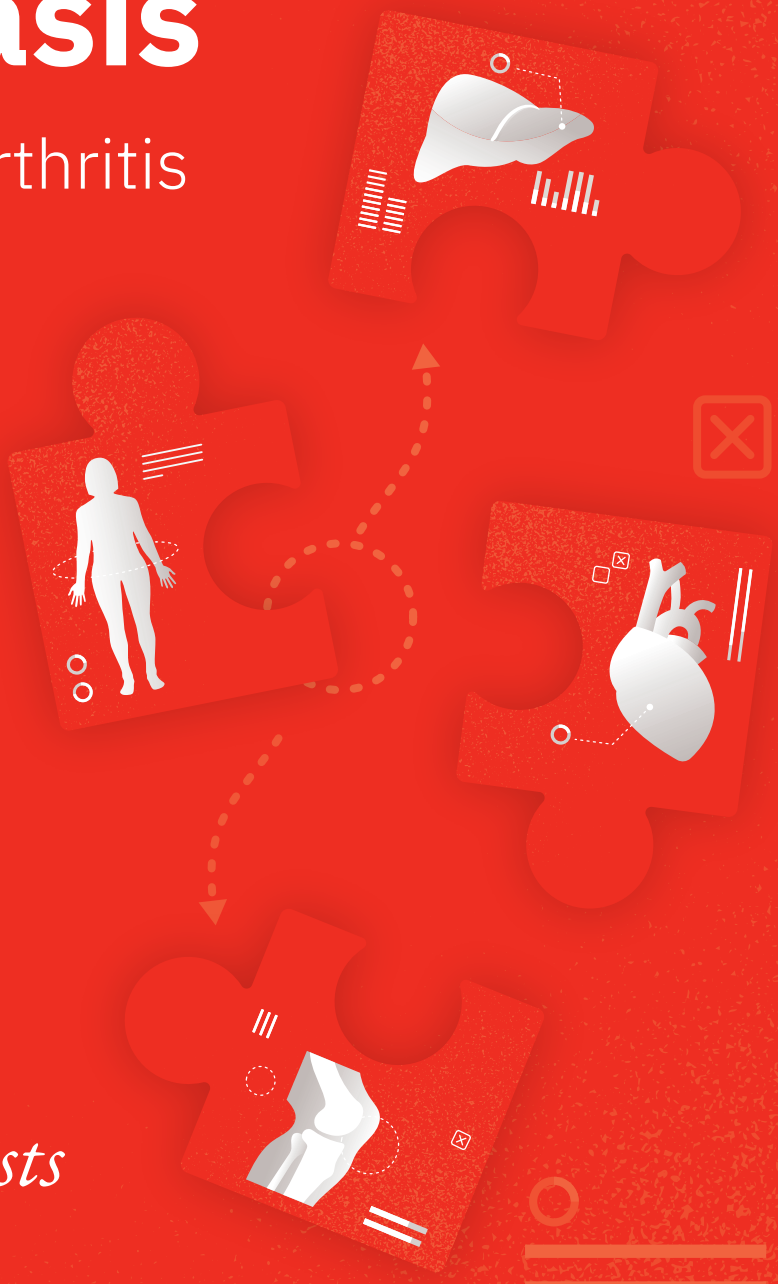
Comorbidities in Psoriasis

From Psoriatic Arthritis to Obesity



Key Takeaways for *Dermatologists*

Impact of Race/Ethnicity

PSOLAR: Registry of Patients With Moderate-to-Severe PsO – North American Dataset[1]

Prevalence of PsO comorbidities by self-reported race/ethnicity

	Obesity (BMI ≥30 kg/m²)	Cardiovascular disease	PsA
White (n=8338)	50.7%	39.9%	37.3%
Black (n=404)	**58.9%**	**48.3%**	34.2%
Asian (n=436)	23.2%	29.8%	30.5%
Hispanic/Latino (n=668)	**57.8%**	30.8%	36.8%
Other (n=261)	44.8%	39.9%	34.9%

Patients with moderate-to-severe PsO who are Black have higher rates of obesity and CVD, and are more likely to have a poorer QoL due to the impact of disease[1]

- 80.0% of Black patients reported a DLQI ≥2, vs. 68.6% of White patients

Presentation of PsO in patients with skin of color

- In darker skin, **recognizing inflammation** is nuanced since erythema often appears violaceous, dark brown, or gray[2]
- Patients may be left with **hyper- or hypopigmentation** after psoriatic lesions have resolved[2]
- **Prevalence of PsO varies** between different races[3]
- Race and ethnicity may be associated with socioeconomic disparities that impact **access** and **adherence** to different types of treatments[4]

Obesity

Obesity Impacts the Body's Homeostasis

Pathological increase of **adipose tissue** and dysfunction induces **qualitative and quantitative changes in signal production**[5]

→

These changes induce low-grade systemic inflammation,[5-7] insulin resistance,[5,8] endothelial dysfunction,[8] synthesis of pro-clotting factors,[8] and other metabolic disorders[5]; ultimately leading to the **impairment of multiple organs and their functions**[5]

Patients With PsO and Comorbid Obesity Are More Likely to Have Involvement of Challenging Body Areas

Up to 38% of patients with PsO have **comorbid obesity**[a-c,9,10]

Palms and Soles
3.5× higher prevalence in patients with **comorbid obesity**[d,e,11]

Inverse PsO (intertriginous areas)
2.2× higher prevalence in patients with **comorbid obesity**[c,d,12]

Nails
1.8× higher prevalence in patients with **comorbid obesity**[c,d,13]

Treatment Considerations

- Patients with PsO and comorbid obesity[c] may have a lower response to some biologics for PsO, compared to those without comorbid obesity[14]
- Weight loss is associated with a numerical reduction in PASI score[15]

1.5× to 3×[f] higher risk of PsA in patients with **PsO** and **comorbid obesity**[g,16]

AAD/NPF Recommendations for Dermatologists[17]

- Inform patients regarding the association between metabolic syndrome components and PsO
- Advise patients to practice a healthy lifestyle (appropriate diet, regular exercise, smoking cessation, and mental wellness)
- Ensure that the patient is engaged with their PCP for appropriate screening
- Communicate with the patient's PCP to have them evaluated and appropriately treated for obesity/comorbidities (including referral to the appropriate HCP specialist to confirm diagnosis and treatment)

[a]The value of 38% differs from that shown on page 2, which was based on data from the PSOLAR registry,[1] as the NHANES data encompass a broader population.[9,10] [b]NHANES is a nationally representative survey of the US civilian, non-institutionalized population conducted by the CDC NCHS. The cross-sectional survey includes an in-home interview to obtain sociodemographic characteristics and medical history, and a physical examination and laboratory measures, including BMI, taken at a mobile examination center. Patients self-reported being diagnosed with PsO. [c]Obesity defined as BMI ≥30 kg/m². [d]Studies involved a small number of patients and not all studies consistently reported the same prevalence. [e]Obesity defined as BMI ≥25 kg/m². [f]Based on data from a study in US women. [g]Obesity definition ranged from BMI ≥30 kg/m² to ≥35 kg/m².

Cardiovascular Disease

PsO is an Independent Risk Factor for CVD[18]

PsO and cardiometabolic disorders may be associated with each other via systemic **inflammation**[19]

The development of atherosclerosis in PsO may result from a combination of induced immune system activation and pan-arterial inflammation, alongside comorbid cardiometabolic conditions[20]

Pathophysiological variables[20]

- *T cells, platelets, myeloid lineage cells, adipocytes, inflammasome signaling*

Clinical factors[20]

- *For example, hypertension, hyperlipidemia*

PsO and atherosclerosis share common disease pathways:[18]

- *Reduced T-regulatory cell numbers result in decreased production of anti-inflammatory and increased activity of Th1 and Th17 cells*
- *Th1 cells release pro-inflammatory cytokines that activate macrophages, keratinocytes, and vascular cells, triggering additional cytokine production*

Patients with PsO are up to 50% more likely to develop CVD compared to those without PsO[20]

Severe PsO confers the highest CV risk (compared with control subjects), including up to[20]

- *3-fold increased odds of myocardial infarction*
- *60% higher odds of stroke*
- *40% higher odds of CV-related mortality*

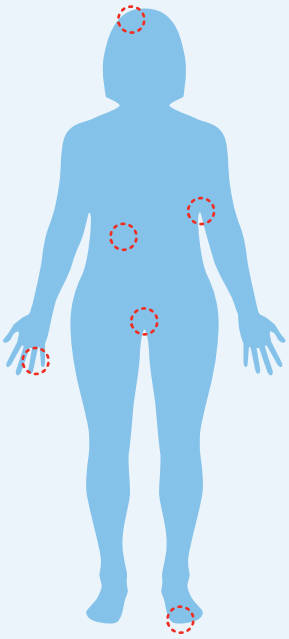
Biologic therapy for PsO is associated with reduced coronary inflammation[21]

AAD/NPF Recommendations for Dermatologists[17]

- Dermatologists should inform patients about the association between CVD and PsO and ensure that the patient is receiving care from their primary care provider or cardiologist for screening purposes
- CV risk assessment (screening for hypertension, diabetes, and hyperlipidemia) with national guidelines is recommended for all patients with PsO
- Consider early and more frequent screening for hypertension, diabetes, and hyperlipidemia in PsO patients who are candidates for systemic or phototherapy or who have PsO involving >10% of the BSA
- Risk score models should be adapted for patients with PsO
- CV risk management in PsO for hypertension and dyslipidemia should be carried out according to national guidelines

Psoriatic Arthritis

There are several risk factors that may contribute to the development of PsA in patients with PsO



Effect Size (95% CI)[a]

BMI ≥35 kg/m² [b,c,16]
In general population:
up to RR 6.46 (4.11-10.16)
In patients with PsO:
up to RR 2.98 (1.86-4.78)

Inverse PsO[16]
Intergluteal/perianal involvement:
HR 1.95 (1.07-3.56)

Severity of PsO[d,16]
RR 5.39 (1.64-17.7)

Scalp PsO[22]
HR 3.89 (2.18-6.94)

Nail dystrophy[22]
HR 2.93 (1.68-5.12)

Physical trauma (all)[16]
HR 1.32 (1.13-1.54)

Other risk factors include family history of PsA, smoking, and duration of PsO; however, for the latter two, results for their impact on risk are mixed[16]

Treatment Considerations

In PsA, irreversible joint damage[23]

- Can happen with a delay in diagnosis of just 6 months
- Can lead to worse long-term physical function

Simple Mnemonic: PsA[24]

Joint
PAIN
STIFFNESS
AXIAL
involvement

after waking in the morning, or after a period of inactivity.
Swelling/Sausage digit (dactylitis)

AAD/NPF Recommendations for Dermatologists[17]

- Patients with PsO should be informed about the association between PsO and PsA
- PsA should be considered in all patients with cutaneous PsO
- Patients with signs and symptoms suspicious for PsA should be fully evaluated for PsA. Initiate appropriate PsA therapy if comfortable with the diagnosis or otherwise consult with a rheumatologist for assessment and management

Note: Risk factors for the development of PsA in patients with PsO are from cohort studies unless otherwise stated.
[a]Adjusted for other covariates. [b]BMI ≥35.0 kg/m² vs. normal (BMI <25.0 kg/m²). [c]Time varying exposure. [d]PASI score >20 vs. <10.

Hepatic Disease

Patients With PsO Are at an Increased Risk of Developing Hepatic Disease

MAFLD encompasses a spectrum of liver diseases ranging from steatosis, which is relatively benign, to MASH – a severe form where fatty infiltration is accompanied by inflammation and hepatocellular ballooning[25]

The **pathogenic link** between **PsO and MAFLD/MASH** may be **bi-directional**[17,25-27]

- Skin lymphocyte-derived cytokines may circulate through and potentially damage the liver, **and/or**[17]
- Hepatic inflammatory cytokines may circulate systemically and promote keratinocyte hyperproliferation[17]

Patients with PsO have a **higher risk** of MAFLD compared with non-PsO controls[27]:
OR 1.67 (95% CI 1.03-2.70), p=.04[27]

Patients with PsO and PsA are at an increased risk of MASH[28]

In a population of patients with PsO or PsA (N=103)

47% had ***MAFLD***, and of those

48% had ***MASH***

- Patients with MASH are **at risk** of progressing to advanced liver disease[25,26]
- MASH can result in **cirrhosis in 12-25% of cases**[26]
- Hepatocellular cancer **develops at a rate ~2% per year in MASH-related cirrhosis**[29]

Hepatic disease is a comorbid condition without specific recommendations in the AAD/NPF guideline[17]

- Dermatologists should be aware of the increased prevalence of MAFLD in patients with PsO
- Systemic medications may be deleterious to liver function[a]
- Unidentified liver disease can lead to progression of liver damage; early identification allows for management and monitoring

[a]Systemic therapies included methotrexate, cyclosporine, oral retinoids, TNF inhibitors, and IL-12/IL-23 inhibitors.[30]

Abbreviations and References

Abbreviations:

AAD=American Academy of Dermatology; BMI=Body Mass Index; BSA=Body Surface Area; CDC=Centers for Disease Control and Prevention; CI=Confidence Interval; CV=Cardiovascular; CVD=Cardiovascular Disease; DLQI=Dermatology Life Quality Index; HCP=Healthcare Professional; HR=Hazard Ratio; IL=Interleukin; MAFLD=Metabolic Dysfunction-associated Fatty Liver Disease; MASH=Metabolic Dysfunction-associated Steatohepatitis; NCHS=National Center for Health Statistics; NHANES=National Health and Nutrition Examination Survey; NPF=National Psoriasis Foundation; OR=Odds Ratio; PASI=Psoriasis Area and Severity Index; PCP=Primary Care Provider; PsA=Psoriatic Arthritis; PsO=Psoriasis; PSOLAR=Psoriasis Longitudinal Assessment and Registry; QoL=Quality of Life; RR=Relative Risk; Th=T Helper; TNF=Tumor Necrosis Factor.

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