Weigh in on Psoriatic Arthritis and Obesity: Reviewing the Link Between Joints and Weight

Contents

HCP=Healthcare Professional; PsA=Psoriatic Arthritis.

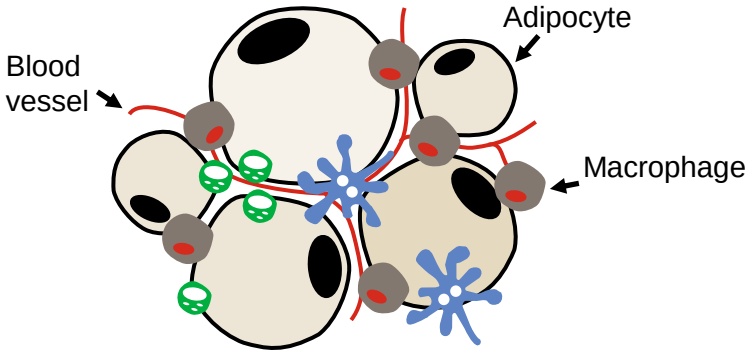
Pathophysiology and Epidemiology of PsA and Obesity

PsA=Psoriatic Arthritis.

Obesity Impacts the Body's Homeostasis

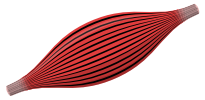
Pathological increase of adipose tissue and dysfunction induces qualitative and quantitative changes in signal production[1]

These changes induce low-grade systemic inflammation,[1-3] insulin resistance,[1,4] endothelial dysfunction,[4] synthesis of pro-clotting factors,[4] and other metabolic disorders[1]; ultimately leading to the impairment of multiple organs and their functions[1]



Molecules synthesized by adipose tissue[1]

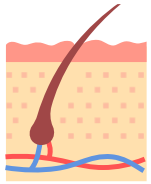
- **Adipokines**: Leptin, adiponectin, FABP4, apelin
- **Lipokines and metabolites**: Fatty acids, ceramides, BCAAs, FAHFAs, diHOMEs
- **Cytokines**: IL-6, TNFα
- **Growth factors** BMPs, FGF21
- **Others**: Exosomes, miRNAs



Sarcopenia[1]

Type 2 diabetes[1]

MAFLD[1]
Hepatocarcinoma[1]

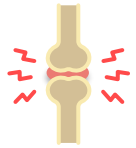


Dermatological diseases (eg, PsO[2], AD[2], HS[5])

Altered food intake and energy expenditure[1]

Coronary heart disease[1]
Cardiovascular risk[3]
Atherosclerosis/atherothrombosis[4]

Altered hematopoiesis[1]
Osteoporosis[1]



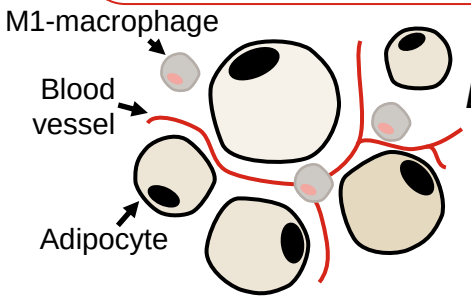
Arthritis[3,4]

AD=Atopic Dermatitis; BCAA=Branched-Chain Amino Acid; BMP=Bone Morphogenetic Protein; diHOME=Dihydroxy Octadecenoic Acid; FABP4=Fatty Acid-binding Protein 4; FAHFA=Fatty Acid Esters of Hydroxy Fatty Acid; FGF=Fibroblast Growth Factor; HS=Hidradenitis Suppurativa; IL=Interleukin; miRNA=Micro Ribonucleic Acid; MAFLD=Metabolic Dysfunction-associated Fatty Liver Disease; PsA=Psoriatic Arthritis; PsO=Psoriasis; TNFα=Tumor Necrosis Factor Alpha.
1. Favaretto F, et al. *Rev Endocr Metab Disord*. 2022;23(1):71-85. 2. Guo Z, et al. *JID Innov*. 2022;2(1):100064. 3. Porta S, et al. *Front Immunol*. 2021;11:590749. 4. Russolillo A, et al. *Rheumatology (Oxford)*. 2013;52(1):62-67. 5. Krajewski PK, et al. *Br J Dermatol*. 2023;188(3):320-327.

Excess Adipose Tissue May Contribute to PsA Development

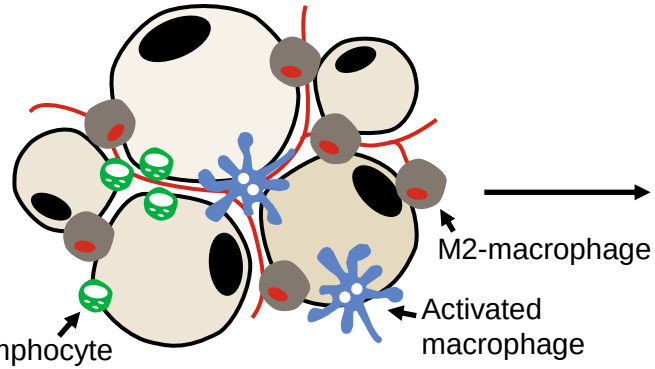
Obesity results from an excessive expansion of white adipose tissue (WAT)[1,2]

- Hypertrophy of existing adipocytes
- Increased infiltration of pro-inflammatory cells
- Decrease in the anti-inflammatory cell population



Lean WAT

Energy intake > expenditure[1]



Obese WAT

The dysfunctional adipose tissue acts as an endocrine organ[2,3]

- Increasing secretion of adipocytokines and pro-inflammatory mediators

Proinflammation		Anti-inflammation	
TNF	Leptin	Adiponectin	
IL-6	Chemerin	Omentin	
IL-8	Visfatin		

Genetic predisposition[2]

Increased mechanical load adds stress to entheses, with resulting microtrauma associated with pathology of PsA[2,3]

Psoriatic arthritis

Functional disability in PsA may reduce physical activity, favoring further weight gain[2]

Note: Genetic predisposition not present in all patients.
IL=Interleukin; PsA=Psoriatic Arthritis; TNF=Tumor Necrosis Factor.

1. Guo Z, et al. *JID Innov*. 2022;2(1):100064. 2. Porta S, et al. *Front Immunol.* 2021:11:590749. 3. Kumthekar A, Ogdie A. *Rheumatol Ther*. 2020;7(3):447-456.

Comorbid Obesity is Highly Prevalent Among Patients with PsA

US prevalence among patients with PsA[1,2]:

Obesity (BMI ≥30 kg/m^2) **up to 48%**

Overweight (BMI 25 to <30 kg/m^2) **up to 35%**

The incidence rate (IR) of PsA increased with higher BMI[a,3]

IR for PsA in BMI 30.0-34.9 kg/m^2: 2.05***

IR for PsA in BMI ≥35.0 kg/m^2: 2.67***

>375,000 (48%) adults with PsA in the US have obesity, according to a US survey[1,2]

For trend: ***p<.001.
[a]IR per 10,000 person-years.
BMI=Body Mass Index; PsA=Psoriatic Arthritis.
1. https://wwwn.cdc.gov/nchs/nhanes/Default.aspx (Accessed January 30, 2024). 2. Data on file. Lilly USA. 3. Love TJ, et al. *Ann Rheum Dis*. 2012;71(8):1273-1277.

Risk Factors For Development of PsA: Effect Size (95% CI)[a]

Predictors of PsA in patients with PsO are from cohort studies unless otherwise stated

Obesity[b,c]

- **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)**

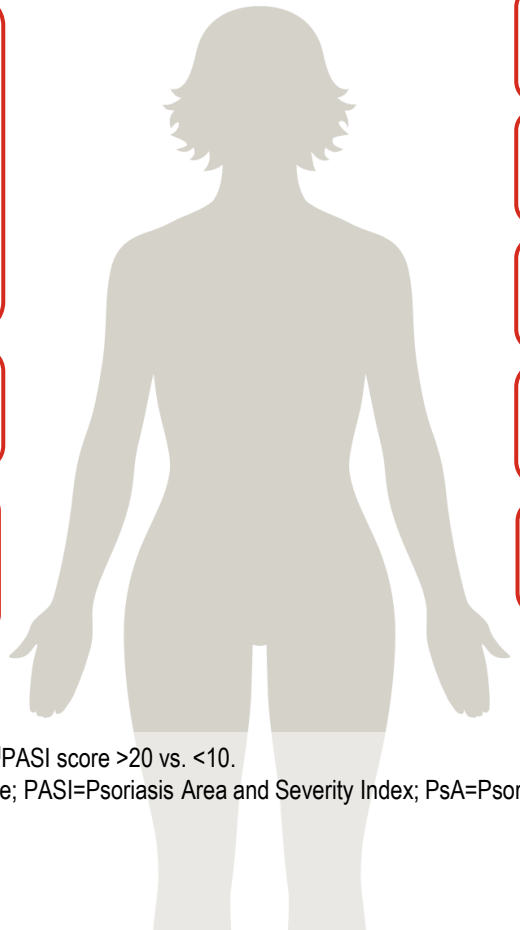
Symptoms[c]

- **Arthralgia** (in females): **HR 5.91 (2.46-14.2)**
- **Back stiffness**: **HR 3.71 (1.95-7.02)**
- **Level of fatigue** (mFSS >5): **HR 3.09 (1.76-5.53)**
- **Level of stiffness** (VAS >2): **HR 3.06 (1.69-5.52)**
- **Level of pain** (VAS >2): **HR 2.66 (1.44-4.81)**
- **Morning joint stiffness: HR 2.25 (1.55-3.25)**

Inverse/Intertriginous PsO

Intergluteal/perianal involvement: HR 1.95 (1.07-3.56)

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



Severity of PsO[d]

RR 5.39 (1.64-17.7)

Scalp PsO

HR 3.75 (2.09-6.71)

Nail Dystrophy

HR 2.24 (1.26-3.98)

Depression

HR 1.41 (1.10-1.80)

Physical Trauma (All)

HR 1.32 (1.13-1.54)

[a]Adjusted for other covariates. [b]BMI ≥35.0 kg/m^2 vs. normal (BMI <25.0 kg/m^2). [c]Time varying exposure. [d]PASI score >20 vs. <10.
BMI=Body Mass Index; CI=Confidence Interval; HR=Hazard Ratio; mFSS=Modified Fatigue Severity Scale; PASI=Psoriasis Area and Severity Index; PsA=Psoriatic Arthritis; PsO=Psoriasis; RR=Relative Risk; VAS=Visual Analog Scale. Scher JU, et al. *Nat Rev Rheumatol.* 2019;15(3):153-166.

Burden of Disease for Patients With PsA and Obesity

PsA=Psoriatic Arthritis.

Comorbid Obesity is Associated With an Increased Disease Burden for Patients With PsA

Compared with those without obesity, patients with PsA and comorbid obesity are more likely to have[1-3]:

Depression

Anxiety

Fatigue/sleep disturbances

Reduced physical function

Impaired quality of life

PsA patients with obesity report a greater disease burden, as measured by PsAID12 and RAPID3, compared with PsA patients without obesity[1,4]

PsA=Psoriatic Arthritis; PsAID12=Psoriatic Arthritis Impact of Disease 12; RAPID3=Routine Assessment of Patient Index Data 3.

1. Leung YY, et al. *RMD Open*. 2023;9(3):e003157. 2. Gok K, et al. *Rheumatol Int*. 2022;42(4):659-668. 3. Haugeberg G, et al. *Arthritis Res Ther*. 2020;22:198. 4. Walsh JA, et al. *J Rheumatol*. 2020;47(10):1496-1505.

Patients with PsA and Obesity Tend to Have More Severe Disease at Baseline, vs. Those Without Obesity

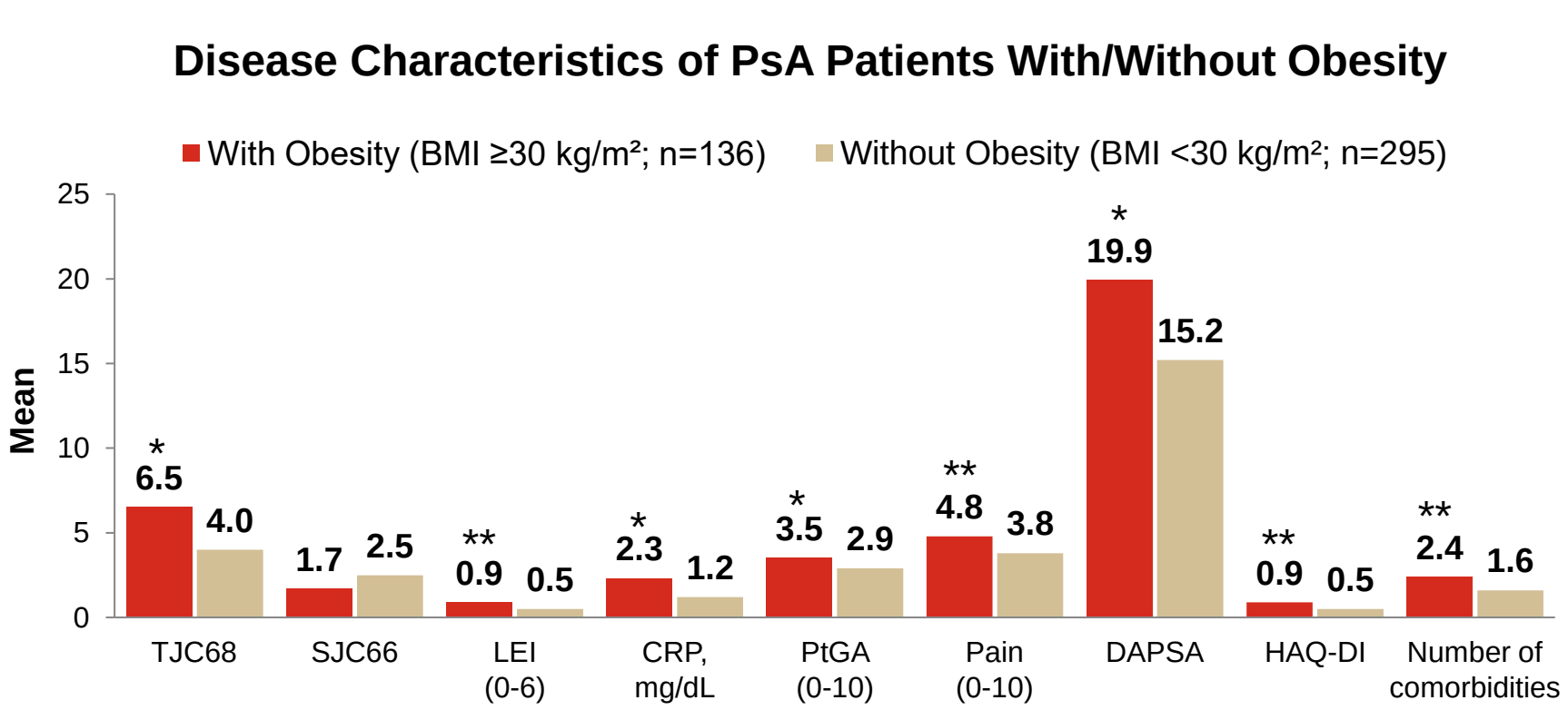
Compared with those without obesity, patients with PsA and obesity had significantly higher tender joint counts, enthesitis scores, and CRP levels

Methodology

Multicenter cohort study (N=431)

Demographic and clinical data collected for adult patients with physician-diagnosed PsA and ≥2 years disease duration

- Mean age: 52.4 years
- Female: 49.3%



vs. patients without obesity: *p<.05; **p<.01.
CRP=C-reactive Protein; DAPSA=Disease Activity in Psoriatic Arthritis; LEI=Leeds Enthesitis Index; HAQ-DI=Health Assessment Questionnaire – Disability Index; PtGA=Patient Global Assessment of Disease Activity; PsA=Psoriatic Arthritis; SJC=Swollen Joint Count; TJC=Tender Joint Count. Leung Y, et al. *RMD Open*. 2023;9(3):1-8.

Cross-sectional Cohort Study

Effect of Obesity on Nail PsO and Clinical Characteristics in Patients With PsA

Obesity was independently associated with the presence of nail involvement in PsA patients

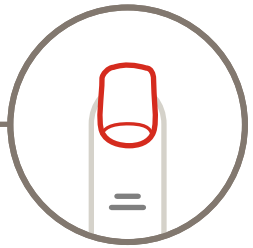
Methodology

Cross-sectional study in patients with PsA with and without obesity (N=82)

Aim: To compare nail PsO prevalence and disease activity between PsA patients with and without obesity

Results

PsA Patients Without Obesity (N=41)	Clinical Characteristics	PsA Patients With Obesity (N=41)
27%	Hypertension	**56%****
29%	Dyslipidemia	**59%****
22%	NAPSI >0	**46%***
9.3 (4.0, 19)	DAPSA, median (IQR)	**19 (10, 35)****



- PsA patients with obesity have higher disease activity (as measured by DAPSA and NAPSI), with a higher BMI associated with a higher NAPSI score

vs. PsA patients without obesity: *p<.05; **p<.01.
BMI=Body Mass Index; DAPSA=Disease Activity in Psoriatic Arthritis; IQR=Interquartile Range; NAPSI=Nail Psoriasis Severity Index; PsA=Psoriatic Arthritis; PsO=Psoriasis.
Galarza-Delgado DA, et al. *Int J Dermatol.* 2024;63(1):e1-e2.

Impact of Obesity on PsA Treatment Outcomes

PsA=Psoriatic Arthritis.

Obesity is a Negative Predictor of Achieving and Maintaining MDA for Patients with PsA

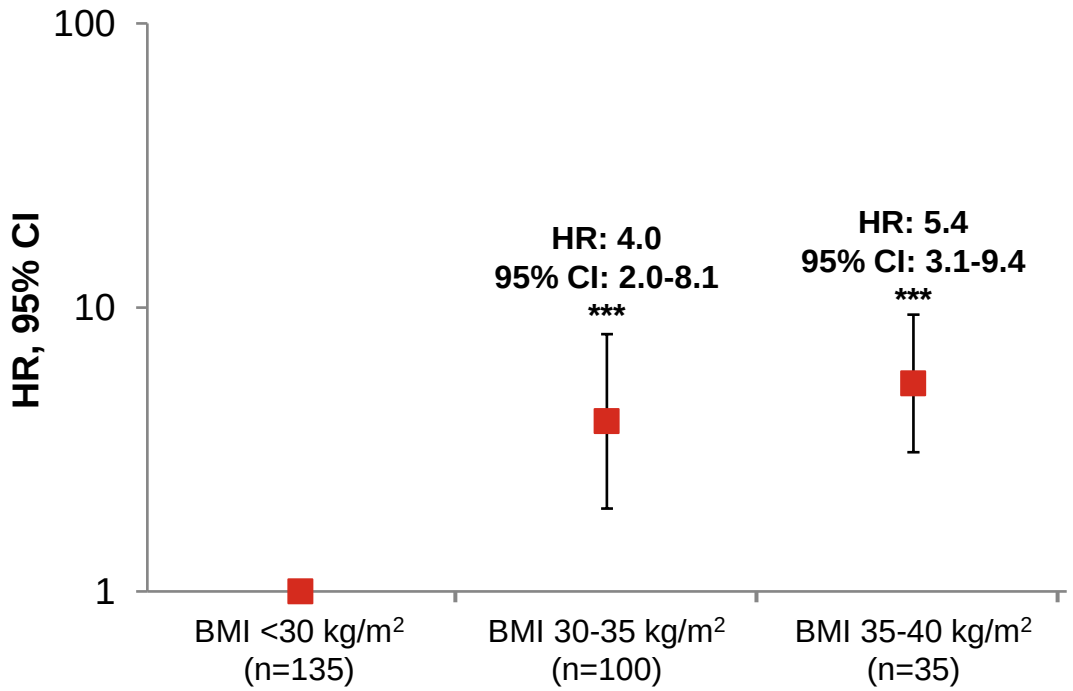
High BMI, particularly with high visceral fat, can be an indicator of **more active psoriatic disease**[1-3]

Increased BMI is associated with a **less favorable outcome for patients**, reducing the likelihood of achieving and sustaining MDA and remission[1,3,4]

This association has been shown to be **independent of DMARD or TNFi use**[3]

In one study, PsA patients with comorbid obesity (BMI >30 kg/m^2) were **2.5-3.0 fold less likely** to be in remission/VLDA, and **1.6 times less likely** to have achieved MDA, compared with patients without obesity[1]

Risk of Not Achieving MDA After 12 Months of TNFi Therapy, According to BMI[4]



vs. BMI <30 kg/m^2: ***p<.001. BMI=Body Mass Index; CI=Confidence Interval; DMARD=Disease-modifying Antirheumatic Drug; HR=Hazard Ratio; MDA=Minimal Disease Activity; PsA=Psoriatic Arthritis; TNFi=Tumor Necrosis Factor Inhibitor; VLDA=Very Low Disease Activity.

1. Leung YY, et al. *RMD Open.* 2023;9(3):e003157. 2. Blake T, et al. *Arthritis Res Ther.* 2023;25:108 (updated 25(1):115). 3. Eder L, et al. *Ann Rheum Dis.* 2015;74(5):813-817. 4. di Minno MND, et al. *Arthritis Care Res (Hoboken).* 2013;65(1):141-147.

Observational Cohort Study

Effect of Obesity on PsA Disease Activity

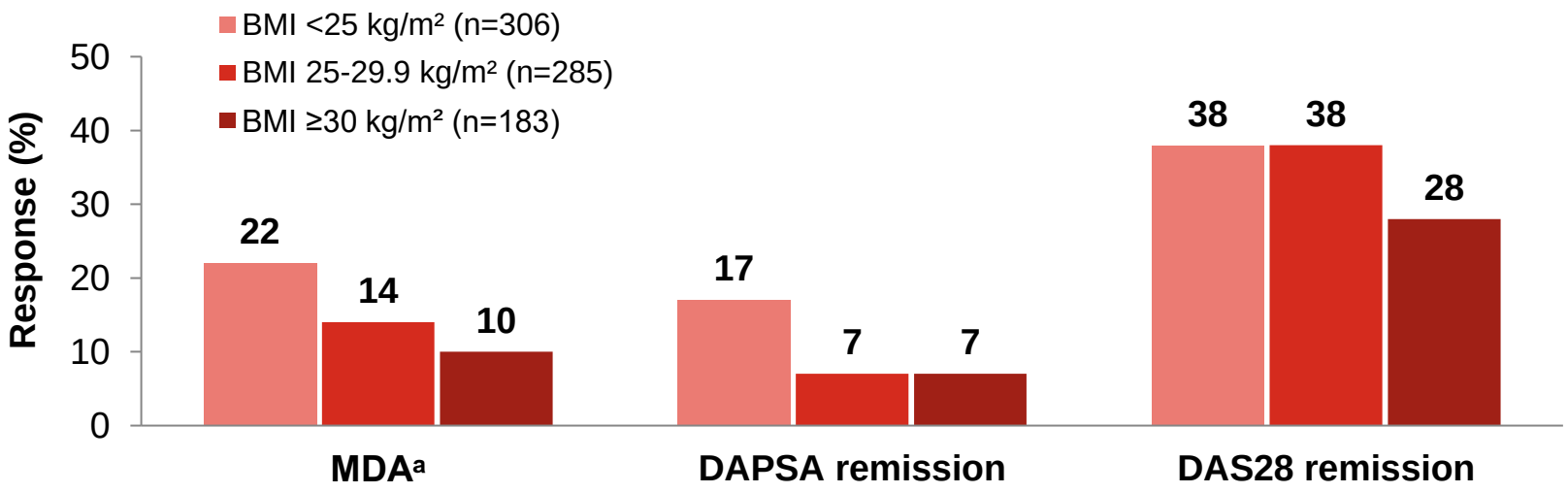
Patients with BMI ≥30 kg/m^2 were half as likely to achieve MDA, compared with patients with BMI <25 kg/m^2

Methodology

Observational cohort study in PsA patients ≥18 years old starting their first b/tsDMARD (N=774)

Aim: To assess the impact of BMI on the achievement of MDA and remission in patients with PsA

Achievement of MDA and Remission at Month 12, by BMI Category



- Patients with BMI ≥30 kg/m^2 had significantly reduced odds (49–58%) of achieving MDA, as well as DAPSA, cDAPSA, or DAS28 remission within 12 months of treatment, compared with patients with BMI <25 kg/m^2
- BMI ≥30 kg/m^2 was neither associated with the likelihood of achieving low disease activity nor with changes in treatment persistence

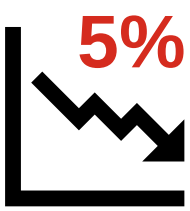
[a]MDA was achieved if at least five of the following seven criteria were met: number of TJC ≤1; number of SJC ≤1; skin manifestation none or almost none; patient's joint pain by VAS (0–100) ≤15; patient's assessment on PsA activity by VAS ≤20; HAQ ≤0.5; enthesis points ≤1. See speaker notes for abbreviations. Vallejo-Yagüe E, et al. *BMJ Open*. 2022;12(9):e061474.

Impact of Weight Loss on PsA Treatment Outcomes

PsA=Psoriatic Arthritis.

Weight Loss Improves Outcomes for Patients With PsA and Obesity

Weight loss can improve pre-existing PsA, and may prevent the onset of PsA in individuals with obesity and PsO[1,2]



In patients with PsA, a **5% weight loss through a low-calorie diet** improves the response to TNFis; a greater response to treatment is observed with further weight loss[3,4]

- Patients with ≥5% weight loss had higher odds of achieving MDA, compared with patients who lost <5% of their body weight[4]

Effect of Weight Loss on PsA Patient Outcomes[3]

	Disease Activity	MDA Response
Low-calorie diet (RCT)	↓	↑

MDA=Minimal Disease Activity; PsA=Psoriatic Arthritis; PsO=Psoriasis; RCT=Randomized Controlled Trial; TNFi=Tumor Necrosis Factor Inhibitor.

1. Mahil SK, et al. *Br J Dermatol*. 2019;181(5):946-953. 2. Green A, et al. *Br J Dermatol.* 2020;182(3):714-720. 3. Tournadre A, Beauger M. *Joint Bone Spine*. 2024;91(3):105647.
4. Di Minno MND, et al. *Ann Rheum Dis*. 2014;73(6):1157-1162.

Prospective Interventional Study

Effect of Diet-Based Weight Loss on PsA Treatment Response

Weight loss treatment was associated with significant long-term positive effects on measures of disease activity, self-reported function, and markers of the metabolic syndrome in patients with PsA and obesity[1]

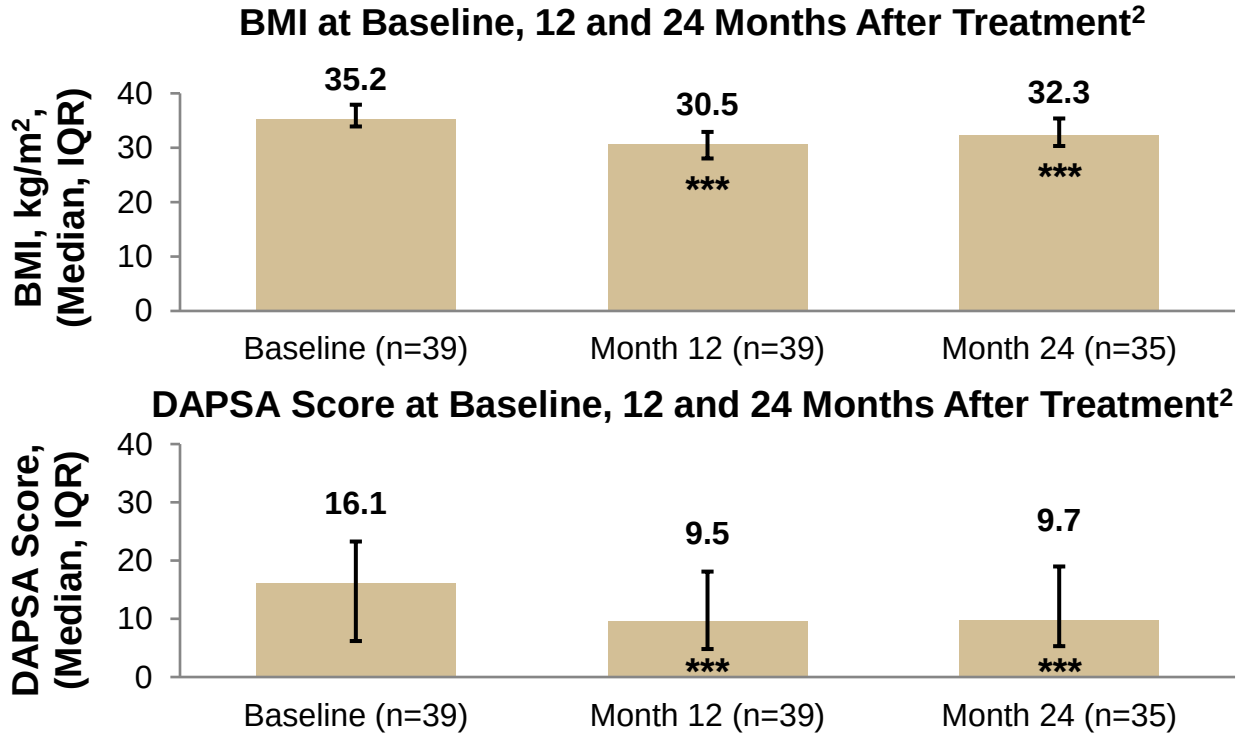
Methodology

Multicenter study in patients with PsA and BMI ≥33 kg/m² (N=41)

Aim: To evaluate the effects of weight loss treatment with a very-low-energy diet (VLED) on disease activity in patients with PsA and obesity[1]

Intervention: VLED (640 kcal/day) was taken over 12-16 weeks, depending on pre-treatment BMI. After, an energy-restricted diet was gradually reintroduced[1] with follow up at 12- and 24-months post treatment[2]

Results



vs. Baseline: *p<.05; **p<.01; ***p<.001. Note: Data are as observed. BMI=Body Mass Index; DAPSA=Disease Activity in Psoriatic Arthritis; IQR=Interquartile Range; n=Number of Responders; PsA=Psoriatic Arthritis.

1. Klingberg E, et al. *Arthritis Res Ther*. 2019;21:17. 2. Klingberg E, et al. *Arthritis Res Ther*. 2020;22:254.

Guidelines and the Role of HCPs in Weight Management

HCP=Healthcare Professional.

Clinical Guidelines

Treatment of Patients With Active PsA and Comorbid Obesity

ACR/NPF Recommendations[1]

- Recommend weight loss over no weight loss for patients who have overweight/obesity
- Conditional recommendation based on low-quality evidence; may consider no weight loss due to additional patient burden involved with weight-loss program

GRAPPA Guidelines[2]

- Patients should be encouraged to maintain a healthy weight in order to improve disease activity and minimize disease impact
- Several studies have demonstrated that obesity is associated with reduced functional ability, greater PsO severity and disease activity, and reduced response to therapy
- Patients with obesity have a higher prevalence of fatty liver disease. For this reason, patients initiating MTX or LEF should be counseled on the increased probability of elevated LFTs with these medications and LFTs should be monitored more carefully[a]

[a]MTX and LEF should be used with caution in patients with obesity and avoided in patients with a diagnosis of fatty liver disease.

ACR=American College of Rheumatology; GRAPPA=Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; LEF=Leflunomide; LFT=Liver Function Test; MTX=Methotrexate; NPF=National Psoriasis Foundation; PsA=Psoriatic Arthritis; PsO=Psoriasis.

1. Singh JA, et al. *Arthritis Rheumatol.* 2019;71(1):5-32. 2. Coates LC, et al. *Nat Rev Rheumatol*. 2022;18(8):465-479.

Role of the Rheumatologist in the Management of Patients With PsA and Metabolic Syndromes

Encourage patients to maintain a healthy weight to improve disease activity and minimize disease impact[1]

Include healthy eating and dietary weight reduction in disease management plans[2]

Review comorbidities such as comorbid obesity or metabolic syndromes when deciding on a treatment plan[1]

Consider an integrated approach to management that includes both the metabolic and inflammatory burden of disease[3]

Ensure therapeutic decisions are individualized and made jointly with the patient, taking their views into account[1,4]

PsA=Psoriatic Arthritis.

1. Coates LC, et al. *Nat Rev Rheumatol*. 2022;18(8):465-479. 2. Ford AR, et al. *JAMA Dermatol*. 2018;154(8):934-950. 3. Blake T, et al. *Arthritis Res Ther*. 2023;25(1):108 (updated 25(1):115).
4. Leung YY, et al. *RMD Open*. 2023;9(3):1-8.

A Healthy Lifestyle Should be Promoted for All Patients With PsA

Lifestyle changes including a healthy diet, increased exercise, and prioritization of sleep, may help to improve patient QoL and reduce the burden of disease[1-3]

A hypocaloric diet can help improve disease activity in all patients with PsA, regardless of weight loss[2]

In addition to weight loss benefits, exercise can help manage symptoms, reduce disability, and prevent the development of further comorbidities[1]

Prioritizing time for sleep could help improve patient QoL and aid weight-loss efforts[1,4]

PsA=Psoriatic Arthritis; QoL=Quality of Life.

1. Lubrano E, et al. *RMD Open*. 2023;9(3):e003339. 2. Leite BF, et al. *Adv Rheumatol.* 2022;62(1):12. 3. Porta S, et al. *Front Immunol.* 2021:11:590749. 4. Papatriantafyllou E, et al. *Nutrients*. 2022;14(8):1549.

Conclusions

An **excess of adipose tissue** may contribute to PsA development[1]

Comorbid obesity is highly prevalent among patients with PsA[2,3] and is associated with an **increased disease burden** and **more severe disease at baseline**, compared with those without obesity[4,5]

Weight loss has been demonstrated to **improve patient outcomes,** with a greater response to treatment observed with larger weight loss[6,7]

PsA treatment **guidelines recommend weight loss over no weight loss** for patients who have overweight or obesity; patients should be encouraged to **maintain a healthy weight** to improve disease activity and minimize disease impact[8,9]

BMI=Body Mass Index; PsA=Psoriatic Arthritis.

1. Porta S, et al. *Front Immunol*. 2021:11:590749. 2. https://wwwn.cdc.gov/nchs/nhanes/Default.aspx (Accessed January 30, 2024). 3. Data on file. Lilly USA. 4. Leung YY, et al. *RMD Open*. 2023;9(3):e003157.
5. Gok K, et al. *Rheumatol Int*. 2022;42(4):659-668. 6. Tournadre A, Beauger M. *Joint Bone Spine*. 2024;91(3):105647. 7. Di Minno MND, et al. *Ann Rheum Dis*. 2014;73(6):1157-1162.
8. Singh JA, et al. *Arthritis Rheumatol.* 2019;71(1):5-32. 9. Coates LC, et al. *Nat Rev Rheumatol*. 2022;18(8):465-479.

US Medical Education

Scan the Code Below for Additional Resources on PsA

SCAN HERE

PsA=Psoriatic Arthritis.

Appendix

Bariatric Surgery May Lead to Improved Outcomes for Patients with PsA and Obesity

Current evidence suggests improved outcomes after bariatric surgery in populations with obesity and rheumatic disorders; however, controlled trials with long follow-up periods are needed to draw concrete conclusions[1]

Population-Based Cohort Study[2]

- The incidence and prognosis of new onset PsO and PsA in all patients undergoing bariatric surgery was examined (N=13,435)
- In patients who underwent a gastric bypass, there was a decreased risk of PsA (adjusted HR: 0.29; 95% CI, 0.12-0.71; p=.01)
- This was not observed in patients following gastric banding (adjusted HR: 0.53; 95% CI, 0.08-3.56; p=.52)

Retrospective Monocentric Study[3]

- In the 21 patients who had a pre-operative diagnosis of PsA:
  - 62% reported subjective improvement in their disease
  - Disease severity rating decreased[a] from 6.4 to 4.5 (p=.01)
  - This decrease[a] was more pronounced amongst patients with severe disease (8.2 vs. 4.8; p<.01)

Bariatric procedures have deleterious effects on bone and are associated with an increased risk of fractures[1]

[a]Decrease is from prior to surgery to 1-year post surgery. CI=Confidence Interval; HR=Hazard Ratio; PsA=Psoriatic Arthritis; PsO=Psoriasis.

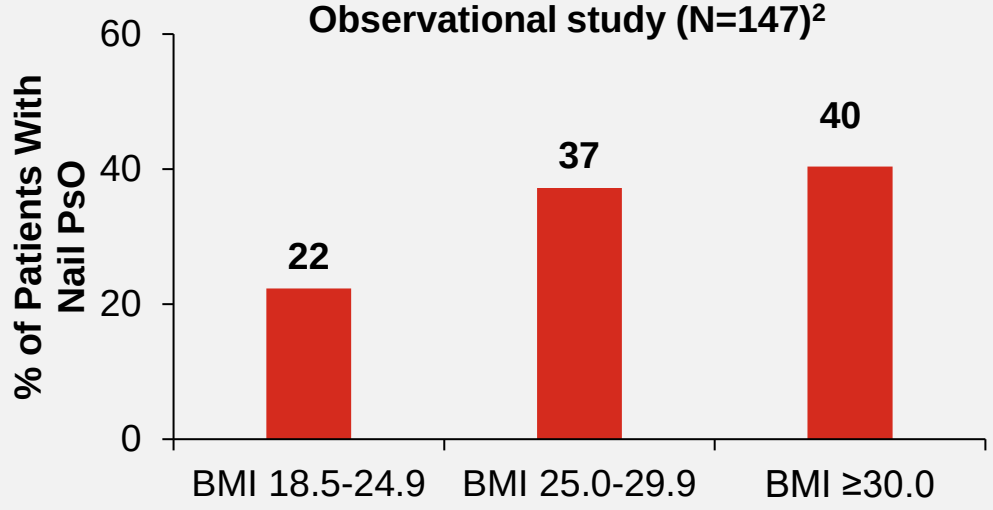
1. Lespessailles E, et al. *Arthritis Res Ther*. 2019;21(1):83. 2. Egeberg A, et al. *JAMA Surg*. 2017;152(4):344-349. 3. Sethi M, et al. Presented at: *ACR/ARHP 2015*. Abstract 688.

Nail PsO

Prevalence and Comorbidities

- Affects up to **40-50%** of patients with PsO[1]
- Increased prevalence in patients who are **overweight** or with comorbid **obesity**[a] and PsO[2]

Observational study (N=147)[2]



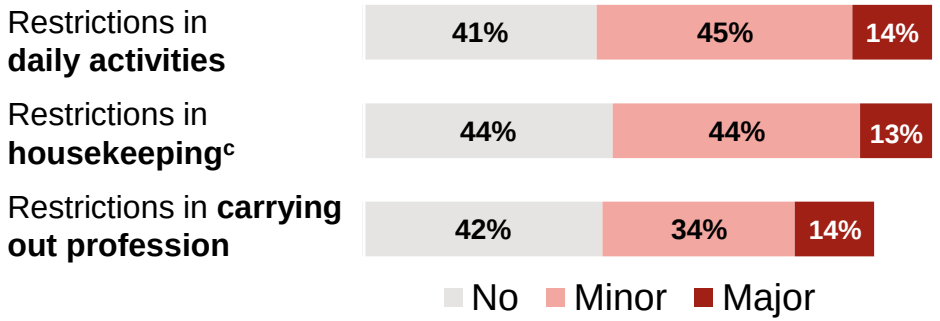
Impact on Quality of Life

Survey: Patients with plaque PsO (N=1728)[3]

93% experienced **cosmetic problems** due to nail PsO

52% experienced **pain** due to nail PsO

Majority of Patients Reported Restrictions on Daily Activities Due to Nail PsO[b]



[a]Normal defined as BMI 18.5-24.9 kg/m^2, overweight defined as BMI 25.0-29.9 kg/m^2, and obesity defined as ≥30.0 kg/m^2. [b]Full percentages of restrictions not reported. [c]Housekeeping is not a subset of daily activities.
BMI=Body Mass Index; PsO=Psoriasis.

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