of T-cell activation, with T helper 1 (Th1) and Th17 cytokine upregulation, as well as increased local and systemic expression of adhesion molecules and endothelins because of displacements of inflammatory cells among active psoriatic skin, peripheral circulation, and atherosclerotic plaques of coronary vasculature.⁶ Therefore, once there is an endothelial injury, there is a release of cytokines that stimulates more Th17, which in turn fuels its release in positive feedback. This process consequently potentiates the release of further proinflammatory cytokines, such as tumor necrosis factor- α (TNF- α), adhesion molecules, and chemokines.⁶ Eventually, TNF- α and interleukin (IL)-17 work collaboratively to upregulate other key cytokines, such as IL-6.⁶ It has been demonstrated that these inflammatory cascades enhance local oxidative stress and contribute to both cutaneous plaque

angiogenesis and systemic plaque atherogenesis.⁷ This systemic inflammation leads to subsequent hypertension, CVD, coronary microvascular dysfunction, and metabolic syndrome. Management for these disease entities ranges from non-pharmacologic interventions to immunomodulatory therapy directed at reversing the pathways. This article aims to elucidate the current and proposed preventive strategies for both disease entities as well as the recommendations for management. A multidisciplinary team involving a panel of cardiologists, endocrinologists, and dermatologists has provided their consensus opinion based on clinical practice and the available literature sourced from multiple databases including PubMed and Google Scholar.

Proposed screening guidelines for the prevention and control of CVD and metabolic syndrome

The Strength of Recommendation Taxonomy (SORT) was utilized to grade the quality of the evidence available for the new/adjunctive recommended preventive guidelines discussed throughout the manuscript (Table 1, Table S1).⁸ The new/adjunctive recommendations listed throughout this document are primarily SORT level C, in keeping with the limited randomized controlled trials conducted to analyze the evidence provided. The bulk of recommendations discussed are based on consensus, usual practice, disease-oriented evidence, case series for studies of diagnosis, treatment, prevention, or screening and/or opinion. Of note, a strength of recommendation level "C" does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective. Nonetheless, the recommendations outlined in this manuscript serve as screening considerations for physicians in primary practice and dermatology. For definite recommendations, we refer to national guidelines regarding comorbidity screening and management.^{9–11}

Screening for cardiovascular disease

The risk of CVD is commonly underestimated in the psoriasis population, as current scoring criteria used to assess CV risk in the general population do not consider the underlying inflammation as an independent risk factor.¹² Eder et al.¹³ found that the Framingham score has a limited ability to stratify patients with psoriasis. The majority of patients in the intermediate-risk group based on that score and almost half of the patients in the low-risk group were reclassified in a higher-risk group after a carotid ultrasound evaluation. Additionally, it was found that the underestimation of risk was higher in patients with psoriatic arthritis.¹³

The stratification of cardiovascular risk is important as patients with CVD and psoriasis are likely to have worse

outcomes. The presence of carotid atherosclerotic plaques has also been observed commonly in patients with psoriasis and psoriatic arthritis.^{3,12,14} Furthermore, Ahlehoff et al. assessed the prognosis of patients with previous myocardial infarction and concluded that the presence of psoriasis leads to a statistically significant worse prognosis.¹⁵ Additionally, there is emerging evidence that severe psoriasis is not only associated with CV risk factors but also with worse left ventricular performance index even in the absence of cardiac diseases.³

The current recommendations for screening and management of CVD are as follows, with new recommendations denoted by the symbol "O":

- The European Society of Cardiology (ESC) Guidelines on Cardiovascular Disease Prevention in Clinical Practice recommends a stepwise approach starting with prevention goals for all, regardless of CVD risk.¹⁶ In patients without a prior personal or family history of atherosclerotic cardiovascular disease (ASCVD), this involves considering 10 years risk of fatal and non-fatal CVD events using Systemic Coronary Risk Estimation 2 (SCORE2) algorithm, identifying modifiable risk factors and determining a treatment plan using a collaborative approach.
- The American College of Cardiology recommends the initiation of moderate-intensity statin therapy if the ASCVD is calculated to be "intermediate risk," that is, ≥ 7.5 to $< 20\%$, and the patient has the presence of risk enhancers such as psoriasis or other inflammatory skin diseases.¹⁷
- Risk stratification should be adapted by introducing a 1.5 multiplication factor for patients with either $> 10\%$ body surface area involvement or those who are candidates for systemic treatment or phototherapy.¹¹ However, due to the evidence that coronary microvascular dysfunction is not only associated with severe psoriasis but also young patients with no prior evidence of CVD, the authors propose that^{3,4}:
- Risk scores for the initial stratification of cardiovascular risk in patients with psoriasis should be adjusted by a multiplier factor of 1.5 in all patients with psoriasis, to account for the underlying inflammation.¹²
- In patients with psoriasis stratified as low risk, after a multiplier factor of 1.5 has been applied to the Framingham Risk Score, QRISK3 or SCORE2, a cardiovascular evaluation would be appropriate at least every 3 years.¹²
- At intermediate risk after the aforementioned modified risk assessment, the evaluation should be annual.¹² Additionally, clinicians should consider early and more frequent screening for hypertension, diabetes, and hyperlipidemia in patients with psoriasis who are candidates for systemic or phototherapy or who have psoriasis involving $> 10\%$ of the BSA.
- Patients classified as high risk require intensive preventive interventions, without the need for a new evaluation.¹²
- Consider vessel wall volume analysis, coronary artery calcium (CAC) score, CT artery angiography, lipoprotein(a), and the

Table 1 Summary of the current and proposed recommendations for the screening of comorbidities contributing to CVD and metabolic syndrome in patients with psoriasis

Comorbidity	Current recommendation	New/adjunctive recommendation	Level of evidence (LOE)	Strength of recommendation
Cardiovascular disease	1. Risk stratification using the 10-year CVD risk factor calculators should be adapted by introducing a 1.5 multiplication factor for patients with either >10% body surface area involvement or those who are candidates for systemic or phototherapy ¹¹	Risk scores for the initial stratification of cardiovascular risk in patients with psoriasis should be adjusted by a multiplier factor of 1.5 in all patients with psoriasis, to account for the underlying inflammation ¹²	3	C
	2. Moderate-intensity statin therapy can be initiated if the ASCVD is calculated to be "intermediate risk," i.e., ≥7.5% to <20%, and the patient has the presence of risk enhancers such as psoriasis or other inflammatory skin diseases ¹⁷	Frequency of screening as per recommendations by Masson et al. ⁶⁰	2	B
	Perform an initial non-fasting lipid panel at the time of diagnosis: Total low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides (TG). If abnormal (initial total cholesterol >200, HDL < 45 or non-HDL > 145 mg/dl), confirm with fasting lipid panel ²⁰	Consider coronary artery calcium (CAC) scoring for initial risk stratification in patients aged greater than 30 with indications found in the statement by the National Lipid Association ¹⁰	3	C
	Evaluate lipid levels every 2 years due to ongoing risk factors	Consider lipoprotein(a) as a risk stratification tool. No treatment target for lipoprotein(a) is currently recommended. Elevated levels are commonly treated with the lowering of low-density lipoprotein (LDL) ²¹		
Hypertension	Patients aged >40 years and those at increased risk for high blood pressure (BP: 130–139/85–89 mm Hg, overweight/obese, Black) are recommended to have annual adequate office blood pressure measurement and, if indicated, confirmation with ambulatory blood pressure monitoring. Meanwhile, patients aged 20–39 years with a normal BP (<120/80 mm Hg) or no risk factors and BP < 130/85 mm Hg are recommended to be screened every 3–5 years	Target lipid levels in keeping with the national guidelines. Consult with lipid specialist to determine benefit of starting statin therapy if LDL >160 mg/dl or more than one risk factor for dyslipidemia present (Table S2)		
		Consider evaluating TSH levels: patients with underlying autoimmune problems are at risk of developing autoimmune hypothyroidism. ²² Untreated hypothyroidism can present with dyslipidemia that may be improved with thyroid replacement ^{23,24}		
		Measure blood pressure at least annually from age ≥ 20, starting at the time of psoriasis diagnosis. Target SBP < 120–130 mm Hg, DBP < 80 mm Hg	3	C
Heart rate	Evaluate for tachycardia and irregular rhythm at least every 2 years (increased incidence of atrial fibrillation) ³²	Screen for sleep dysfunction every 2–3 years using the insomnia severity score. Assess common causes of insomnia such as pain and pruritus by using subjective QOL measures such as the insomnia severity index. Also assess for associated differential diagnoses (restless leg syndrome, periodic limb movement disorder, and obstructive sleep apnea)	3	C
		Consider a cardiology referral for tachycardia without an underlying cause		
Type 2 diabetes mellitus	Evaluate the fasting plasma glucose (FPG) or glycated hemoglobin (HbA1c) every 5 or 2 years if risk factors are present (see supplementary table 4, with a target FPG of ≤100 mg/dl, HbA1c < 5.7%	Consider a cardiology referral or Holter monitor for symptomatic palpitations		
		Evaluate FPG or HbA1c at least every 2 years. Screening may be performed more frequently in patients with moderate–severe PASI scores or BSA > 10%	3	C

Comorbidity	Current recommendation	New/adjunctive recommendation	Level of evidence (LOE)	Strength of recommendation
	Recommend measuring body mass index, FPG, and triglyceride (TG) plasma values in the diagnosis of insulin resistance	Furthermore, studies are needed to confirm the ideal percentiles for homeostasis model of insulin resistance (HOMA-IR), insulin sensitivity index (ISI), adipose tissue insulin resistance index (Adipo-IR), or lipoprotein IR (Lipo-IR), and their clinical utility Consider medications for insulin resistance such as peroxisome proliferator-activated receptor-gamma (PPAR γ) agonists and biguanides, as well as the natural alkaloid berberine	3	C
Obesity	Patients with moderate-to-severe psoriasis should have their obesity status (height, weight, waist circumference, BMI) determined annually ^{11,32}	For patients with a normal initial BMI, the BMI should be evaluated at least every 2 years; target <25 kg/m ² . Additionally, waist circumference should be evaluated at least every 2 years; target: <35 inches for women, <40 inches for men	3	C
	Refer to nutritionist to determine ideal macronutrient and micronutrient intake	Advise vitamin D supplementation for serum concentrations of 25(OH)D to begin at 75 nmol/l (30 ng/ml), with the goal being 90–100 nmol/l (36–40 ng/ml)	3	C
		Consider intake of fruit rich in resveratrol as appropriate	3	C
	Reinforce adherence to exercise: At least 150 to 300 min/week of aerobic exercise, combined with at least twice weekly strength/resistance training. Recommended BMI < 25 ^{32,58}	Also recommend goal of average or above average skeletal muscle mass index	3	C
	Screen for comorbid conditions such as obstructive sleep apnea (OSA) and gastroesophageal reflux disease (GERD)	–	1	A
Mental health status	Perform anxiety and depression screening yearly	Screening can be done using tools such as the Beck's Depression Inventory II (BDI-II) or through clinical discussion Consider performing dermatology life quality index (DLQI) yearly or when step-up therapy indicated	3	C
	Screen yearly for substance abuse Inquire about tobacco smoking status and encourage smoking cessation as indicated		3	C

- CAC score has demonstrably superior diagnostic power compared to carotid artery measurements and should be used in accordance with the American Heart Association guidelines, generally in patients older than 30.^{15,18} Clinicians reporting CAC scores should report both the absolute Agatston CAC score and the age, sex, and race/ethnicity-based CAC percentiles. Furthermore, information about CAC scoring and indications can be found in the statement by the National Lipid Association.¹⁹

Initial non-fasting lipid panel at the time of diagnosis: total low-density lipoprotein (LDL) cholesterol, high-density

- Consider lipoprotein(a) as a risk stratification tool. No treatment target for lipoprotein(a) is currently recommended. Elevated levels are commonly treated with more aggressive LDL lowering.²¹ Target lipid levels in keeping with the national guidelines. Consult with lipid specialist to determine benefit of starting statin therapy if LDL > 160 mg/dl or more than one risk factor for dyslipidemia present (Table S2)
- Consider evaluating TSH levels: patients with underlying autoimmune problems are at risk of developing autoimmune hypothyroidism.²² Untreated hypothyroidism can present with

dyslipidemia that may be improved with thyroid replacement.^{23,24}

- Other secondary causes of hypercholesterolemia should be ruled out including, but not limited to: liver disease, nephrotic syndrome, diabetes mellitus, pregnancy, drugs (isotretinoin, antiretroviral medications, corticosteroids, alcohol, etc.).²⁵
- Management: Use SCORE2 to determine the indication for starting statin therapy and use the United States Preventive Services Task Force (USPSTF) guidelines as a tool for statin selection.^{9,16}
- CVD risk in inflammatory conditions should be treated with similar interventions as in the general high-risk population, as there is evidence that traditional methods to lessen risk (e.g., lipid-lowering treatment) are just as beneficial in preventing ASCVD (Table S3).
- In addition to pharmaceutical intervention and CVD prophylaxis, it is recommended to guide patients with psoriasis to suitable dietary interventions, low/moderate alcohol intake, smoking cessation, physical training, and weight loss interventions to achieve a BMI < 25.

Screening for hypertension

Raised blood pressure is a major cause of both ASCVD and non-atherosclerotic CVD (particularly heart failure [HF]).¹⁶ In patients with psoriasis, raised PASI scores have been demonstrated as positively correlated with blood pressure levels. It should also be noted that some medications used to treat psoriasis can induce or worsen hypertension. For example, cyclosporine commonly causes new-onset hypertension or worsening of preexisting hypertension. The calcium channel blocker amlodipine is often found to successfully reverse the effects of cyclosporine-induced hypertension.¹¹

The following recommendations for screening are below, with new recommendations denoted by the symbol “○”:

- The Joint AAD-NPF guidelines suggest that adults aged 18–39 with no risk factors should screen for hypertension every 3–5 years. If aged >40 and at increased risk for high blood pressure, screen yearly with adequate office blood pressure measurement and, if indicated, confirm the blood pressure with ambulatory blood pressure monitoring.¹¹
- Because of the strong positive correlation of HTN with psoriasis, these authors recommend the evaluation of blood pressure at least annually, especially in people with moderate–severe PASI scores or BSA involvement >10%.
- Screen for sleep dysfunction:
The recommended hours of sleep per 24 hours (including naps) on a regular basis for optimal health are as follows: 8–10 hours for teenagers, 7–9 hours for young adults and adults, and 7–8 hours of sleep for older adults.²⁶ Non-restorative sleep and a sleep duration that varies significantly up or down from the optimum of 7 hours are

associated with increased CV risk.¹⁶ Pruritus, variations in patient expectations, sleep hygiene or comorbid depression, and anxiety may result in transient physiological discomfort that impacts sleep and/or subsequent chronic insomnia. However, it should be noted that conditions such as restless leg syndrome and periodic limb movement disorder (PLMD) also have increased prevalence in patients with psoriasis.²⁷ Therefore, alternate causes of sleep disturbance should be considered and patient assessment of sleep disruption using qualitative QOL scoring criteria such as itch severity scale (ISS), insomnia severity index (ISI), or objective sleep studies such as polysomnography should be employed.^{16,28,29}

Heart rate and rhythm

Patients with psoriasis are susceptible to a significantly increased risk of new-onset atrial fibrillation (AF) compared to controls.³⁰ A cohort study of a Danish population demonstrated that in patients with mild psoriasis, the adjusted rate ratios (RRs) for AF were 1.50 (1.21–1.86) and 1.16 (1.08–1.24) in patients aged <50 and >50 years, respectively.¹⁵ Patients with severe psoriasis had a higher risk of AF with RRs 2.98 (1.80–4.92) in patients aged <50 years and 1.29 (1.01–1.65) in patients aged >50 years.¹⁵ This finding is in keeping with Chiu et al.'s findings that patients with psoriasis aged 20–39 years were at higher risk for arrhythmia (aHR: 1.39; 95% CI: 1.26–1.54) compared to middle-aged and elderly patients.³¹ However, the risk of AF was significantly elevated in all, likely secondary to the underlying inflammation in both disease processes.

The authors agree with the current recommendation for screening, which is^{30,32}:

- Evaluate at least every 2 years (increased incidence of atrial fibrillation).

This evaluation should include checking the pulse rate for tachycardia (HR > 100 bpm) and considering a cardiology referral for tachycardia without an underlying cause. Additionally, clinicians should consider a cardiology referral or Holter monitor for symptomatic palpitations.

Screening for type 2 diabetes mellitus and insulin resistance

Psoriasis is an independent risk factor for type 2 diabetes mellitus (T2DM) (OR: 1.59; 95% CI: 1.38–1.83) and earlier age of psoriasis onset (<40 years old) as well as the presence of psoriatic arthritis may impart an even greater risk of T2DM in adults.³³ USPSTF recommends screening for prediabetes and T2DM between the ages 35–70 years in individuals with obesity or an overweight status.¹⁰ Earlier screening is advised in patients with

a disproportionately high incidence of T2DM, such as a history gestational DM, family history of DM, or BMI ≥ 23 kg/m² as in the Asian American population (Table S4).¹⁰ With the caveat of insulin resistance and metabolic syndrome in mind, inflammatory skin diseases such as psoriasis should also be considered. Therefore, these authors also propose earlier screening for T2DM in patients with psoriasis.

Fasting plasma glucose (FPG) levels, BMI, and triglycerides (TG) plasma values have been noted to have clinical utility in the diagnosis of insulin resistance.³⁴ Currently, the ESC/European Association for the Study of Diabetes guidelines on diabetes, prediabetes, and CVD recommend starting with FPG or HbA_{1c} and proceeding to oral glucose tolerance tests (OGTT) if the results are uncertain.³⁵ The American Diabetes Association guidelines equally recommend the use of HbA_{1c}, FPG, and 2-hour postprandial glucose (2hPG).³⁶ Currently, screening for hyperglycemia in patients with coronary artery disease by means of serum insulin, C-peptide, and homeostasis model of insulin resistance (HOMA-IR) has a low sensitivity and specificity to detect glucometabolic abnormalities compared with the gold-standard 2hPG.³⁷

The following recommendations for screening are below, with new recommendations denoted by the symbol “○”:

- T2DM screening should start at age 40 if the patient is overweight and at age 45 if there are no risk factors.
- An FPG and/or hemoglobin A1C should be performed by a healthcare provider in patients with psoriasis according to national guidelines.¹¹ If these studies are conducted by the patient's dermatologist, those with prediabetes or new-onset diabetes should be referred to their primary care provider for further assessment and management.
- The ADA recommends using a confirmatory approach (repeat testing or using a combination of elevated FPG and A1C in a single blood sample) if either one of the glycemic markers is elevated, that is, FPG > 126 mg/dl or HbA_{1c} $\geq 6.5\%$.³⁸
- The National Psoriasis Foundation recommends evaluating the FPG every 5 or 2 years if risk factors (Table S4) are present, with a target FPG of ≤ 100 mg/dl, HbA_{1c} $< 5.7\%$.
 - Evaluate FPG at least every 2 years. Screening may be performed more frequently in patients with moderate-severe PASI scores or BSA $> 10\%$.
- Recommend measuring BMI, FPG, and triglycerides (TG) plasma values in the diagnosis of insulin resistance: The best measure of insulin resistance is still unknown.
- Further studies are needed to confirm the ideal percentiles for HOMA-IR, insulin sensitivity index or adipose tissue insulin resistance index (Adipo-IR), or lipoprotein IR (Lipo-IR) and their clinical utility.³⁹
- Consider medications for insulin resistance such as PPAR γ agonists and biguanides, as well as the natural alkaloid berberine.
- These authors recommend consultation with an endocrinologist for optimal, individual dosage of the above-recommended

medications for patients with insulin resistance.⁴⁰ Esmaeili et al. observed a significant decrease in the expression of catalase gene in patients with psoriasis ($P = 0.02$), likely as a result of sustained exposure to ROS leading to decreased expression of the catalase gene.⁴¹ This finding could provide utility of PPAR γ agonists, such as thiazolidinediones, as PPAR γ regulates catalase production and is decreased in patients with psoriasis.⁴² By virtue of this replacement, and the other characteristics of thiazolidinediones such as adipocyte differentiation, decreasing FFA, TNF- α , and leptin, the mitochondrial regulation of PPAR γ may have a role in the prevention of metabolic syndrome in patients with psoriasis.⁴³ Furthermore, studies are needed to reinforce this point. AMP-activated protein kinase (AMPK) dysfunction is also believed to be implicated in the pathogenesis of metabolic disorders; AMPK activates PGC1 α within the mitochondria enhancing the biogenesis and inhibition of ROS, similar to the sirtuin pathway. Thiazolidinediones and biguanides share a common effect on AMPK potentiation, and their potential clinical utility for insulin resistance treatment is being evaluated.⁴⁴ Additionally, berberine prevents the development of atherosclerosis, T2DM, and cardiovascular disorders by lowering blood glucose, hemoglobin A1c, TC, LDL-C and triglycerides, and reducing body weight and fat mass.⁴⁵ Furthermore, it seems to have beneficial effects on endothelial function.⁴⁵ The principal mechanism responsible of its insulin-sensitizing action is the upregulation of insulin receptor expression, accompanied by activation of AMPK and inhibition of intestinal disaccharides. Multiple clinical trials are currently underway to determine optimal dosage and compare the efficacy against other agents such as biguanides.⁴⁶

For follow-up of T2DM or insulin resistance, once diagnosed, we use recommendations in keeping with the USPSTF and the National Psoriasis Foundation.^{10,32}

Screening for obesity

Increased waist circumference has been directly correlated with the incidence of developing psoriasis and having increased PASI scores. This is likely because of the production of inflammatory cytokines in visceral obesity representing the link involved in the complex mechanisms leading to the exacerbation of psoriasis and psoriasis comorbidities.⁴⁷

The following recommendations for screening are given, with new recommendations denoted by the symbol “○”:

- Patients with moderate-to-severe psoriasis should have their obesity status determined annually. This includes measuring height, weight, waist circumference, and calculating BMI.¹¹
- For patients with a normal initial BMI, the BMI should be evaluated at least every 2 years; target < 25 kg/m². Additionally, waist circumference should be evaluated at least every 2 years; target: < 35 inches for women, < 40 inches for men.³²

- The fibrosis-4 index (FIB-4) should be calculated in patients with metabolic risk factors or unexplained liver chemistries. Patients >35 years old with 1–2 metabolic risk factors in the absence of T2DM/prediabetes should be reevaluated every 2–3 years. Patients <35 years with metabolic risk factors should have secondary evaluation with either vibration-controlled elastography (VCTE), enhanced liver fibrosis (ELF), or referral to a hepatologist/specialist.⁴⁸
- Refer to nutritionist to determine ideal macronutrient and micronutrient intake.
- Consider intake of fruit rich in resveratrol as appropriate: Resveratrol is naturally occurring in foods such as berries, nuts, red grapes with its use as an active ingredient due to its antioxidant properties as an activator of SIRT1.^{49,50} It notably improves mitochondrial function and promotes mitochondrial biogenesis, therefore having a role in chronic inflammatory diseases such as psoriasis, which have associated mitochondrial dysfunction.⁴⁹ For example, murine models have demonstrated the anti-atherosclerotic activity of resveratrol, likely due to its modulatory activity over the PI3K/AKT/mTOR signaling pathway.⁵¹ However, further studies are needed to clarify the effect on additional pathways, optimal dosing, and adverse effects.⁵²
- Vitamin D supplementation for serum concentrations of 25 (OH)D of at least 75 nmol/l (30 ng/ml), with goal being 90 and 100 nmol/l (36–40 ng/ml): An inverse relationship has been demonstrated between BMI status and vitamin D levels, likely due to sequestration of vitamin D in the adipose tissue, volumetric dilution related to the greater volume of distribution of 25(OH)D, and/or less exposure of skin to sunlight because of less outdoor activity and air pollution.^{53,54} Therefore, with the associations of low vitamin D status with obesity and low vitamin D status with psoriasis, a hypothesis exists for considering vitamin D as a further link between obesity and psoriasis. In this context, a vicious cycle could operate among low vitamin D status, obesity, and psoriasis, with additive detrimental effects on cardiometabolic risk in patients with psoriasis and obesity. According to this hypothesis, vitamin D supplementation might be of particular usefulness for the prevention of psoriasis-related comorbidities.⁴⁷ Vitamin D is additionally suspected to have multiple effects on the cardiovascular system. On the heart, it exerts antihypertrophic effects, modulates contractility, regulates the extracellular matrix turnover, and suppresses the renin-angiotensin aldosterone system. On the vessels, it exerts anti-atherosclerotic effects, inhibits vascular calcification, and improves endothelial function.⁵⁵
- Screen for comorbid conditions such as obstructive sleep apnea (OSA) and gastroesophageal reflux disease (GERD): OSA has increased prevalence in patients with psoriasis compared to the general population, with a prevalence of 36–81.8% in the former compared to 2–4% in the latter.²⁷

These two syndromes have an overlap in their associated comorbidities of obesity, hypertension, diabetes, metabolic syndrome, and psychiatric disorders. Therefore, the underlying inflammation and endocrine disruption would need to be treated in conjunction with the symptoms of OSA and psoriasis to see improvement when these conditions present simultaneously.

- For all patients, reinforce adherence to exercise: At least 150–300 min/week of aerobic exercise combined with at least twice weekly strength/resistance training:
- Recommend goal of average or above average skeletal muscle mass index + BMI < 25: Kim G et al. found an inverse association between baseline skeletal muscle mass index (SMI) and metabolic syndrome development in a 7-year longitudinal follow-up study.⁵⁶ These findings were variable in subjects with obesity but consistent in subjects without obesity. However, an increase in relative muscle mass over a single year was significantly associated with low risk of metabolic syndrome even in people with obesity who have a high cardiometabolic risk, suggesting that an increase in relative skeletal muscle mass is a potent preventive parameter for metabolic syndrome.⁵⁶ Additionally, skeletal muscle hosts glucose transporter 4 (GLUT 4) and is a major site of postprandial glucose utilization. Overall, SMI changes were negatively correlated with changes in waist circumference, SBP, HOMA-IR, and concentrations of HbA_{1c}, fasting glucose, triglycerides, and LDL cholesterol, but not significantly so with CRP levels.⁵⁶ Lastly, it has been observed that the number of steps per day is directly related to insulin growth factor-1 (IGF-1) levels and inversely related to high-sensitivity C-reactive protein (hsCRP).⁵⁷

Furthermore, guidelines for exercise recommendations can be found in the Physical Activity Guideline for Americans, 2nd ed.⁵⁸

Mental health screening in adults

The risks of depression, anxiety, and suicidality are increased even among patients with mild psoriasis.⁵⁹ Mental disorders with either significant functional impairment or decreased use of healthcare systems should be considered as influencing total CVD risk. Additionally, the treatment of an unhealthy lifestyle via exercise therapy, healthy dietary practices, and abstinence from substance use reduces CVD risk as well as improves mental health. The recommendations for mental health screening are as follows:

- Perform anxiety and depression screening yearly.
- Screening can be done using tools such as the BDI-II or through clinical discussion. Refer to a mental health provider for formal evaluation if positive.
- Screen yearly for substance abuse.

- Inquire about tobacco smoking status and encourage smoking cessation as indicated.
- Consider performing dermatology life quality index (DLQI) yearly or when step-up therapy indicated.

Discussion

Psoriasis is a chronic inflammatory disease with much potential for intervention to reduce the incidence and progression of associated comorbidities such as CVD and metabolic syndrome. Thorough screening and management are essential for these patients at risk of insulin resistance, cardiovascular dysfunction, and psychiatric comorbidities. This manuscript provided background regarding the role of lipoprotein(a) in lipid panels, recommendations for exercise, and weight management to decrease insulin resistance, as well as guidance for heart rate, blood pressure management, and glucose control. These supplements serve as a guide for future studies and reinforce the collaborative effort needed by clinicians to reduce the “psoriatic march” and additional sequelae.

Conclusion

The evidence provided in this literature expounds on existing guidelines and recommendations for comorbidity screening in adult patients with psoriasis. Future high-quality studies are needed to strengthen the evidence provided throughout this review, which serves primarily as a framework for screening and managing adult patients with psoriasis with allopathic medications and lifestyle interventions for the reduction of CVD and metabolic syndrome.

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Questions

- 1 What is the recommended value to modify 10 years CVD risk scores in patients with psoriasis?
 - a 2
 - b 3
 - c 1.5
 - d No modification required
- 2 An inverse relationship exists between skeletal muscle mass index and metabolic syndrome.
 - a True
 - b False
- 3 What is currently the most reliable clinical marker for measuring insulin resistance?
 - a Homeostasis model of insulin resistance (HOMA-IR)
 - b Adipose tissue insulin resistance index (Adipo-IR)

- c Insulin Sensitivity Index (ISI)
 - d A combination of BMI, FBG, and triglyceride plasma values
- 4 Intake of which food groups provides a diet rich in resveratrol? (More than one may be selected)
 - a Grains
 - b Dairy
 - c Fruits
 - d Legumes
 - 5 Thiazolidinediones and biguanides share a common effect on which of the following receptors?
 - a AMPK
 - b SIRT1
 - c PPAR γ
 - d Insulin
 - 6 Untreated hypothyroidism can present with dyslipidemia.
 - a True
 - b False
 - 7 Psoriasis has no known association with which of the following?
 - a Obstructive sleep apnea
 - b Restless leg syndrome
 - c Parasomnias
 - d Periodic limb movement disorder
 - 8 Which age group has a higher risk of developing atrial fibrillation as a complication of psoriasis?
 - a 20–39 years
 - b 50–59 years
 - c 60–69 years
 - d 70–79 years
 - 9 Non-alcoholic fatty liver disease should be evaluated in all patients with psoriasis
 - a True
 - b False
 - 10 What is the current recommendation for the frequency of formal screening for anxiety and depression in patients with psoriasis?
 - a Every 3 years
 - b Every 2 years
 - c Every follow-up
 - d Every year

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Answers to Questions

- 1 c
- 2 a
- 3 d
- 4 c, d
- 5 a
- 6 a
- 7 c
- 8 a
- 9 a
- 10 d

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Outlining the requisites for the SORT grading system.⁶¹

Table S2. Outlining risk factors for dyslipidemia. Adapted from Kang et al.⁶²

Table S3. Demonstrating the indications for starting statin therapy in patients with psoriasis. Adapted from Masson et al.⁶⁰

Table S4. Outlining the risk factors for T2DM. Adapted from the American Diabetes Association.³⁸