Adiposity in Juvenile Psoriatic Arthritis

Aaida Samad, Matthew L. Stoll, Idit Lavi, Joyce J. Hsu, Vibeke Strand, Thomas N. Robinson, Elizabeth D. Mellins, and Devy Zisman, for the CARRA Legacy Registry Investigators

ABSTRACT. ***Objective.*** Adult patients with psoriatic arthritis are at increased risk for obesity and metabolic syndrome, but data regarding adiposity in children with juvenile psoriatic arthritis (JPsA) are limited. Our study assessed adiposity in children with JPsA in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry.

Methods. Patients with JPsA in the CARRA registry were divided into nonoverweight and overweight groups using recommendations from the US Centers for Disease Control, and differences in demographic and clinical characteristics between groups at baseline and after 1-year followup were assessed using chi-square test, Fisher's exact test, T test, or Mann-Whitney U test, as appropriate. The prevalence of overweight status in the JPsA registry patients was compared to rheumatoid factor–positive and –negative polyarticular juvenile idiopathic arthritis (RF+polyJIA; RF–polyJIA) registry cohorts and the US pediatric population, using a chi-square goodness-of-fit test.

Results. Overweight children represented 36.3% of this JPsA cohort (n = 320). Compared to nonoverweight children, they were significantly older at symptom onset and rheumatologist's first assessment, and scored significantly worse on patient/physician outcome measures. At 1-year followup, changes in body mass index were not associated with changes in clinical features or outcome measures. The prevalence of overweight and obesity in patients with JPsA was significantly higher than in RF+polyJIA patients, RF–polyJIA patients, and the US pediatric population.

Conclusion. In this registry, almost 1 in 5 patients with JPsA were obese and more than one-third were overweight. This is significantly more than expected compared to the US pediatric population, and appropriate longterm followup of this JPsA subgroup is warranted. (First Release December 15 2017; J Rheumatol 2018;45:411–18; doi:10.3899/jrheum.170598)

Key Indexing Terms:
JUVENILE IDIOPATHIC ARTHRITIS PSORIATIC ARTHRITIS
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Juvenile psoriatic arthritis (JPsA), a subgroup of juvenile idiopathic arthritis (JIA), is a chronic inflammatory joint disease with onset under 16 years of age, characterized as arthritis associated with psoriasis, or in the absence of frank psoriasis, supportive minor criteria (dactylitis, nail changes, family history)[1,2]. Patients with JPsA represent an estimated 5–20% of patients with JIA, depending on patient series and diagnostic criteria used[1]. JPsA can cause significant joint damage, physical impairment, chronic pain, and functional limitation, underscoring the need for early recognition and treatment[3,4].

Increasing body mass index (BMI) and obesity are associated with a dose-dependent increased risk for PsA in adults[5]. Specifically, obesity during early adulthood has been

From the School of Medicine, Case Western Reserve University, Cleveland, Ohio; Department of Pediatrics, Division of Rheumatology, University of Alabama at Birmingham, Birmingham, Alabama; Department of Medicine and Department of Pediatrics, and divisions of Allergy, Immunology and Rheumatology, and Human Gene Therapy, and General Pediatrics, Stanford University, Palo Alto, California, USA; Department of Rheumatology and the Department of Community Medicine and Epidemiology, Carmel Medical Center; The Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel.

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A. Samad, BA, Case Western Reserve University School of Medicine; M.L. Stoll, MD, PhD, MSCS, Department of Pediatrics, Division of Rheumatology, University of Alabama at Birmingham; I. Lavi, MA, Department of Community Medicine and Epidemiology, Carmel Medical Center; J.J. Hsu, MD, Department of Pediatrics, Division of Allergy, Immunology and Rheumatology, Stanford University; V. Strand, MD, MACR, FACP, Department of Medicine, Division of Immunology and Rheumatology; T.N. Robinson, MD, Departments of Pediatrics and Medicine, Division of General Pediatrics; E.D. Mellins, MD, Department of Pediatrics, divisions of Human Gene Therapy and Allergy, Immunology and Rheumatology, Program in Immunology, Stanford University; D. Zisman, MD, Department of Rheumatology, Carmel Medical Center and the Ruth and Bruce Rappaport Faculty of Medicine, Technion.

Dr. Mellins and Dr. Zisman contributed equally to this paper and are listed alphabetically.

Address correspondence to Dr. D. Zisman, Rheumatology Unit, Carmel Medical Center, 7 Michal St., Haifa, Israel. E-mail: devyzisman@gmail.com, devyzi@clalit.org.il

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suggested to predict development of PsA in adults: patients with psoriasis who are obese at age 18 are twice as likely to develop PsA than patients with a normal BMI[6]. Adult patients with PsA are at a markedly increased risk for obesity, with higher BMI compared to patients with psoriasis without arthritis, patients with rheumatoid arthritis (RA), and the general population[7]. Obesity has been associated with a lower probability of achieving minimal disease activity among adult patients with PsA[8,9]. Conversely, weight loss has been associated with increased achievement of minimal disease activity in patients with PsA starting treatment with tumor necrosis factor (TNF)-α inhibitors (TNFi), potentially because of a reduction in inflammatory mediators or changes to pharmacodynamics (i.e., volume of distribution) of these medications occurring secondarily to weight loss[10].

Previous studies have addressed the relationship between adiposity and psoriatic disease in adults. In pediatric populations, there are several studies of obesity in childhood psoriatic skin disease that show increased risk of being overweight and of metabolic syndrome in children and adolescents with psoriasis[11]. However, fewer studies of obesity in JPsA have been done, and the results are conflicting. In a large cohort of German children with JIA, patients with JPsA were more likely to be overweight than patients with other JIA subtypes[12]. Similarly, in a study assessing longterm outcomes of Canadian patients with JPsA, while patients had linear growth along predicted percentiles, their weight percentiles grew significantly out of step with changes to their height[13]. However, in a US single-center study, children with JPsA were not significantly more obese than a reference population of healthy children[14]. With the increasing prevalence of childhood obesity worldwide[15], it is of interest what relationships, if any, exist between adiposity and JPsA.

Thus, our study objective was to assess the adiposity of children diagnosed with JPsA in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry at baseline and after 1 year of followup, comparing overweight and nonoverweight patients. Additionally, the adiposity of patients with JPsA was compared to rheumatoid factor–positive (RF+polyJIA) and –negative (RF–polyJIA) polyarticular JIA groups in the registry and to the general US population.

MATERIALS AND METHODS

Patient population. Patient data were obtained from the CARRA registry, a multicenter registry including data on 9450 children with rheumatic diseases. The registry (also referred to as the CARRA legacy registry) was started in May 2010 and closed to enrollment in December 2013, and has entries from more than 425 physicians and health professionals from over 100 sites in the United States and Canada. For our study, data were collected using a standard protocol; patients at any stage of disease were eligible, and all patients in the database diagnosed with JPsA by their treating physicians were included. Defining disease-specific cohorts by physician diagnosis was most feasible given the design of the CARRA registry, and this method has been used by other published reports[16,17,18,19].

The study population included all patients with JPsA in the registry for whom age, sex, height, and weight were recorded at the baseline visit. Data analyzed included demographic variables; family history of psoriasis; clinical features such as number of joints involved (oligoarthritis: < 5 joints, polyarthritis: ≥ 5 joints), and nail pitting, dactylitis, psoriasis, enthesitis, sacroiliitis, and uveitis; laboratory values (RF, antinuclear antibodies, HLA-B27 status); radiographic information (joint damage and active inflammation); therapies ever prescribed; and patient/physician outcome measures. The outcome measures included Childhood Health Assessment Questionnaire [CHAQ; scored between 0 (best) and 3 (worst)]; physician's global assessment [PGA; scored 0 (best)–10 (worst) on a visual analog scale]; health-related quality of life [HRQOL; scored between 1 (excellent) and 5 (very poor)]; parent/subject overall well-being and parent/subject pain scale [each scored 0 (best)–10 (worst) on a visual analog scale]; and American College of Rheumatology functional class (I–IV). Data regarding therapies included present or past use of nonsteroidal antiinflammatory drugs, glucocorticoids (intraarticular injection, intravenous pulses, or oral), disease-modifying antirheumatic drugs, and biologics, e.g., TNFi. For a subset of patients with JPsA, data were available at both baseline and 1-year followup, which allowed for evaluation of change in adiposity over time, as well as assessment of whether any changes in adiposity were correlated with changes to clinical features or outcome measures. We compared the adiposity of patients with JPsA to patients with RF+polyJIA in the registry, considered the most similar subtype of JIA to adult RA[20] and to the more prevalent childhood subtype, RF–polyJIA.

Assessment of adiposity. Adiposity was assessed using BMI percentiles (BMI compared to a reference value that accounts for age and sex). Using baseline visit data, adiposity was assessed according to US Centers for Disease Control (CDC) 2010 recommendations. In patients < 2 years old, ratio of weight for length, plotted on World Health Organization (WHO) curves, was used, and in patients ≥ 2 years, BMI was plotted against CDC/National Center for Health Statistics growth references[21,22,23,24]. In patients < 2 years of age, weight for length percentiles were calculated using a calculator provided by UpToDate online[25]. BMI percentiles were calculated for patients age ≤ 20 years using the CDC BMI Tool for Schools[26], which uses height, weight, sex, and age at baseline. Age at baseline was rounded to the nearest month for infants < 2 years of age and to the nearest one-quarter–year for children 2 to 20 years old, per CDC recommendations[26,27]. In our study, there was a subset of patients (n = 21) enrolled at baseline age > 20 years old who met the registry inclusion criteria (onset of disease prior to age 16). For these patients, raw BMI rather than BMI percentile was used.

Children were divided into the following groups, based on cutoffs defined by the CDC, WHO, and the US National Heart, Lung, and Blood Institute[21,22,23,24,28]:

- Nonoverweight: children classified as underweight (weight for length < 2.3rd percentile for age and sex for infants < 2 yrs old, calculated BMI < 5th percentile for age and sex for children ≥ 2–20 yrs old, BMI < 18.5 kg/m^2 for patients > 20 yrs old) and normal weight (weight for length between the 2.3rd and 97.7th percentile for infants < 2 yrs old, calculated BMI ≥ 5 to < 85th percentile for age and sex in children ≥ 2–20 yrs old, calculated BMI ≥ 18.5 to < 25 for patients > 20 yrs old).
- Overweight: children classified as overweight (weight for length > 97.7th percentile for age and sex for infants < 2 yrs old, calculated BMI ≥ 85th percentile for age and sex in children ≥ 2–20 yrs old, calculated BMI ≥ 25 to < 30 for patients > 20 yrs old) and obese (BMI ≥ 95th percentile for age and sex for children ≥ 2–20 yrs, BMI ≥ 30 for patients > 20 yrs old).

Raw BMI. Previous studies have shown that BMI percentiles are not appropriate for assessing change in adiposity because they are sensitive to changes in the middle of the adiposity range and insensitive to changes at the extremes (i.e., percentiles of obese and very underweight children change less than those of nonobese/normal weight children[29,30]). For this reason, for analyses comparing patients with JPsA at baseline and 1-year followup, changes to raw BMI were analyzed.

Statistical analysis. Descriptive analysis of BMI subgroups was performed

using proportion and percent for the categorical characteristics and mean ± SD, or median and range for continuous variables. Comparisons between 2 independent groups for categorical characteristics were assessed by chi-square test or Fisher's exact test. Comparison of continuous variables between the BMI subgroups was performed by T test or Wilcoxon-Mann-Whitney test, as appropriate. A multivariable ordinal logistic model was used to assess the association between JPsA versus RF+polyJIA and RF–polyJIA and weight status, adjusted for age at baseline, sex, race, and ethnicity (variables described as affecting BMI in the US population[31]). Chi-square goodness-of-fit test was used to compare prevalence of overweight status in JPsA and RF+polyJIA and RF–polyJIA with prevalence of overweight in the US general pediatric population. All significance tests were 2-sided, and statistical significance was defined as $p \leq 0.05$. Data analysis was performed using SPSS version 22.0 (IBM PASW Statistics, SPSS Inc.). The study was approved by human subjects review at Stanford University (Institutional Review Board 31221) and by the CARRAnet Data/Sample Share committee.

RESULTS

Patient characteristics. Of a total of 361 patients with JPsA in the CARRA legacy registry, 320 (88.6%) for whom age, sex, height, and weight were recorded at baseline visit were included in our study (Table 1). In this group, 116 patients (36.3%) were overweight [55 (17.2%) overweight and 61 (19.1%) obese], and 204 (63.8%) were nonoverweight [9 (2.8%) underweight and 195 (60.9%) normal weight]. The majority were white (94.1%), non-Hispanic (91.3%), and female (64.7%; Table 1).

Nonoverweight versus overweight. Between nonoverweight and overweight JPsA groups (Table 1), overweight children were significantly older at symptom onset (9.26 ± 4.48 yrs vs 7.74 ± 4.67 yrs, p = 0.005) and at first assessment by a rheumatologist (10.59 ± 4.30 yrs vs 8.72 ± 4.65 yrs, p = 0.0005). There were no significant differences between the 2 groups for other demographic variables, clinical manifestations, laboratory values, and radiographic data. Regarding outcome measures, overweight patients scored worse on parent/subject overall well-being (2.15 ± 2.15 vs 2.64 ± 2.32, p = 0.05) and had higher CHAQ scores (0.31 ± 0.48 vs 0.42 ± 0.52, p = 0.05). A greater proportion of overweight children had been treated with etanercept (ETN; 47.4% vs 31.4%, p = 0.004) and hydroxychloroquine (6.9% vs 2.5%, p = 0.05) when compared to nonoverweight patients with JPsA.

One-year followup. Data were available for 189 patients with JPsA (Table 2) at 1-year followup. At followup, 15 children (7.9%) had changed to a higher BMI group, 160 (84.7%) remained in the same BMI group, and 14 changed to a lower BMI group. Changes in BMI were not accompanied by changes in clinical features (nail pitting, psoriasis, enthesitis, sacroiliac joint tenderness) or outcome measures (HRQOL, CHAQ, PGA, parent/subject overall well-being, and parent/subject pain scale).

Prevalence of overweight status in JPsA versus RF+polyJIA and RF–polyJIA. Of 436 patients with RF+polyJIA and 1907 children with RF–polyJIA in the CARRA registry, 415 (95.2%) and 1819 (95.4%), respectively, had age, sex, height, and weight recorded at baseline and were included for comparison to patients with JPsA (Table 3). In the RF+polyJIA population, 128 patients (30.8%) were classified as overweight, and 471 (25/9%) in the RF–polyJIA group. Initially there was no significant difference between the JPsA and RF+polyJIA groups in the proportion of patients in overweight and nonoverweight categories (p = 0.32). However, after adjustment for age, sex, race, and ethnicity in an ordinal logistic regression model, patients with JPsA were significantly more overweight than patients with RF+polyJIA (OR 1.49, 95% CI 1.03–2.18, p = 0.03). The JPsA group was more overweight than the RF–polyJIA group in the univariable (p = 0.001) and multivariable ordinal logistic models (OR 1.54, 95% CI 1.20–1.97, p = 0.001). These weight-based differences between children with JPsA [overweight, 114 (36.7%), and with RF–polyJIA, overweight 455 (26.8%)] were observed only in children with age of symptom onset > 4 years (p < 0.0001).

Prevalence of overweight status in JPsA versus the US pediatric population. The prevalence of overweight/obesity in this cohort of patients with JPsA was compared to the general US pediatric population using data reported by Ogden, *et al* from the US National Health and Nutrition Examination Survey (NHANES)[31]. In the United States, the prevalence of childhood obesity differs among racial/ethnic groups, with prevalence in African Americans, Mexican Americans, and Native Americans exceeding that of other groups[32]. Compared to the US pediatric population, our study population (JPsA, RF+polyJIA, and RF–polyJIA) was more racially/ethnically homogeneous, with the vast majority being non-Hispanic white (Table 3). Therefore, to compare our cohort to a similar group of children in the US population, and owing to a lack of statistical power to compare other racial/ethnic groups, we restricted our analysis to non-Hispanic white JPsA (n = 279), RF+polyJIA (n = 250), and RF–polyJIA patients (n = 1543) in our CARRA registry cohort and non-Hispanic white children in the national data.

The prevalence of overweight/obesity in non-Hispanic white children in the CARRA registry was significantly higher in patients with JPsA (35.1%) than in RF+polyJIA (26.8%, p = 0.015) and RF–polyJIA patients (24.5%, p < 0.0001)[31]. Patients with JPsA were significantly more overweight than would be expected based on the US population (28.5%, p = 0.01)[31]; in contrast, compared to the general population, RF+polyJIA patients in the registry were not more overweight and RF–polyJIA patients were leaner (p < 0.0001; Table 4).

DISCUSSION

More than one-third of patients with JPsA in the CARRA registry were overweight, and of these children, about 19% were obese. Overweight patients with JPsA developed symptoms at a later age and had worse patient-reported

Table 1. Characteristics of the study population.

Characteristics	Total JPsA	Nonoverweight	Overweight	p
Patients, n (%)	320	204 (63.8)	116 (36.3)	
Age at symptom onset, yrs, mean ± SD	8.29 ± 4.65	7.74 ± 4.67	9.26 ± 4.48	0.005
Age at first rheumatologist visit, yrs, mean ± SD	9.40 ± 4.60	8.72 ± 4.65	10.59 ± 4.30	0.0005
Interval between onset and first assessment, yrs, mean ± SD	1.03 ± 1.45	0.91 ± 1.17	1.25 ± 1.82	NS
Sex, n (%)				
Male	113 (35.3)	67 (32.8)	46 (39.7)	NS
Female	207 (64.7)	137 (67.2)	70 (60.3)	
Race, n (%)				
White	301 (94.1)	195 (95.6)	106 (91.4)	NS
Other	19 (5.9)	9 (4.4)	10 (8.6)	
Ethnicity				
Hispanic or Latino	28 (8.8)	18 (8.8)	10 (8.6)	NS
Not Hispanic or Latino	292 (91.3)	186 (91.2)	106 (91.4)	
Family history, n (%)				
Psoriasis	103 (32.2)	70 (34.3)	33 (28.4)	NS
JIA	10 (3.1)	5 (2.5)	5 (4.3)	NS
RA	32 (10.0)	19 (9.3)	13 (11.2)	NS
Clinical characteristics, n (%)				
Affected joints				
< 5	140 (44.2)	92 (45.5)	48 (41.7)	NS
≥ 5	177 (55.8)	110 (54.5)	67 (58.3)	
Nail pitting	103 (34.1)	58 (30.2)	45 (40.9)	NS
Dactylitis	94 (29.4)	60 (29.4)	34 (29.3)	NS
Psoriasis	211 (68.5)	129 (66.5)	82 (71.9)	NS
Enthesitis	91 (30.1)	58 (30.2)	33 (30.0)	NS
SI joint tenderness	53 (17.5)	28 (14.7)	25 (22.5)	NS
Uveitis	35 (11.4)	22 (11.3)	13 (11.5)	NS
Laboratory values, n (%)				
IgM RF	4 (1.3)	3 (1.5)	1 (0.9)	NS
ANA				
Negative	136 (2.5)	82 (40.2)	54 (46.6)	NS
Not done	59 (18.4)	37 (18.1)	22 (19.0)	
Positive	125 (39.1)	40 (34.5)	85 (41.7)	
HLA-B27–positive	22 (10.4)	13 (9.9)	9 (11.3)	NS
Radiological variables, n (%)				
Evidence of joint damage	67 (25.1)	38 (22.5)	29 (29.6)	NS
Active inflammation of SI joint	8 (28.6)	4 (22.2)	4 (40.0)	NS
Outcome measures, mean ± SD				
HRQOL	2.17 ± 0.85	2.12 ± 0.85	2.27 ± 0.83	NS
Parent/subject overall well-being	2.33 ± 2.22	2.15 ± 2.15	2.64 ± 2.32	0.05
Parent/subject pain score	2.54 ± 2.65	2.37 ± 2.60	2.83 ± 2.72	NS
CHAQ	0.35 ± 0.49	0.31 ± 0.48	0.42 ± 0.52	0.05
PGA	1.53 ± 1.76	1.50 ± 1.83	1.59 ± 1.63	NS
ACR functional class, n (%)				
Class I	250 (79.9)	166 (83.4)	84 (73.7)	NS
Class II	57 (18.2)	30 (15.1)	27 (23.7)	
Class III	6 (1.9)	3 (1.5)	3 (2.6)	
Therapy				
Nonbiologics, immune modulators, or DMARD, n (%)	257 (80.3)	163 (79.9)	94 (81.0)	NS
HCQ	13 (4.1)	5 (2.5)	8 (6.9)	0.05
LEF	12 (3.8)	9 (4.4)	3 (2.6)	NS
MTX	167 (52.2)	106 (52.0)	61 (52.6)	NS
SSZ	27 (8.4)	20 (9.8)	7 (6.0)	NS
Biologics	160 (50.0)	94 (46.1)	66 (56.9)	NS
ADA	63 (19.7)	37 (18.1)	26 (22.4)	NS
ETN	119 (37.2)	64 (31.4)	55 (47.4)	0.004
IFX	30 (9.4)	21 (10.3)	9 (7.8)	NS
Glucocorticoids	167 (52.2)	101 (49.5)	66 (56.9)	NS
NSAID (daily)	148 (46.3)	97 (47.5)	51 (44.0)	NS

BMI: body mass index; JPsA: juvenile psoriatic arthritis; JIA: juvenile idiopathic arthritis; RA: rheumatoid arthritis; RF: rheumatoid factor; IgM: immunoglobulin M; ANA: antinuclear antibodies; SI: sacroiliac; HRQOL: health-related quality of life; CHAQ: Childhood Health Assessment Questionnaire; PGA: physician's global assessment score; ACR: American College of Rheumatology; DMARD: disease-modifying antirheumatic drug; HCQ: hydroxychloroquine; LEF: leflunomide; MTX; methotrexate; SSZ: sulfasalazine; ADA: adalimumab; ETN: etanercept; IFX: infliximab; NSAID: nonsteroidal antiinflammatory drug; NS: nonsignificant.

Table 2. Change in adiposity in JPsA cohort: baseline versus 1-year followup.

Variables	Baseline			
	Under/normal Weight	Overweight	Obese	Total
Under/normal weight, n (%)	117 (92.9)	*9 (25.0)*	*0 (0)*	126 (66.7)
Overweight, n (%)	**9 (7.1)**	21 (58.3)	*5 (18.5)*	35 (18.5)
Obese, n (%)	**0 (0)**	**6 (16.7)**	22 (81.5)	28 (14.8)
Total	126 (100)	36 (100)	27 (100)	189 (100)

Bold face indicates change from lower to higher BMI. Italics indicate change from higher to lower BMI. BMI: body mass index; JPsA: juvenile psoriatic arthritis.

Table 3. Patient characteristics: JPsA versus RF+ polyarticular JIA and versus RF– polyarticular JIA in the CARRA registry.

Characteristics	JPsA	Poly RF+JIA	p*	Poly RF–JIA	p**
No. patients	320	415		1819	
Age at symptom onset, yrs, median (range)	8.74 (0.21–16.81)	10.43 (0.21–18.32)	< 0.0001	5.44 (0.02–16.62)	< 0.0001
Age at first rheumatology visit, yrs, median (range)	10.15 (0.37–17.27)	11.29 (0.24–18.48)	< 0.0001	6.89 (0.17–20.57)	< 0.0001
Sex, n (%)					
Male	113 (35.3)	62 (14.9)		389 (21.4)	
Female	207 (64.7)	353 (85.1)	< 0.0001	1430 (78.6)	< 0.0001
Race, n (%)					
White	301 (94.1)	320 (77.1)		1680 (92.4)	
Other	19 (5.9)	95 (22.9)	< 0.0001	139 (7.6)	0.28
Ethnicity, n (%)					
Hispanic or Latino	28 (8.8)	97 (23.4)		176 (9.7)	
Non-Hispanic or Latino	292 (91.3)	318 (76.6)	< 0.0001	1643 (90.3)	0.60
BMI group, n (%)					
Underweight	9 (2.8)	19 (4.6)		86 (4.7)	
Normal weight	195 (60.9)	268 (64.6)	0.03#	1262 (69.4)	0.001†
Overweight	55 (17.2)	62 (14.9)		243 (13.4)	
Obese	61 (19.1)	66 (15.9)		228 (12.5)	

* p value comparing JPsA to polyarticular RF+JIA. ** p value comparing JPsA to polyarticular RF–JIA . # Significant after adjustment for age, sex, and race, ethnicity, OR 1.49, 95% CI 1.03–2.18. † Significant after adjustment for age, sex, and race, ethnicity, OR 1.54, 95% CI 1.20–1.97. JPsA: juvenile psoriatic arthritis; RF: rheumatoid factor; JIA: juvenile idiopathic arthritis; CARRA: Childhood Arthritis and Rheumatology Research Alliance; poly: polyarticular; BMI: body mass index.

Table 4. Prevalence of overweight status in JPsA and RF+/RF– polyarticular JIA versus US population.

Variables	JPsA, n = 279*			Poly RF+JIA, n = 250*			Poly RF–JIA, n = 1543*		
	CARRA	Expected	p	CARRA	Expected	p	CARRA	Expected	p
Nonoverweight, no. patients	181	199.5	0.014 *	183	178.8	0.55	1165	1103.2	< 0.001
Overweight, no. patients	98	79.5		67	71.3		378	439.8	

* White, non-Hispanic subgroup of total JPsA and poly RF+/RF– JIA. JPsA: juvenile psoriatic arthritis; RF: rheumatoid factor; JIA: juvenile idiopathic arthritis; poly: polyarticular; CARRA: Childhood Arthritis and Rheumatology Research Alliance (registry).

outcomes by parent/subject overall well-being and CHAQ scores as compared to nonoverweight patients with JPsA. A significantly higher proportion of patients with JPsA was overweight/obese (35.1% of this cohort) than has been reported for the US general pediatric population (28.5%) for non-Hispanic white children[31].

Outside of our study, there are limited data previously published regarding the prevalence of overweight and obesity in patients with JPsA. Of note, a published abstract including 48 patients with JPsA evaluated at a single center in the United States reported that about 16.8% of children were overweight and 10.4% were obese (compared to 17.2% and 19%, respectively, in the CARRA registry)[14]. The abstract assessed differences in clinical and demographic characteristics between overweight and nonoverweight patients with JPsA, similarly to our study, and found that female sex was associated with decreased odds of being overweight, while other clinical features such as age, disease duration, psoriasis,

and active joint count at diagnosis were not associated with overweight status. The proportion of overweight patients with JPsA was not significantly different compared to a reference population of 909 healthy children. The abstract noted that the lack of association between obesity and JPsA was potentially secondary to limited sample size[14].

Overweight children in our study were older at symptom onset than their leaner counterparts. Older-onset patients with JPsA have been shown to have a clinical phenotype that more closely mirrors adult PsA, with male predominance, more sacroiliitis, psoriasis, and enthesitis than the early-onset group, and as observed in our study, this is true for increased BMI as well[7,19,33].

In our study, a greater proportion of overweight children were treated with ETN (47.4% vs 31.4%, p = 0.004, n = 119). However, the CARRA registry contains data on exposure (Yes/No) to medication without doses, start dates, or stop dates, making it impossible to determine whether children became more overweight after treatment with the TNFi ETN, or whether children who were more overweight were treated more often with ETN. In a previous study evaluating changes in BMI over more than 2 years, significant increases in BMI were not observed among patients with JIA receiving TNFi therapy[34]. In contrast, in a second study assessing the effects of longterm ETN treatment on growth of patients with JIA over 3 years, significant increases in mean weight percentile from baseline were observed each year in the ETN and ETN plus methotrexate groups versus those receiving methotrexate alone[35].

Adjusting for age, sex, and race/ethnicity, patients with JPsA in this registry were about 50% more likely to be overweight than RF+polyJIA patients. Similarly, a previous study of more than 12,000 German patients with JIA found that patients with systemic JIA and JPsA were more likely to be overweight, whereas the overweight prevalence of the overall JIA cohort was comparable to children/adolescents in the general population. Analyses in that study showed that predictors of overweight status were male sex, higher functional limitation, higher disease activity, use of high-dose glucocorticoids, and lower level (or lack) of participation in school sports[12]. In patients with JPsA in the CARRA registry, glucocorticoid use (ever) was not significantly different between overweight (56.9%) and nonoverweight groups (49.5%).

In our study, after 1-year followup, 84.7% of children remained in the same BMI group, and changes in BMI were not accompanied by significant changes in clinical features. Several previous studies have also investigated BMI trajectories of JIA and patients with JPsA. In an abstract assessing height, weight, and BMI change of more than 1000 Canadian patients with JIA over 5 years, mean BMI Z scores decreased slightly among children with JPsA, while remaining stable or increasing in other JIA subtypes[36]. In another study specifically assessing 53 Canadian patients with JPsA, weight increased out of step with height, with median percentiles for weight at last followup significantly higher compared with first visit, with no significant change in height percentiles over that same period[13].

From an immunological standpoint, the relationship between obesity and PsA is potentially explained by overlapping inflammatory pathways[8]. Adiposity and obesity are associated with higher levels of inflammatory cytokines such as interleukin 1 (IL-1), IL-6, IL-8, and TNF-α, which act synergistically with inflammation associated with psoriatic conditions[5,6]. Some have suggested that the relationship between obesity and PsA is bidirectional, with cytokines produced by adipose tissue increasing severity/susceptibility to psoriatic disease, and in turn, cytokines associated with psoriatic disease perpetuating obesity and other comorbid conditions[8,37,38]. In addition, it is hypothesized that mechanical wear and biomechanical abnormalities in load-bearing joints, secondary to obesity, could trigger PsA in these joints, with the eventual spread of inflammatory arthritis to other joints[5,8,39].

Alterations or imbalance to microbiome composition (termed *dysbiosis*) have been proposed as potentially explaining the relationship between obesity and inflammatory arthritis[40,41]. Previous studies have established that children with multiple different subtypes of JIA have altered intestinal microbiota[42,43]. Under this proposed mechanism, alterations to microbiota composition influence obesity status; specifically, obese individuals have microbiota that are less diverse and that are more efficient at extracting calories in food, a condition that perpetuates obesity[44]. In turn, obesity status indirectly modulates both the severity and risk of inflammatory arthritis[40,45].

Our study results should be interpreted in the context of their limitations. Although the CARRA legacy registry includes children from more than 100 sites across the United States and Canada, the cohort is a convenience sample, with children enrolled at any stage of disease. The registry data include exposures to medication/treatment (Yes/No) without doses or start/stop dates, making it difficult to determine temporal relationships between treatment and BMI changes. The prevalence of overweight/obesity in this cohort of patients with JPsA was compared to the prevalence of overweight/obesity in the United States using data from the NHANES. A limitation of our approach is that the cohorts being compared were recruited and sampled differently, and differences between the 2 groups regarding factors that potentially contribute to the prevalence of obesity (sex, parental BMI, urban vs rural environments, socioeconomic status, etc.) could not be taken into account and adjusted for. Last, BMI was chosen as a surrogate measure of adiposity because it could be calculated based on data available in the CARRA registry. However, previous studies have shown that patients with JIA can have altered body compositions, with reduced muscle mass and bone mineral density/bone mass and

increased fat/truncal obesity[46,47,48,49]. In the context of potential altered body composition, adiposity may not be adequately represented by BMI, because BMI does not account for different distributions of fat mass, which are perhaps better measured by more direct methods of quantifying body fat[50].

The primary strength of our study is that it represents a first investigation of the prevalence of overweight/obesity in North American patients with JPsA using data from a large, multicenter registry. In our study, more than one-third of patients with JPsA were overweight, and almost 1 in 5 were obese. Consistent with what has previously been reported in adult populations with PsA, patients with JPsA were significantly more overweight than RF+polyJIA and RF–polyJIA patients and the general US population. Longterm followup studies of patients with increased adiposity and/or BMI are needed to help identify the best monitoring and treatment practices and to assess growth and health outcomes in JPsA.

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APPENDIX 1.

List of study collaborators. CARRA registry site principal investigators and research coordinators: L. Abramson, E. Anderson, M. Andrew, N. Battle, M. Becker, H. Benham, T. Beukelman, J. Birmingham, P. Blier, A. Brown, H. Brunner, A. Cabrera, D. Canter, D. Carlton, B. Caruso, L. Ceracchio, E. Chalom, J. Chang, P. Charpentier, K. Clark, J. Dean, F. Dedeoglu, B. Feldman, P. Ferguson, M. Fox, K. Francis, M. Gervasini, D. Goldsmith, G. Gorton, B. Gottlieb, T. Graham, T. Griffin, H. Grosbein, S. Guppy, H. Haftel, D. Helfrich, G. Higgins, A. Hillard, J.R. Hollister, J. Hsu, A. Hudgins, C. Hung, A. Huttenlocher, N. Ilowite, A. Imlay, L. Imundo, C.J. Inman, J. Jaqith, R. Jerath, L. Jung, P. Kahn, A. Kapedani, D. Kingsbury, K. Klein, M. Klein-Gitelman, A. Kunkel, S. Lapidus, S. Layburn, T. Lehman, C. Lindsley, M. Macgregor-Hannah, M. Malloy, C. Mawhorter, D. McCurdy, K. Mims, N. Moorthy, D. Morus, E. Muscal, M. Natter, J. Olson, K. O'Neil, K. Onel, M. Orlando, J. Palmquist, M. Phillips, L. Ponder, S. Prahalad, M. Punaro, D. Puplava, S. Quinn, A. Quintero, C. Rabinovich, A. Reed, C. Reed, S. Ringold, M. Riordan, S. Roberson, A. Robinson, J. Rossette, D. Rothman, D. Russo, N. Ruth, K. Schikler, A. Sestak, B. Shaham, Y. Sherman, M. Simmons, N. Singer, S. Spalding, H. Stapp, R. Syed, E. Thomas, K. Torok, D. Trejo, J. Tress, W. Upton, R. Vehe, E. von Scheven, L. Walters, J. Weiss, P. Weiss, N. Welnick, A. White, J. Woo, J. Wootton, A. Yalcindag, C. Zapp, L. Zemel, and A. Zhu.

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