The Association Between Obesity and Clinical Features of Psoriatic Arthritis: A Case-control Study

Lihi Eder, Fatima Abji, Cheryl F. Rosen, Vinod Chandran, and Dafna D. Gladman

ABSTRACT. ***Objective.*** To assess whether obesity is associated with distinct psoriatic arthritis (PsA) features and whether it interacts with PsA HLA susceptibility alleles.

Methods. Patients with early PsA were compared with patients with psoriasis without arthritis (PsC). The primary predictor was the body mass index (BMI) at the first visit to the clinic. The clinical features across 3 BMI groups were compared by linear trend test and Cochrane-Armitage trend test. The interaction between BMI and HLA risk alleles for psoriatic disease (HLA-B*27, B*3901, B*3801, B*0801, B*4402, B*4403, and C*0602) were assessed using logistic regression analysis.

Results. There were 314 patients with early PsA, and 498 patients with PsC were analyzed. Obesity was more frequent in patients with PsA compared with PsC (OR 1.77; p = 0.002). Higher BMI was associated with older age at onset of PsA (p < 0.0001) and psoriasis (p = 0.009). The frequency of HLA-B*27 was higher in patients with normal weight compared with those with higher BMI (p = 0.002). A significant interaction was found for the combined effect of HLA-B*27 and obesity in logistic regression analysis (p = 0.036). In patients who were HLA-B*27–negative, the association between obesity and PsA was statistically significant (OR 2.39; p < 0.001), but obesity was less frequent in patients with PsA who were HLA-B*27–positive.

Conclusion. Obesity is linked with late-onset psoriasis and PsA, while normal weight is associated with the presence of the HLA-B*27 allele and an earlier onset of the disease. These results highlight the differential risk factors that may drive the inflammatory process in psoriatic disease. (First Release February 15 2017; J Rheumatol 2017;44;437–43; doi:10.3899/jrheum.160532)

Key Indexing Terms:
PSORIATIC DISEASE OBESITY INFLAMMATION GENE ENVIRONMENT HLA-B27

Psoriasis is a chronic immune-mediated inflammatory skin disease affecting 2%–3% of the population. About 30% of the patients with psoriasis develop inflammatory arthritis, termed psoriatic arthritis (PsA)[1]. Both psoriasis and PsA are strongly linked with obesity and its related metabolic abnormalities[2]. The prevalence of obesity is increased among patients with PsA compared with patients with psoriasis alone (PsC) and with the general population[3]. Being obese increases the risk of psoriasis among healthy subjects and of PsA among patients with psoriasis[4,5,6,7]. Obesity is also associated with psoriasis and arthritis severity and with poorer response to therapy, while weight loss is associated with better outcomes[8,9,10,11].

Both environmental and genetic factors are involved in psoriatic disease susceptibility. HLA class I genes, in particular HLA-B*27, B*39, B*38, C*06, and B*08 alleles, are strongly linked with psoriatic disease risk and can affect the clinical expression of the disease[12,13]. These alleles are associated with clinical manifestations of PsA, such as the age at onset of the disease, the interval between psoriasis and PsA, axial involvement, and the extent of joint damage[14]. In rheumatoid arthritis, different environmental risk factors are associated with clinical features of the disease as defined by the presence of the shared epitopes and seropositivity[15]. Refining PsA phenotype may strengthen the association between environmental risk factors and the disease, and elucidate different underlying mechanisms driving the clinical expression of the different subtypes.

In a previous study, we found that obesity was associated with an older age at onset of psoriasis and PsA[11]. In our current study, we aimed to further investigate the association between obesity and PsA clinical features. We hypothesized that there was a differential effect of obesity on PsA risk

From the Division of Rheumatology, Women's College Research Institute, Women's College Hospital; Department of Medicine, University of Toronto; Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital; Division of Dermatology, Toronto Western Hospital, Toronto, Ontario, Canada.

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L. Eder, MD, PhD, Division of Rheumatology, Women's College Research Institute, Women's College Hospital, and Department of Medicine, University of Toronto; F. Abji, MSc, Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital; C.F. Rosen, MD, FRCPC, Division of Dermatology, Toronto Western Hospital; V. Chandran, MD, DM, PhD, Department of Medicine, University of Toronto, and Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital; D.D. Gladman, MD, FRCPC, Department of Medicine, University of Toronto, and Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital.

Address correspondence to Dr. L. Eder, Women's College Research Institute, Women's College Hospital, 76 Grenville St., Toronto, Ontario M5S 1B2, Canada. E-mail: lihi.eder@wchospital.ca

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depending on PsA features. In other words, obesity may be driving the inflammatory process leading to distinct subtypes of PsA while other factors (i.e., genetic factors) may be driving the pathogenic process in other PsA subtypes. We investigated this hypothesis by assessing the prevalence of obesity in PsA features as defined by HLA alleles and by age at PsA onset and compared them to patients with PsC.

MATERIALS AND METHODS

Cases. Adult patients with recent PsA (less than 2 yrs since diagnosis) who satisfied the ClASsification for Psoriatic ARthritis criteria[16] were identified from the University of Toronto PsA cohort. This cohort has been previously described[17]. Patients were followed in the PsA clinic according to a standard protocol at 6- to 12-month intervals. The clinic database was searched for patients with recent PsA who attended the clinic as of 2002, because height and weight had not been routinely measured prior to that year.

Controls. The control group included patients with PsC recruited from the Toronto Psoriasis cohort. This cohort was established in 2006 to study risk factors for PsA in patients with psoriasis[18]. Patients were enrolled if they were free of PsA at baseline after a rheumatologist assessment, and were followed annually for signs and symptoms of PsA. If PsA is diagnosed, the subject was considered to have developed the outcome of interest and was censored. This process ensured that all the psoriasis cohort subjects were free of arthritis at baseline. All patients with complete information about height and weight were included.

The study was approved by the University Health Network Research Ethics Board and all patients gave their informed consent.

Exposure and covariates. Height and weight were measured at enrollment using a standard scale, and the body mass index (BMI) was calculated. We used the World Health Organization BMI classification of underweight (BMI < 18.5 kg/m^2), normal weight (BMI ≥ 18.5 to < 25 kg/m^2), overweight (BMI ≥ 25 to < 30 kg/m^2), and obese (BMI ≥ 30 kg/m^2). Since only a small proportion of patients had BMI < 18.5 kg/m^2, the categories for underweight and normal weight were combined. Because BMI is related to several other lifestyle factors that can potentially explain the association with PsA, we adjusted for smoking (never/current/past) and alcohol consumption (none/social/daily). Level of education (university/college vs high school graduate or less) was used as a marker of socioeconomic status.

Additionally, age was considered a major confounder because it tends to correlate strongly with BMI. Therefore, we controlled for the effect of age by adjustment or stratification in the statistical analysis.

Outcome measures of psoriatic disease. The following variables assessed at the baseline visit were included in the analysis: age at diagnosis of psoriasis and PsA, duration of musculoskeletal (MSK) symptoms prior to diagnosis of PsA, tender and swollen joint count, the presence of enthesitis, Psoriasis Area and Severity Index, nail pitting, and onycholysis. In addition, the following radiographic features were recorded: radiographic joint damage as assessed by modified Steinbrocker score and tuft resorption; entheseal involvement as assessed by the presence of calcification at the attachment of the Achilles tendon, plantar fascia, and along the pelvis rim; axial damage as assessed by the presence of radiographic sacroiliitis (according to the modified New York criteria); and classic and Dixon-Bywater syndesmophytes.

HLA genotyping. HLA-B and HLA-C genotyping of DNA extracted from peripheral blood was performed using LabType SSO typing kits according to the manufacturer's instructions (One Lambda). The following HLA alleles that were validated as PsA susceptibility alleles were analyzed[12,19]: B*27, B*3801/B*3901, B*4402/B*4403, B*0801, and C*0602. The following HLA alleles were associated with PsA characteristics: (1) HLA-B*27 — characterized by early onset of PsA, short psoriasis-arthritis interval, symmetric sacroiliitis; (2) HLA-B*0801 — characterized by asymmetric sacroiliitis and joint fusion; (3) HLA-C*0602 — characterized by early-onset psoriasis, prolonged psoriasis-arthritis interval[13].

Statistical analysis. Descriptive statistics were computed with continuous variables summarized by their means and SD, and categorical variables summarized by proportions (%). Continuous variables were compared by the Student t test and the linear trend test, and categorical variables were compared by the chi-square and Cochrane-Armitage trend tests. The association between BMI categories and PsA compared with PsC was calculated using logistic regression analysis. We investigated the effect of overweight and obesity using normal weight as the reference. The initial model included BMI categories as a single variable in the regression model. Age, sex, smoking status, alcohol consumption, and education levels were then added as covariates to the regression model. To further assess whether the effect of BMI on PsA risk varies by PsA features, we performed subgroup analyses according to age at onset of PsA (< 30, 30–50, > 50 yrs). These cutoff points were roughly based on tertiles. Subsequently, effect modification of HLA risk alleles on BMI was assessed by including the interaction term of the respective HLA allele (HLA-B*27, HLA-C*0602, HLA-B*3801/B*3901, HLA-B*4402/B*4403, and HLA-B*0801) and BMI category in separate regression models. Because a statistically significant interaction was found between HLA-B*27 and BMI category, we performed a subgroup analysis by HLA-B*27 status to assess the association between BMI category and PsA versus PsC using logistic regression models. All analyses were performed using SAS software, version 9.2.

RESULTS

We analyzed 314 patients with PsA and 498 patients with psoriasis. Their baseline characteristics are shown in Table 1.

Table 1. Characteristics of the study population. Values are mean ± SD or n (%).

Characteristics	PsA, n = 314	PsC, n = 498
Age, yrs	44 ± 13.1	46.4 ± 13.5
Male	173 (55.1)	285 (57.2)
Age at onset of psoriasis, yrs	30.2 ± 15.4	30.5 ± 16.1
Age at onset of PsA, yrs	43.2 ± 13	—
Smoking		
Past	89 (28.4)	136 (27.5)
Current	59 (18.9)	118 (23.8)
Alcohol consumption		
Social	166 (59.5)	275 (56.1)
Daily	32 (11.5)	60 (12.2)
BMI		
Normal	87 (27.7)	175 (35.1)
Overweight	112 (35.7)	192 (38.6)
Obese	115 (36.6)	131 (26.3)
Level of education		
Low	96 (30.8)	106 (21.4)
High	216 (69.2)	390 (78.6)
PASI	5.4 ± 8.6	5.5 ± 5.6
Nail psoriasis	220 (71.4)	237 (48.0)
Pitting	154 (50.0)	177 (36.0)
Onycholysis	148 (48.1)	157 (32.0)
Tender joint count	7.2 ± 9	—
Swollen Joint count	3.8 ± 5.8	—
Enthesitis	80 (25.5)	—
HLA-B*27	31 (11.0)	19 (3.8)
HLA-C*0602	58 (20.6)	210 (42.2)
HLA-B*0801	56 (19.8)	61 (12.3)

PsA: psoriatic arthritis; PsC: psoriasis without arthritis; BMI: body mass index; PASI: Psoriasis Area and Severity Index.

Association between BMI and PSA manifestations. PsA manifestations were compared across the 3 BMI categories among patients with PsA (Table 2). The most notable differences between the groups were the earlier age at onset of PsA and psoriasis in patients with normal weight compared with overweight and obese. In addition, obese patients tended to have a longer interval from the onset of symptoms to the diagnosis of PsA. Regarding radiographic damage, obese and overweight patients had a higher prevalence of tuft resorption, Achilles and calcaneal spurs, and pelvic enthesitis. Last, HLA-B*27 allele was unevenly distributed across the BMI categories. Obese and overweight patients were less likely to be HLA-B*27 carriers. This trend was unchanged when the analysis was restricted to whites (data not shown). The distribution of the remaining HLA alleles was balanced across the BMI groups.

The association between BMI and age at onset of PsA. To further investigate the association between a later age at onset of PsA and obesity, we performed a case-control comparison with patients with PsC. Results are shown in Table 3. The prevalence of obesity was higher in patients with PsA compared with those with PsC (36.6% vs 26.3%, respectively). This association remained statistically significant in the multivariable model after adjusting for potential confounding factors.

In addition to the global comparison between cases and controls, we conducted a subgroup analysis to assess variation in the effect size of BMI across age groups. In this analysis, the effect size was highest in the late-onset PsA group (OR 3.12), lower in the middle age of onset patients with PsA (age 30–50 yrs, OR of 1.72), and lowest and nonsignificant OR of 1.38 in patients with early-onset PsA (age ≤ 30 yrs). The association between overweight and PsA was statistically significance only in patients above 50 years of age (p = 0.04). These findings suggested that the strength of association between BMI and PsA risk may be dependent on age at onset of PsA, and it was stronger in late-onset PsA.

The association between BMI and HLA risk alleles for PSA.

Table 2. PsA manifestations by BMI categories at clinic entry. Values are mean ± SD or n (%).

Variables	Normal, BMI < 25, n = 87	Overweight, BMI 25–30, n = 112	Obese, BMI ≥ 30, n = 115	p*
Age at onset PsA, yrs	**38.1 ± 13.6**	**44.1 ± 13.5**	**46.2 ± 11**	**< 0.0001**
Age at onset psoriasis, yrs	**27.6 ± 16**	**29.2 ± 15.1**	**33 ± 14.9**	**0.01**
Interval PsA-psoriasis	10.6 ± 12.7	14.8 ± 14.8	13.3 ± 12.4	0.17
Interval from onset of symptoms to diagnosis of PsA	**2.8 ± 5.7**	**3.8 ± 9.9**	**5.7 ± 9.2**	**0.02**
Nail lesions	54 (62.1)	86 (76.8)	80 (69.6)	0.32
Pitting	43 (49.4)	57 (50.9)	54 (45)	0.70
Onycholysis	35 (40.2)	55 (49.1)	58 (50.4)	0.16
PASI	4.8 ± 7.3	4.8 ± 7.5	6.5 ± 10.3	0.16
Tender joint count	6.6 ± 7.7	6.6 ± 7.9	8.1 ± 11.7	0.26
Swollen joint count	3.9 ± 5.7	3.9 ± 5.3	3.6 ± 6.3	0.75
Enthesitis	20 (23)	30 (26.8)	30 (26.1)	0.64
Corticosteroid, current use	2 (2.3)	5 (4.5)	2 (1.7)	0.73
DMARD, current use	16 (18.4)	28 (25)	28 (24.4)	0.34
TNFi, current use	3 (3.5)	3 (2.7)	6 (5.2)	0.47
Radiographic damage				
mSteinbrocker score, Time 0	2.5 ± 5.3	3.3 ± 5.9	4.1 ± 7.8	0.11
Erosions	22 (29.7)	49 (45.4)	48 (44)	0.075
mSteinbrocker score, Time 2	4.7 ± 7.3	4.8 ± 8.6	5.7 ± 9.4	0.53
Tuft resorption	**15 (20.5)**	**30 (27.8)**	**38 (35.2)**	**0.03**
Periostitis	22 (29.3)	34 (31.8)	25 (23.4)	0.32
Plantar spur	**16 (27.1)**	**30 (32.3)**	**50 (53.2)**	**0.0006**
Achilles spur	**10 (17)**	**25 (26.9)**	**40 (42.6)**	**0.0006**
Axial involvement	13 (19.4)	20 (21.5)	20 (20.6)	0.87
Classic syndesmophyte	7 (11.9)	8 (8.6)	10 (10.6)	0.88
Paramarginal syndesmophytes	1 (1.7)	3 (3.2)	6 (6.4)	0.14
Pelvis enthesitis	**14 (19.2)**	**30 (28)**	**47 (43.5)**	**0.0004**
HLA alleles				
C*0602	15 (20.6)	23 (22.1)	20 (19.1)	0.76
B*27	**12 (16.4)**	**16 (15.2)**	**3 (2.9)**	**0.002**
B*0801	12 (16.4)	20 (19.1)	24 (22.9)	0.28

* p value by linear trend test for continuous variables and Cochrane-Armitage trend test for categorical variables. Significant data are in bold face. PsA: psoriatic arthritis; BMI: body mass index; PASI: Psoriasis Area and Severity Index; DMARD: disease-modifying antirheumatic drug; TNFi: tumor necrosis factor inhibitor; mSteinbrocker: modified Steinbrocker.

Table 3. The association between BMI category and PsA versus PsC by age group. Logistic regression model. Values are n (%) unless otherwise specified.

Variables	PsA, n = 314	PsC, n = 498	Univariate Model		Full Regression Model*	
			OR (95% CI)	p	OR (95% CI)	p
All						
Normal	87 (27.7)	175 (35.1)				
Overweight	112 (35.7)	192 (38.6)	1.17 (0.83–1.67)	0.36	1.25 (0.87–1.79)	0.23
Obese	115 (36.6)	131 (26.3)	1.77 (1.23–2.53)	0.002	1.77 (1.23–2.56)	0.002
Age of onset ≤ 30 yrs						
Normal	25 (45.5)	34 (51.5)				
Overweight	20 (36.4)	22 (33.3)	1.24 (0.56–2.74)	0.60	1.20 (0.52–2.79)	0.67
Obese	10 (18.2)	10 (15.5)	1.36 (0.49–3.76)	0.55	1.38 (0.46–4.11)	0.56
Age of onset 30–50 yrs						
Normal	47 (29.8)	86 (36.4)				
Overweight	54 (34.2)	91 (38.6)	1.09 (0.67–1.78)	0.74	1.10 (0.66–1.84)	0.72
Obese	57 (36.1)	59 (25)	1.77 (1.06–2.94)	0.028	1.72 (1.03–2.89)	0.04
Age of onset > 50 yrs						
Normal	15 (14.8)	55 (28.1)				
Overweight	38 (37.6)	79 (40.3)	1.76 (0.89–3.52)	0.11	2.19 (1.03–4.65)	0.04
Obese	48 (47.5)	62 (31.6)	2.84 (1.43–5.62)	0.003	3.12 (1.49–6.52)	0.002

* The model for all groups combined adjusted for age, sex, alcohol consumption, smoking, and education level. Models for each age category adjusted for sex, alcohol consumption, smoking, and education level. BMI: body mass index; PsA: psoriatic arthritis; PsC: psoriasis without arthritis.

To further investigate whether the differential effect of obesity on age at onset of PsA was related to differences in carriage of HLA alleles, we assessed the interaction between PsA susceptibility HLA alleles and BMI categories using a multivariate logistic regression model. A significant association was found between HLA-B*27 allele and BMI category (Table 4). While in patients who were HLA-B*27–negative the association between obesity and PsA was statistically significant (OR 2.39, 95% CI 1.59–3.60), there was an inverse association between obesity and patients with PsA who were HLA-B*27–positive (OR 0.55, 95% CI 0.08–3.76), although the latter did not reach statistical significance. The relationship between BMI, HLA-B*27, and age at onset of PsA are illustrated in Figure 1. The majority of the HLA-B*27 carriers are concentrated in the left lower corner of the plot, indicating lower BMI and younger age at onset of PsA. The interaction between the remaining HLA alleles and BMI categories was not statistically significant (data shown in Appendix 1). A sensitivity analysis was conducted among whites to account for potential population stratification bias. The results of the multivariable regression analysis were essentially similar with a significant association between obesity and PsA in HLA-B*27–negative individuals (OR 2.42, p = 0.0003), and a nonsignificant inverse association between obesity and PsA in HLA-B*27–positive patients (OR 0.26, p = 0.23).

DISCUSSION

In our large study of patients with early PsA and controls with PsC, obesity was differentially associated with PsA onset. Higher BMI is associated with a later onset of PsA and psoriasis, while normal weight was linked with early age of onset and the presence of the HLA-B*27 allele. These findings suggest a potentially differential effect of obesity on PsA risk depending on the genetic factors.

Table 4. The association between BMI category and PsA versus PsC by HLA-B*27. Logistic regression model.

Variables	Unadjusted Regression Model		Fully Adjusted Regression Model*	
	OR (95% CI)	p	OR (95% CI)	p
HLA-B*27	6.68 (2.27–19.5)	0.0006	7.02 (2.33–20.9)	0.0005
Overweight vs normal	1.35 (0.93–1.95)	0.12	1.43 (0.97–2.09)	0.08
Obese vs normal	2.24 (1.51–3.32)	< 0.0001	2.20 (1.47–3.25)	0.0001
BMI category*HLA-B*27		0.056		0.036
HLA-B*27–negative				
Overweight vs normal	1.35 (0.92–1.99)	0.12	1.51 (1.01–2.27)	0.046
Obese vs normal	2.25 (1.52–3.34)	< 0.0001	2.39 (1.59–3.60)	< 0.0001
HLA-B*27–positive				
Overweight vs normal	0.74 (0.20–2.78)	0.65	0.93 (0.17–5.15)	0.93
Obese vs normal	0.25 (0.04–1.46)	0.13	0.55 (0.08–3.76)	0.54

* Adjusted for age, sex, alcohol consumption, smoking, and education level. BMI: body mass index; PsA: psoriatic arthritis; PsC: psoriasis without arthritis.

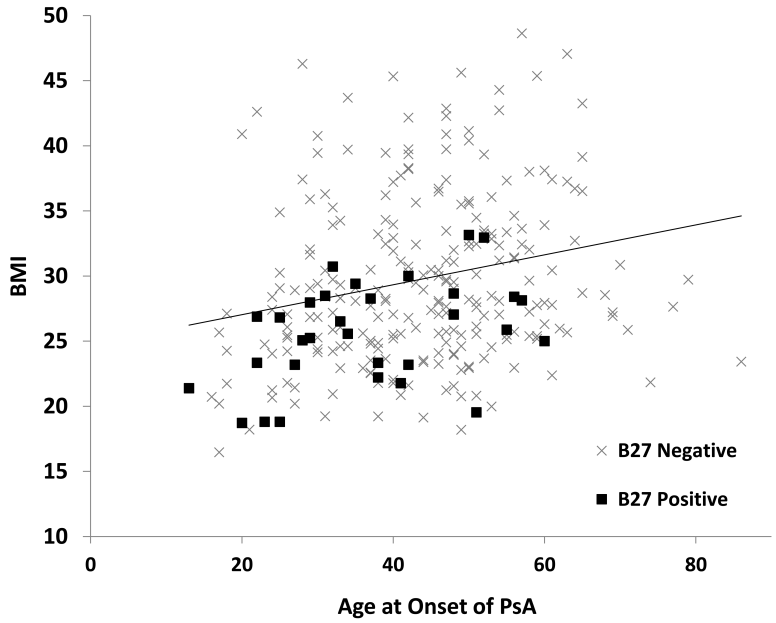

Figure 1. The correlation between BMI and age at onset of PsA by HLA-B*27 status in patients with PsA. Carriers of the HLA-B*27 allele tended to be leaner and in general, develop PsA before the age of 45. BMI: body mass index; PsA: psoriatic arthritis.

The strong link between obesity and PsA is well recognized and has been observed in numerous epidemiological studies[4,5,6,7,20]. It is unclear whether obesity has a direct causal effect on psoriasis and PsA susceptibility or whether a noncausal association exists. Considering the Bradford Hill criteria, accumulating evidence from recent studies points toward a potential causal relationship between obesity and psoriatic disease[21]. A temporal relationship and dose-effect between increased BMI and psoriasis and PsA risk were observed in several large population-based cohort studies from independent populations[4,5,7]. Additional studies demonstrated a strong and consistent association between obesity and PsA with 2–3× higher risk for obese people[6]. While risk reduction with weight loss has not been reported yet, studies have shown dramatic improvements in PsA and psoriasis disease activity following diet-induced and surgical weight reduction[9,22,23], thus strengthening the causal relationship between obesity and psoriatic disease. Adipose tissue functions as an endocrine organ that produces a variety of proteins called adipokines that have diverse physiological functions including involvement in chronic inflammation[24]. The levels of several of these adipokines, including leptin and adiponectin, are abnormal in patients with psoriasis and PsA, and correlate with the extent of skin and joint inflammation[25,26,27]. The adipose tissue is also a substantial source of proinflammatory cytokines, such as tumor necrosis factor-α (TNF-α), that drive systemic and organ-specific inflammation in psoriatic disease[28]. Our study provides novel information that contributes to the understanding of the pathophysiology of PsA and highlights the complex relationships between obesity and psoriatic disease.

In our study, obesity was associated with late-onset psoriasis and PsA, and with a long interval between the onset of MSK symptoms and diagnosis, which may indicate a more insidious onset of PsA. This long interval may be influenced by physicians' failure to recognize arthritis symptoms in obese individuals, instead attributing them to strain problems caused by heavy weight. Age is a major confounder of BMI; therefore, to account for the tendency to gain weight with aging, we performed an age-stratified comparison between patients with PsA and psoriasis who have not developed arthritis. The strong association between higher BMI and PsA was significant only in the older age groups (i.e., people who developed PsA at an older age), supporting the notion that obesity may be involved in the development of late-onset PsA.

In addition to environmental/external factors, such as obesity, genetic factors — in particular HLA-class I genes — are involved in PsA pathogenesis. We assessed the interaction between obesity and known HLA susceptibility markers of PsA. We hypothesized that obesity may be less important in triggering PsA in patients who carry strong genetic markers for PsA, and thus in such individuals obesity will be less prevalent. Indeed, we found an inverse association between obesity and HLA-B*27, the strongest genetic marker for PsA. Patients with HLA-B*27 tended to be significantly leaner than the remaining PsA study patients who were HLA-B*27–negative. While 36% of the patients with early PsA in our study population were obese, fewer than 10% of the patients who were HLA-B*27 carriers were obese. This association was independent of age, sex, and other known confounders that may affect body mass. HLA-B*27 allele marks a distinct subgroup of PsA that has similar clinical features to axial spondyloarthritis, with an early onset of disease and a short psoriasis-arthritis interval[13,29]. The lack of association

between the presence of HLA-B*27 and obesity in our study is in accordance with the weak association between ankylosing spondylitis and obesity[30,31], and suggests that obesity may not play a significant role in the pathophysiology of this subgroup of PsA.

Our finding of an association between obesity and later onset of psoriasis and PsA is in line with similar observations from other studies. Herédi, *et al* reported that higher BMI and central obesity were more frequent in patients with late-onset psoriasis (after 40 yrs of age) compared with early onset disease[32]. Among patients with PsA, patients with metabolic syndrome, which is strongly linked with central obesity, were reported to have a later age of onset of psoriasis and PsA[33]. Recent reports from patients with juvenile PsA support the notion that obesity may play a more important role in late-onset PsA. No significant difference was found in the prevalence of overweight and obesity in patients with juvenile PsA compared with a reference population of nonpsoriatic children[34]. In another study, an analysis of 320 patients with juvenile PsA found that overweight and obesity were associated with an older age at onset of MSK symptoms[35]. Overall, the predominance of obesity rates in late-onset psoriasis and PsA compared to the association of HLA alleles with early onset disease point toward heterogeneity in the driving factors of psoriatic disease. Obesity may play a predominant role in the pathogenesis of late-onset psoriasis and PsA, despite an overall similar clinical phenotype.

There is no known explanation for the association between obesity and psoriatic disease. Obesity is associated with systemic low-grade inflammation, as evident by increased inflammatory cytokines (interleukin 6, TNF-α) and changes in related molecules such as leptin and adiponectin, which may contribute to the development of psoriatic disease in susceptible individuals[2,36]. These cytokines and adipokines have been linked with the severity of established psoriasis and PsA[11,26,37]. An alternative hypothesis holds that elevated body mass leads to PsA through biomechanical stress, resulting in joint and enthesis microtrauma. Aberrant response to microtrauma at the enthesis and within the joint may trigger uncontrolled MSK inflammation resulting in PsA[38]. The exact mechanisms whereby adipose mass contributes to the development of psoriatic disease remain unknown and await further research.

Our study was limited in several aspects. First, a cross-sectional analysis as performed in our study cannot assess the temporal relationship between the exposure and the outcome. However, several studies have shown that obesity precedes the onset of psoriasis and PsA; therefore, there is substantial literature to infer causal relationships. Although it is possible that patients with PsA gain weight over time because of limitation in physical function, we limited the study population to patients with recent-onset PsA; therefore, it is unlikely that disease activity had a substantial effect on their weight and it is unlikely to explain the inverse association between HLA-B*27 and obesity. Second, obesity is linked to various factors that may confound the association between obesity and PsA. We adjusted for several potential variables including demographic and lifestyle factors in the statistical analysis. However, we cannot rule out other variables that were not accounted for. Last, our reference group was of people with psoriasis without arthritis; we did not have a control group of nonpsoriatic individuals.

Our present study analyzed the correlation between obesity and features of PsA. We have found that obesity is linked with late-onset psoriasis and PsA, while normal weight is associated with the presence of an identifiable genetic component, the HLA-B*27 allele, and an earlier onset of the disease. These results highlight the differential risk factors that may drive the inflammatory process in psoriatic disease.

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APPENDIX 1. Association between BMI category and PsA versus PsC. Logistic regression model.

Variables	Unadjusted Regression Model		Fully Adjusted Regression Model*	
	OR (95% CI)	p	OR (95% CI)	p
HLA-C*0602	0.30 (0.16–0.57)	0.0002	0.24 (0.13–0.47)	< 0.0001
Overweight vs normal	1.16 (0.76–1.69)	0.49	1.32 (0.84–2.07)	0.22
Obese vs normal	1.69 (1.07–2.66)	0.02	1.78 (1.12–2.85)	0.01
BMI category*HLA-C*0602		0.76		0.56
HLA-B*0801	1.21 (0.82–1.78)	0.35	1.11 (0.52–2.38)	0.78
Overweight vs normal	1.39 (0.92–2.07)	0.12	1.39 (0.92–2.07)	0.12
Obese vs normal	1.69 (1.11–2.55)	0.01	1.80 (1.17–2.77)	0.007
BMI category*HLA-B*0801		0.36		0.56
HLA-B*3801/B*3901	0.88 (0.39–2.01)	0.77	0.98 (0.42–2.27)	0.96
Overweight vs normal	1.26 (0.85–1.85)	0.25	1.44 (0.96–2.18)	0.07
Obese vs normal	1.75 (1.15–2.63)	0.007	1.95 (1.27–2.97)	0.002
BMI category*HLA-B*3801/B*3901		0.57		0.68
HLA-B*4402/B*4403	1.07 (0.48–1.80)	0.84	1.12 (0.56–2.27)	0.76
Overweight vs normal	1.27 (0.84–1.92)	0.25	1.43 (0.93–2.20)	0.09
Obese vs normal	1.84 (1.20–2.82)	0.005	2.05 (1.33–3.15)	0.001
BMI category*HLA-B*4402/B*4403		0.92		0.94

* Adjusted for age, sex, alcohol consumption, smoking, and education level. BMI: body mass index; PsA: psoriatic arthritis; PsC: psoriasis without arthritis.