Higher bodily adiposity, fat intake, and cholesterol serum levels are associated with higher disease activity in psoriatic arthritis patients: is there a link among fat and skin and joint involvement?

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Abstract

Introduction/ objectives: Assuming that there is a link between lipid and glucose metabolism and inflammation in patients with psoriatic arthritis (PsA), our aim was to evaluate the relationships among body composition measurements, food intake, and disease activity in patients with PsA.

Methods: A total of 97 patients with PsA, according to the CASPAR criteria, were included in this cross-sectional study. Body composition measurements (whole-body DXA, GE-Lunar), food intake (3-day registry) and biochemical and inflammatory serum markers were evaluated. Skin and joint disease activity were assessed by using PASI, BSA, DAS28, and minimal disease activity (MDA). The level of significance was set as p < 0.05.

Results: A higher prevalence of obesity, according to the fat mass index (FMI) (92.7%), and metabolic syndrome (MetS) (54%) were found, but no significant changes regarding lean or bone mass were found. Joint disease activity was positively correlated with total body fat (r = 0.4; p < 0.001), FMI (r = 0.33; p < 0.001), body mass index (r = 0.20; p < 0.049) and waist circumference (r = 0.27; p = 0.009). In addition, joint disease activity was negatively associated with muscle mass (r = −0.38; p < 0.001). Skin disease activity was positively correlated with total cholesterol (r = 0.3; p = 0.003) and LDL-cholesterol (r = 0.28; p = 0.006). After multiple adjustments, patients with severe joint disease activity had higher body adiposity than patients in remission or with low disease activity. Skin disease activity was associated with higher trans-fat intake and lower omega-6 consumption.

Conclusions: Our data suggest a possible harmful link among fat (body adiposity, saturated fat consumption, LDL-cholesterol serum levels) and joint and skin disease activity in patients with PsA.

Keywords: Psoriatic arthritis, Body composition measurements, Adipose tissue, Metabolic syndrome, Food intake
Introduction
Psoriatic arthritis (PsA) is a chronic systemic inflammatory disease characterized by red scaly skin patches and nail and joint involvement is associated with multiple comorbidities, particularly metabolic syndrome (MetS) [1–3], characterized by higher obesity and body adiposity [4] and poor lipid profiles [2, 5]. This close relationship between adipose tissue and skin and joint disease may be explained by complex interactions among inflammation, innate immune changes, insulin uptake, lipid processing, and alterations in adipogenesis and neoangiogenesis [6–8].

Some authors have found significant association between body mass index (BMI) and disease activity in psoriasis (Ps) and PsA patients [9–13], especially in patients with a longer duration of disease [14]. Moreover, better response to cyclosporine was observed in obese patients with Ps with low calorie intake and restricted diet, suggesting that lifestyle modifications may contribute to the pharmacological therapy [9, 15]. Additionally, higher carbohydrate and saturated fat intakes were associated with skin disease activity and a higher rate of comorbidities [16].

Assuming that there is a link between lipid and glucose metabolism and the inflammation in patients with PsA, our aim was to evaluate the relationship among body composition (BC) measurements, food intake, and disease activity in patients with psoriatic arthritis (PsA).

Patients and methods
A total of 97 patients were included in this cross-sectional study (Fig. 1).

As an inclusion criterion, patients with PsA must have been diagnosed according to the Classification Criteria of Psoriatic Arthritis (CASPAR) and must have signed an informed consent form, according to the Declaration of Helsinki. Specific medications for PsA and physical activity levels were required to be stable for the last 3 months. Patients with gastrointestinal, endocrine, pulmonary, kidney, hepatic, and neuromuscular diseases, as well as patient who were HIV-positive, pregnant or breast-feeding or had a previous history of cancer were excluded. Patients taking sex steroid hormones, protein supplements, vitamins, multivitamins, nutraceuticals or antioxidants were not included.

Clinical risk factors for MetS and CVD were evaluated in all PsA patients. To classify MetS, the Harmonizing Guideline for Metabolic Syndrome was used [17]. The criteria for clinical diagnosis were the presence of any three of five risk factors: 1) elevated waist circumference, according to population and country specific definitions; 2) elevated triglycerides (≥ 150 mg/dL or 1.7 mmol/L) or drug treatment for elevated triglycerides; 3) reduced high-density lipoprotein cholesterol (HDL-C) (< 40 mg/dL or 1.0 mmol/L in males; < 50 mg/dL or 1.3 mmol/L in females); 4) elevated blood pressure (systolic ≥130 and/or diastolic ≥85 mmHg) or antihypertensive drug treatment; 5) elevated fasting glucose (≥ 100 mg/dL) or drug treatment for elevated glucose. In addition, medical history including current drug use, lifestyle habits, duration of disease, and details about skin and joint involvement were also recorded.

A 3-day food-record (FR) was used to quantify the intake of energy (kcal), carbohydrates (g), protein (g), total fat (g), saturated fat (g), monounsaturated fat (g), polyunsaturated fat (g), cholesterol (mg), trans-fat (g), sugar (g), fiber (g), vitamin E (mg), vitamin A (mcg), vitamin C (mg), magnesium (mg), zinc (mg), copper (mg), selenium (mg), omega 3 (ω-3) (g), omega 6 (ω-6) (g), carotene (RE), beta-carotene (mg), and sodium (mg). A well-trained dietitian prospectively administered these FR. Energy was adjusted using the residual method described by Willet and Stamper (1998) [18]. Data were calculated using he Food Processor SQL – Professional Nutrition Analysis Software and Databases – ESHA Research, USA, 2010. Dietetic data were compared with reference values, according to the Dietary Reference Intake (DRI) [19].

Anthropometric assessment was performed by measuring weight (Filizola®) and height (stadiometer). Nutritional

![Fig. 1 Patient disposition. Intent to treat analysis. CASPAR: CIAssification of psoriatic arthritis](image-url)
status was categorized based on the World Health Organization (WHO) criteria for BMI (kg/m²). Waist circumference was measured halfway between the lowest rib and the top of hipbone and was classified using a cutoff of 90 cm for males and 80 cm for females, values proposed by Ethnic Central and South American populations by the International Diabetes Federation (IDF) and Metabolic Syndrome Harmonizing Guidelines [17].

Body composition assessment was performed by using dual x-ray absorptiometry (DXA) technology (GE-Lunar Radiation Corporation, DPX MD +, Madison, WI, USA), according to the standard protocol for acquisition and analysis suggested by International Society Clinical Densitometry (ISCD). The measurements included total lean mass (kg), skeletal lean mass (kg), total and regional adipose tissue (kg and %), total bone mineral density (g/cm²), and bone mineral content (g). The coefficients of variation were 1.14, 1.64, 1.53, 1.62, 0.67, and 1.72%, respectively [20]. To classify low appendicular lean mass (ALM), Baumgartner’s method was used for patients older than 50 years, and Rosetta’s method was used for those under 50 years, according to sex [21, 22]. The fat mass index (FMI) was calculated using the equation proposed by NHANES III, considering reference values of 5–9 kg/m² for females and 3–6 kg/m² for males [23].

To evaluate the activity and severity of skin disease, the psoriasis area severity index (PASI) [24] and body surface area (BSA) [25] were used. To evaluate peripheral joint activity, the disease activity score (DAS28-ESR and DAS28-CRP) (interobserver coefficient of variation of 0.81 and intraobserver coefficient of variation of 0.79) [26] were used. For axial involvement, the Bath Ankylosing Spondylitis disease activity index (BASDAI) was chosen [27]. The functional capacity was evaluated using the health assessment questionnaire (HAQ) [28] and minimal disease activity (MDA) was used to classify remission status in PsA patients [29].

Physical activity status was analyzed using the International Physical Activity Questionnaire (IPAQ) – short form, and the patients were classified as being inactive, being minimally active, or participating in health enhancing physical activity (HEPA; i.e., highly active) [30, 31].

In the morning, after the participant had fasted for 12 h, a 10 mL blood sample was collected by a trained nurse using disposable material. All the samples were then centrifuged at 2000 rpm for 10 min at room temperature to test high-sensitivity C-reactive protein (hs-CPR), erythrocyte sedimentation rate (ESR), hemoglobin A1c, fasting insulin and glucose levels, total cholesterol and its fractions and triglycerides. HOMA-IR it was also used to calculate insulin resistance. All data were analyzed using SPSS software, version 19.0. The Kolmogorov-Smirnov test was used to evaluate the normality of distributions.

Descriptive analysis was expressed as mean, standard deviation, and frequency (%). The sample was calculated by using chi-square test. A power of 80% power and a significance of 5% were used, and the required sample size was determined to be 97. Inferential statistics included Student’s t-test to compare means of numeric variables that were normally distributed. The Pearson correlation coefficient was used to test associations among continuous variables, including PASI, DAS-28, BASDAI, HAQ, number of swollen joints (NSJs) and number of tender joints (NTJs), age, weight, height, BMI, and waist circumference. To perform the multiple regression analyses, a model was created for each outcome: PASI for skin disease activity and MDA for joint disease activity. Both PASI and MDA were considered as dependent variables, while biochemical (fasting glucose, HOMA-IR, cholesterol, triglycerides), body composition measurements (waist circumference, lean mass, fat mass, BMI), dietary and activity habits, pharmacological treatments, and clinical conditions were considered independent variables. The final regression model was adjusted for sex, weight and age. The level of significance was set as p < 0.05.

The study was approved by the Ethics Committee of Research from Federal University of Sao Paulo (CAAE: 00591412.5.0000.5505).

Results

Patients with PsA were equally distributed according to sex (54.6% females), and there were more adults (68%) than elderly with long-term disease. Most PsA patients were inactive (35.1%) or minimally physically active (39.2%), according to the IPAQ. Approximately 60% of women were postmenopausal (60.4%), and almost 20% were taking hormone replacement therapy (data not shown).

More than 60% had skin involvement primarily, and only 14% had arthritis as the initial manifestation. Almost 25% of the sample had both manifestations concomitantly. Methotrexate (MTX) was used by the majority of patients as monotherapy or in combination with TNF-blockers. Approximately 20% of patients were taking TNF-blockers, and less than 10% of the sample was using nonsteroidal anti-inflammatory drugs (NSAIDs) or glucocorticosteroids. There was a high prevalence of obesity, according to BMI, and abdominal fat tissue excess (Table 1).

After sex and age-adjustments, there was a high prevalence of abdominal fatness (android pattern) in both male and female PsA patients, but no significant lean or bone mass impairment was observed (Table 2). More than 90% of PsA patients, regardless of sex, had excess adipose tissue (FMI), 5.2% had sarcopenia and 3.1% had sarcopenic obesity, according to DXA measurements.
and NHANES III cutoffs. Comparing FMI and BMI, there was a divergence between these two measurements in almost 20% of patients in the classification of fat excess. PsA patients also had a high rate of MetS (54.6%), hypertension (46.9%), and dyslipidemia (44.3%).

Regarding dietary intake, there was a high average energy consumption, especially in men, but there was no significant difference in macro or micronutrient intake, according to sex. Furthermore, low consumption of fiber was found, as well as consumption of sodium above the international recommendations (Table 3). The ω-6/ω-3 ratio was 5.8/1.

Biochemical analysis showed that insulin resistance (HOMA-IR), fasting blood glucose levels, and hemoglobin A1c were above the reference values (Table 4). Approximately 30% of the sample had values above the recommended values and were being treated for glucose intolerance (20.6% metformin and 7.2% insulin therapy). However, almost 70% of subjects with abnormal HOMA-IR had not yet been diagnosed with diabetes mellitus. In contrast, serum cholesterol levels were adequate in most patients. Statins or fibrates were being used by 34% of the patients.

There was a slightly moderate correlation between the values of joint disease activity and body composition measurements, including DAS28-ESR and FMI ($r = 0.33, p = 0.001$), bodily fat ($r = 0.40, p < 0.001$) and BMI ($r = 0.20, p = 0.049$). On the other hand, there was a negative correlation between DAS28-ESR and appendicular skeletal lean mass index ($r = -0.38, p < 0.001$). Similarly, a positive correlation was found between DAS28-CRP and

| Table 1 Characteristics of patients with psoriatic arthritis |
|---------------------------------|----------------|----------------|
| Age (years) | 53.12 (13.10) | 53 (54.6) |
| Sex (Female) | 53 (54.6) | 77.93 (15.98) |
| Height (cm) | 159.1 (20.2) | 30.50 (5.73) |
| Body Mass Index (kg/m²) | 103.13 (13.26) | 104.44 (13.40) |
| Waist circumference (cm) | 101.43 (13.49) | 12.29 (14.42) |
| Time of Disease (years) | 19.27 (15.26) | 12.98 (14.43) |
| Skin activity | 3.61 (6.84) | 4.22 (9.31) |
| Joint activity | DAS28-ESR | 3.54 (1.38) |
| Arthritis | 72 (74.2) | 21 (22.1) |
| Dactylitis | 30 (30.9) | 17 (17.9) |
| Axial | 8 (8.72) | 57 (60.0) |
| DAS28-CRP | 3.05 (1.31) | 32 (33.9) |
| Remission | 34 (35.1) | 21 (22.3) |
| Low | 39 (41.5) | 39 (41.5) |
| Moderate/Severe | BASDAI | 3.15 (2.06) |
| < 4 | 47 (52.8) | 47 (52.8) |
| ≥ 4 | 42 (47.2) | 42 (47.2) |
| HAQ | 0.92 (0.69) | 0.92 (0.69) |
| MDA | 22 (23.4) | 22 (23.4) |
| Physical Activity (IPAQ) | Inactive | 60 |
| Minimally active | 27 |
| Sufficiently active | 1 |
| Active | 0 |
| Very active | 0 |
| Drug therapy | GCs | 11 (11.5) |
| NSAIDs | 4 (4.1) |
| Synthetic DMARDs monotherapy | 31 (31.9) |
| Synthetic DMARDs combination therapy | 10 (10.3) |
| TNF-blockers | 17 (17.5) |
| Concomitant Medications | Insulin, n (%) | 7 (7.2) |
| Statins, n (%) | 33 (34.0) |
| Antidiabetic, n (%) | 20 (20.6) |
| Antihypertensive, n (%) | 46 (47.4) |
| Comorbidities | Diabetes, n (%) | 20 (20.6) |
| Hypertension, n (%) | 45 (46.4) |
| Dyslipidemia, n (%) | 43 (44.3) |

Results shown as absolute values and respective percentage or mean and standard deviation (SD). GCs glucocorticoids, NSAIDs non-steroidal anti-inflammatory drugs, MTX methotrexate, LEF leflunomide, CsA cyclosporine A, TJN tender joint number, SJN swollen joint number, DMARDS Disease-modifying antirheumatic drugs, TNF Tumoral Necrosis Factor
fat, as well as FMI (r = 0.27, p = 0.008), body fatness (r = 0.27, p = 0.008), BMI (r = 0.26, p = 0.01) and waist circumference (r = 0.27, p = 0.009) (data not shown).

No significant correlation was found between skin activity and body composition measurements (data not shown), although there was a significant correlation between the PASI and the serum cholesterol levels (r = 0.30; p = 0.003 and r = 0.28; p = 0.006, for total and LDL cholesterol, respectively). However, it is important to mention that the mean PASI was low in this population. Thus, the correlations related to skin activity might be more relevant in patients with more severe psoriasis.

Patients in remission had significantly higher lean mass than those with active arthritis. Nonetheless, those with more severe joint activity had higher FMI and fat intake (Table 5). Unexpectedly, no correlation was found between MDA and body composition measurements, food intake, or biochemical indexes. On the other hand, skin disease activity was more severe in patients with increased consumption of trans fat and sodium and lower ω-6 intake than in patients in remission (Table 6). After multiple statistical adjustments, including adjustments for sex, BMI and age, the final model of multivariate regression model showed that total body fat (R² = 0.065, p = 0.02) and insulin resistance (R² = 0.069, p = 0.016) were significantly associated with joint activity. However, no variable could explain the outcome related to skin activity.

**Discussion**

Our results demonstrated that patients with active PsA had high rate of obesity, metabolic syndrome and adiposity (FMI), as well as high fat intake and insulin resistance, suggesting that these aspects share a possible harmful link with the association between disturbed lipid and glucose metabolism and skin and joint disease. It is worth emphasizing that the fat consumption and cholesterol levels might be more associated with skin activity, whereas the excess of total and abdominal fat mass and lower lean mass were more related to joint activity.

This close relationship between fat and skin and joint disease may be explained by inflammation itself. The increase in macrophages and other immune cells in psoriatic lesions and the synovio-entheseal complex would promote complex metabolic changes in the liver and adipose tissue, especially insulin resistance, as well as increased release of TNF-α and lower production of adiponectin [8]. Furthermore, patients with PsA and psoriasis share some other pathophysiological characteristics (neangiogenesis, insulin uptake, adipogenesis, lipid metabolism, and immune and epidermal proliferation) [6–8] and genetic aspects, such as peroxisome proliferator activated receptor (PPAR) polymorphism. Altogether, they have been considered triggers of inflammatory disorders and immune cell activation [32, 33].

PPARs are ligand-dependent transcription factors, that are activated by fatty acids and their derivates and control the inflammatory response. PPARs are activated by fatty acids and their derivates and control the inflammatory response. PPARs are activated by fatty acids and their derivates and control the inflammatory response. PPARs are activated by fatty acids and their derivates and control the inflammatory response. PPARs are activated by fatty acids and their derivates and control the inflammatory response. PPARs are activated by fatty acids and their derivates and control the inflammatory response. PPARs are activated by fatty acids and their derivates and control the inflammatory response. PPARs are activated by fatty acids and their derivates and control the inflammatory response. PPARs are activated by fatty acids and their derivates and control the inflammatory response. PPARs are activated by fatty acids and their derivates and control the inflammatory response.
injury. Therefore, there is an alteration in PPAR expression in psoriasis and PsA, contributing to the systemic inflammation in both diseases and the alteration of fat and glucose metabolism [33].

It seems that the oral treatment of PPAR synthetic ligand decreases inflammatory cytokines and suppresses angiogenesis, and PPAR synthetic ligand has been used in the treatment of metabolic syndrome, diabetes and dyslipidemia. Pilot studies have also shown that oral administration of the PPAR agonist improved cutaneous symptoms of PsA and psoriasis [33].

Higher cardiovascular risk in patients with PsA can also be attributed to the combination of skin and joint inflammation, releasing higher amounts of pro-inflammatory cytokines, such as tumor necrosis factor (TNF)-α, interleukin (IL)-6, IL-17 and IL-23 [34].

Recent studies have shown the importance of the IL-23/IL-17 axis pathway for the pathogenesis of chronic and autoimmune disease, including PsA, indicating an interaction between components of the innate and adaptive immune system. While IL-23 is critical in the pathogenesis of autoimmunity and producing myeloid cells, granulocytes, macrophages, and mast cells, IL-17 contributes to Th17- and IL17-producing cytotoxic (CD8+) T cells [35, 36].

Adiposity and insulin resistance (IR) also contributes to immunity and inflammation. The adipose tissue produces adipokines, especially leptin, adiponectin, resistin, and visfatin [37].

Leptin is up-regulated by inflammatory mediators and promotes the increase of TNF, IL-12, IL-6 and others inflammatory cytokines. The hyperleptinemia and leptin resistance, a common scenario on obesity, leads to a reduction in adipose tissue-infiltrating regulatory T cells (T_reg), amplifying local inflammation. T_reg cells are a subcategory of CD4+ CD25+ T cells, critical mediators of immune tolerance [37].

Resistin and visfatin are up-regulated with the increase of pro-inflammatory cytokines. While resistin is associated with glucose metabolism, visfatin has an important role in the development of B and T lymphocytes and it operates as a chemotactic factor for lymphocytes and monocytes. In contrast, adiponectin acts decreasing TNF and IL-6, and increasing interleukin-1 receptor associated kinase 1 (IRAK-1) in macrophages, monocytes, and dendritic cells, implying negative feedback between adiponectin and proinflammatory cytokines [37].

Table 3: Daily food intake of patients with psoriatic arthritis, according food intake records

| Nutrient            | Mean (SD) | Recommendation (Male/Female) |
|---------------------|-----------|------------------------------|
| Energy (Kcal)       | 1955.9 (730.0) | 2291.7 (649.7) | 1683.5 (681.0) | – |
| Carbohydrate (g)    | 257.9 (48.2) | 259.7 (53.3) | 256.3 (42.1) | 130/130 |
| Protein (g)         | 85.9 (17.4) | 88.9 (17.0) | 83.5 (17.5) | 56/46 |
| Lipid (g)           | 63.0 (17.1) | 59.8 (14.9) | 65.5 (18.3) | – |
| SFA (g)             | 12.0 (5.4) | 11.9 (5.9) | 12.1 (5.0) | – |
| PUFA (g)            | 4.19 (2.72) | 4.14 (2.23) | 4.22 (3.06) | – |
| Cholesterol (mg)    | 222.5 (93.6) | 217.4 (87.6) | 226.5 (98.8) | ** |
| Trans fat (g)       | 0.99 (0.62) | 0.94 (0.24) | 1.03 (0.08) | ** |
| Sugar (g)           | 88.2 (39.5) | 88.7 (51.4) | 87.8 (27.1) | 143/105 |
| Fibers (g)          | 2.38 (0.38) | 2.40 (0.36) | 2.36 (0.39) | 30/ 21 |
| Omega 3 (g)         | 0.37 (0.12) | 0.37 (0.11) | 0.36 (0.13) | 1.5–3.0/ 1.1–2.2 |
| Omega 6 (g)         | 2.14 (1.49) | 2.13 (1.55) | 2.15 (1.45) | 12.7–25.4/ 9.3–18.7 |
| Sodium (mg)         | 2578.6 (784.4) | 2589.5 (925.7) | 2569.6 (657.0) | 1300/1300 |

Results shown as mean and standard deviation (SD). SFA Saturated fatty acid, MUFA monounsaturated fatty acid, PUFA Polynsaturated fatty acid, REq Retinol equivalent, Energy adjusted (2). Recommendation according Estimated Average Requirements (3)

**As low as possible while consuming a nutritionally adequate diet.

Table 4: Biochemical profile of patients with PsA

| Nutrient                        | Mean ± SD |
|---------------------------------|-----------|
| Fasting glucose levels (mg/dL)  | 102.90 ± 34.75 |
| Hemoglobin A1c (%)              | 6.14 ± 1.27 |
| Insulin (U)                     | 16.88 ± 14.08 |
| HOMA-IR                         | 4.59 ± 5.19 |
| Total Cholesterol (mg/dL)       | 196 ± 42.4 |
| LDL-Cholesterol (mg/dL)         | 121.1 ± 37.6 |
| HDL-Cholesterol (mg/dL)         | 47.7 ± 11.36 |
| Triglycerides (mg/dL)           | 138.87 ± 86.39 |

Cutoff points: a) 99 mg/dL. b) > 6%. c) > 30 U. d) > 2.7(4). e) > 200 mg/dL. f) > 130 mg/dL. g) < 40 mg/dL. h) < 50 mg/dL. i) > 150 mg/dL. j) > 180 mg/dL. k) > 200 mg/dL.
Along these lines, it seems that there is a correlation between levels of IL-17, IL-23 and increased weight adipose tissue. Adiposity is an important source of proinflammatory mediators and infiltrating immune cells, representing a possible cellular source of IL-17 and IL-23 in obese patients [37].

Another aspect that is also related to the higher incidence of atherosclerosis in PsA patients than in the general population is related to the increased prevalence of MetS and each of its components, such as obesity, hypertension, diabetes mellitus and dyslipidemia [34].

Regarding food intake, our data showed that patients with PsA had a high consumption of energy, saturated fat and sodium and low intake of ω-6, ω-3 and fiber. It has been well established that inadequate consumption of these nutrients and a hypercaloric diet are associated with hypertension, diabetes, dyslipidemia and metabolic syndrome [38], conditions which are conditions with high prevalence in PsA patients.

The energy consumption and low fiber intake were quite similar to the findings in the Brazilian population [39]. However, the ω-6/ω-3 ratio was lower than recommended by the World Health Organization [40]. This finding is important to mention because higher ω-6/ω-3 ratio is associated with inflammatory disorders and cardiovascular diseases [41]. Although we did not find any correlation with carbohydrate intake, it was observed that patients with severe skin activity had higher intakes of sodium and trans fat and reduced consumption of ω-6 than patients with moderate activity or without skin lesions. These results highlight that these nutrients may be associated with disease activity, as reported by Medeiros and Sittart [16].

Despite this data seems controversial whereas ω-6 fatty acid is commonly associated with increased inflammation, it is relevant to consider that ω-6 does not produce only pro-inflammatory eicosanoids, but also lipid mediators that play an important role in inflammation resolution. Evidently, in healthy human adults, the increased intake of arachidonic acid (ARA) or linolenic acid (LA) does not increase the many of the levels of the inflammatory markers. Thus, the ratio of omega-3 and omega-6 polyunsaturated fatty acids (PUFAs) seems to be the best option to evaluate in the context of inflammation [42].

Furthermore, the body and abdominal (android pattern) adiposity excess in PsA patients was significantly higher than the normative data from the female Brazilian population [20]. Our data demonstrated that BMI was not fully able to identifying excess fat, unlike DXA measurements. Using different methodologies, such as bioimpedance and plethysmography, previous studies also found similar results [4, 43]. Unexpectedly, we found sarcopenia in only 5% of our sample and binomial obesity-sarcopenia was also only evidenced in 3% of PsA patients, in contrast to the findings of another authors [4, 44].

Beyond inadequate food intake and body composition changes, there was a higher frequency of peripheral insulin resistance, as well as a significant relationship with joint activity, highlighting a high prevalence of undiagnosed diabetes/insulin resistance in patients with PsA. First, this finding was attributed to obesity itself. However, merging our data, we suggest that these conditions might share pathophysiological phenomena and are not derived from each other. The PPAR-γ polymorphisms may be a canonical pathway to both disorders [32, 33].

Supporting this hypothesis, we were able to show a significant correlation between psoriatic disease activity and body composition measurements, including the negative association with lean mass and the positive association with fat mass. In addition, we demonstrated a positive association between skin activity and total and LDL-cholesterol serum levels as well as higher trans fat intake and lower ω-6 consumption. Some studies have demonstrated that weight loss is associated with lower disease activity and improved drug response [45]. Altogether, adipose tissue is a

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**Table 5** Joint activity and body composition measurements in PsA patients

| Body Composition                  | DAS28-ESR          |
|-----------------------------------|--------------------|
|                                   | Severe (> 5.1)     | Moderate (3.2–5.1) | Low (2.6–3.2) | Remission (< 2.6) |
| ASMI (kg/m²)                      | 17.74<sup>a</sup>  | 19.54<sup>a</sup>  | 19.57<sup>a</sup> | 23.91<sup>b</sup> |
| Total body fat mass (kg)          | 45.53<sup>a</sup>  | 40.46<sup>ab</sup> | 37.05<sup>ab</sup> | 31.78<sup>b</sup> |
| FMI (kg/m²)                       | 14.45<sup>a</sup>  | 12.53<sup>ab</sup> | 10.22<sup>b</sup>  | 9.69<sup>b</sup>  |

<sup>ASMI</sup> Appendicular skeletal muscle mass index, <sup>FMI</sup> Fat mass index, <sup>ANOVA</sup> Tukey Test, Same letters in the same line ρ > 0.05; different letters in the same line ρ < 0.05

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**Table 6** Associations between skin activity and food intake in patients with PsA

| Food Intake | PASI | Severe (5.0) | Moderate (0.1–4.9) | Remission (0) |
|-------------|------|--------------|--------------------|---------------|
| Trans fat (g) | 1.59<sup>a</sup> | 1.01<sup>b</sup> | 0.91<sup>b</sup>   |               |
| Sodium (mg)   | 2921.82<sup>a</sup> | 2053.96<sup>b</sup> | 2588.02<sup>b</sup>|               |
| Omega 6 (g)   | 1.65<sup>a</sup>   | 3.12<sup>b</sup>   | 2.11<sup>b</sup>   |               |

<sup>ANOVA and Tukey test; same letters in the same line ρ > 0.05; different letters in the same line ρ < 0.05</sup>
relevant player for modulating skin and joint activity in PsA patients.

Excess adipose tissue is closely associated with a higher risk for MetS and is likely related to PsA, according to our data. Some authors have demonstrated that, in early adulthood, each 1-unit increase in BMI the risk of PsA by 5.3% and that obesity increases this risk three times, suggesting that excess body weight can be a predisposing factor to PsA. Obesity in PsA patients seems to be associated with reduced probability of achieving minimal disease activity and increases the cardiovascular risk. In addition, patients with PsA have some limitation in performing exercises, especially patients with moderate or severe disease activity, increasing sedentarism, similar to what was shown by our data [3]. Altogether, these aspects are associated with systemic inflammation, liver steatosis, insulin resistance, lipid oxidation, atherosclerosis and cardiovascular risk.

Hence, the implementation of nonpharmacological strategies such as weight loss (10% of total body weight), regular physical activity, and counseling about protein, carbohydrate, and fat intake could contribute to drug intervention outcomes and the clinical prognosis of these patients. However, prospective observational studies and randomized trials are needed to demonstrate the true impact of body composition changes and dietary style on disease activity in patients with PsA.

Despite the sample size seems a limitation, the number was calculated by using statistic analyses. All patients of the four biggest centers of rheumatology in Sao Paulo state was recruited to participate of this study. Initially, 140 patients were recruited, but thirty-three did not fill the inclusion criteria. We had a total of 97 patients included in this study, same number calculated by the Chi-square test.

This study had some positive points, such as a comprehensive and integrated view regarding the relationships among food intake, inflammation, body composition measurements, and metabolic changes in PsA patients. However, it also has some limitations, including the lack of a control group, the daily variation in food intake and the exclusion of very obese patients (more than 135 kg) due to the DXA weight limit.

We are aware of the limitations of DAS28 in evaluating PsA joint activity. Although there are many tools to measure disease activity in these patients, including PASDAS, DAPSA and CPDAI, none of them have been used in a majority of clinical trials or in epidemiological studies [46]. In addition, the MDA has been recommended by the EULAR (European League Against Rheumatism) and GRAPPA (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis) to better evaluate the skin and joint outcomes in these patients, and because of that, this instrument it was chosen in our study [29, 47]. More recently, Coates et al. demonstrated a close relationship between MDA and other composite indexes (above 0.9), including PASDAS and CPDAI [48].

Conclusion
Thus, patients with active PsA have higher prevalence of obesity and adiposity and excess total and abdominal fat, as well as MetS, insulin resistance and inadequate fat food intake and higher total and LDL-cholesterol serum levels, suggesting a harmful link among lipid and glucose metabolism and joint and skin disease.

Abbreviations
ALM: Appendicular Lean Mass; ARA: Arachidonic Acid; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASI: Body Surface Area; BC: Body Composition; BMI: Body Mass Index; CASPAR: Classification Criteria of Psoriatic Arthritis; CD8: Cytotoxic; CPDAI: Composite Psoriatic Disease Activity Index; CPR: C-reactive Protein; CVD: Cardiovascular disease; DAPSA: Disease Activity Index for Psoriatic Arthritis; DAS28: Disease Activity Score; DRI: Dietary Reference Intake; DXA: Dual X-ray-absorptiometry; ESR: Erythrocyte Sedimentation Rate; EULAR: European League Against Rheumatism; FMII: Fat Mass Index; FR: Food-record; GRAPPA: Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; HAQ: Health Assessment Questionnaire; HDL-C: high-density lipoprotein; HEPA: Health Enhancing Physical Activity; HOMA-IR: Insulin Resistance; hs-CRP: High-Sensitive C-Reactive Protein; IDF: International Diabetes Federation; IL: Interleukin; IPAC: International Physical Activity Questionnaire; IRAK-1: Increasing Interleukin-1 receptor associated kinase 1; ISCD: International Society Clinical Densitometry; LA: Linolenic Acid; LDL: Low-density lipoprotein; MDA: Minimal Disease Activity; MetS: Metabolic Syndrome; NSAIDs: Non-steroidal Anti-inflammatory drugs; NJ: Number of Swollen Joints; NTJ: Number of Tender Joints; PASDAS: Psoriatic Arthritis Disease Activity Score; PASI: Psoriasis Area Severity Index; PPAR: Proliferator-Activator Receptor; Ps: Psoriasis; PsA: Psoriatic Arthritis; PUFAs: Polyunsaturated Fatty Acids; TNF-α: Tumor Necrosis Factor; Treg: Regulatory T cells; WHO: World Health Organization; ω-3: Omega 3; ω-6: Omega 6.

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Authors’ contributions
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Availability of data and materials
Data supporting our findings can be found at Rheumatology Division in Federal University of Sao Paulo (715 Napoleao de Barros St., Vila Clementino, Sao Paulo/ SP, Brazil. ZIP code: 04024–002).

Ethics approval and consent to participate
Patients signed an informed consent form, according to the Declaration of Helsinki, and the study was approved by the Ethics Committee of Research from Federal University of Sao Paulo (CAAE: 00591412.5.0000.5505).

Consent for publication
All patients signed an informed consent for publication.

Competing interests
The authors have no conflict of interest and no competing interest to declare.

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References

1. Sharma A, Gopalakrishnan D, Kumar R, Vijayvergiya R, Dogra S. Metabolic syndrome in psoriatic arthritis patients: a cross-sectional study. Int J Rheum Dis. 2013;16:667–73.
2. Raychaudhuri SK, Chatterjee S, Nguyen C, Kaur M, Jalal I, Raychaudhuri SP. Increased prevalence of the metabolic syndrome in patients with psoriatic arthritis. Metab Syndr Relat Disord. 2010;8:331–4.
3. Russolillo A, Iervolino S, Peluso R, Lupoli R, Di Minno A, Pappone N, Di Minno MN. Obesity and psoriatic arthritis: from pathogenesis to clinical outcome and management. Rheumatology (Oxford). 2013;52:262–7.
4. Pedreira PG, Pinheiro MM, Szejnfeld VL. Bone mineral density and body composition in postmenopausal women with psoriasis and psoriatic arthritis. Arthritis Res Ther. 2011;13:R16.
5. Rocha-Pereira P, Santos-Silva A, Rebelo I, Figueiredo A, Quintanilha A, Teixeira F. Lipidemia and oxidative stress in mild and in severe psoriasis as a risk for cardiovascular disease. Clin Chim Acta. 2001;303:33–9.
6. Azfar RS, Gelfand JM. Psoriasis and metabolic disease: epidemiology and pathophysiology. Curr Opin Rheumatol. 2008;20:416–22.
7. Felix PF, CEC. Obesity status: preventing and managing the global epidemic. In Compêndio de Psoriase. Edited by Elsevier. Rio de Janeiro 2010.
8. Davidovic BB, Sattar N, Prinz J, Puig L, Emery P, Barker JN, van de Kerkhof P, Stahle M, Nestle FO, Girolomoni G. Krueger JG. Psoriasis and cardiovascular inflammatory diseases: potential mechanistic links between skin disease and co-morbid conditions. J Invest Dermatol. 2010;130:1785–96.
9. Gisondi P, Del Giglio M, Di Francesco V, Zamboni M, Girolomoni G. Obesity and the prediction of minimal disease activity: a prospective longitudinal study of patients with psoriasis. Int J Dermatol. 2008;47:1019–23.
10. Prevoo ML, Van ’t Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van riel PL. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum. 1995;38:44–8.
11. Garrett S, Jenkinson T, Kennedy LG, WhiteLock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing spondylitis disease activity index. J Rheumatol. 1994;21:2286–91.
12. Ferraz MB, Oliveira LM, Araujo PM, Atra E, Tugwell P. Cross-cultural reliability of the physical ability dimension of the health assessment questionnaire. J Rheumatol. 1990;17:813–7.
13. Coates LC, Helliwell PS. Validation of minimal disease activity criteria for psoriatic arthritis using interventional trial data. Arthritis Care Res (Hoboken). 2010;62:965–9.
14. Kurte N, Ranul V, Hustvedt BE. Reliability and validity of the international physical activity questionnaire in the Nord-Trndelag health study (HUNT) population of men. BMC Med Res Methodol. 2008;86:63.
15. Pardini R, Matsudo S, Araújo T, Matsudo V, Andrade E, Bragion G, Andrade D, Oliveira L, Figueira-It A, Raso V. Validation of the international physical activity questionnaire (IPAQ version 6); pilot study in Brazilian young adults. Rev Bras Ciên Cncr. 2001;945–51.
16. Sertznig P, Reichrath J. Peroxisome proliferator-activated receptors (PPARs) in dermatology: challenge and promise. Dermatosen docinol. 2011;13:130–5.
17. Lima EA, Lima WMDA, Marques CDL, Duarte ALDP, Pitta IR, Pitta MGR. Peroxisome proliferator-activated receptor agonists (PPARs): a promising prospect in the treatment of psoriasis and psoriatic arthritis. An Bras Dermatol. 2013;88:1029–35.
18. Labitragto M, Bahn-Labitragto A, Kremer J, Reed G, Greenberg JD, Jordan N, Puttermann C, Broder A. Higher rates and clustering of abnormal lipids, obesity, and diabetes mellitus in psoriatic arthritis compared with rheumatoid arthritis. Arthritis Care Res (Hoboken). 2014;66:600–7.
19. Schön MP, Erpenbeck L. The interleukin-23/Interleukin-17 Axis links adaptive and innate immunity in psoriasis. Front Immunol. 2018;9:1323.
20. Lubberts E, The IL-23-IL-17 axis in inflammatory arthritis. Nat Rev Rheumatol. 2011;5:415–29.
21. Granata M, Skarmoutsou E, Trovato C, Rossi GA, Mazzarino MC, D’Amico F, Obesity, type 1 diabetes, and psoriasis: an autoimmune triple Flip. Pathobiology. 2017;84:71–9.
22. Steenburgo T, D’Alba V, Gross JL, Azevedo MJ. Fatores dietéticos e síndrome metabólica. Arq Bras Endocrinol Metabol. 2007;51:425–33.
23. Pinheiro MM, Crionelli RM, Chavez GW, Aquino L, Juzwiak CR, Gainer Pde S, Ferraz MB. Antioxidant intake among Brazilian adults—the Brazilian osteoporosis study (BRAZOS): a cross-sectional study. Nutr J. 2011;10:39.
24. Martin CA, Almeida WV, Ruiz MR, Visentainer JEL, Matshushita M, Souza NE, Visentainer JV. ácidos graxos poliinsaturados ômega-3 e ômega-6: importância e ocorrência em alimentos. Rev Nutr. 2006;19:761–70.
25. Simopoulos AP. The importance of the ratio of omega-6/omega-3 essential fatty acids. Biomed Pharmacother. 2002;56:365–79.
26. Innes JK, Calder PC. Omega-6 fatty acids and inflammation. Prostaglandins Leukot Essent Fatty Acids. 2018;132:418–8.
27. Solís MV, de Melo NS, Macedo ME, Carneiro FP, Sabbag CY, Lancha Junior AH, Frangella VS. Nutritional status and food intake of patients with systemic psoriasis and psoriatic arthritis associated. Einstein (Sao Paulo). 2004;12:1044–52.
28. Dao HH, Do QT, Sakamoto J. Abnormal body composition phenotypes in Vietnamese women with early rheumatoid arthritis. Rheumatology (Oxford). 2011;52:1250–8.
29. Di Minno MN, Peluso R, Iervolino S, Lupoli R, Russolillo A, Tarantino G, Scarpa R. Hepatic steatosis, carotid plaques and achieving MDA in psoriatic
46. Coates LC, Navarro-Coy N, Brown SR, Brown S, McParland L, Collier H, Skinner E, Law J, Moverley A, Pavitt S, et al. The TICOPA protocol (Tight COntrol of psoriatic arthritis): a randomised controlled trial to compare intensive management versus standard care in early psoriatic arthritis. BMC Musculoskeletal Disorders. 2013;14:101.

47. Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. Ann Rheum Dis. 2010;69:48–53.

48. Coates LC, Helliwell PS. Defining low disease activity states in psoriatic arthritis using novel composite disease instruments. J Rheumatol. 2016;43:371–5.

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