Association of visceral adipose tissue with inflammation and functional impairment in women with Sjögren's disease

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Abstract

Objective

This study aimed to evaluate the association between visceral adipose tissue (VAT) levels and inflammation, disease activity, and functional impairment in women with primary Sjögren's disease (SjD).

Methods

We included 100 female patients with SjD from a tertiary care clinic who met the ACR/EULAR 2016 classification criteria. Disease activity was assessed using the ESSDAI and ESSPRI scores, while cumulative damage was evaluated by the SSDDI. Inflammatory markers, synovitis (via ultrasound), and functional disability using the HAQ were measured. Body composition, including VAT, was analysed using dual-energy X-ray absorptiometry. Handgrip strength and physical activity (Baecke questionnaire) were also assessed. Patients were categorised into VAT tertiles, and comparisons were made to healthy controls. Correlations between VAT, disease activity, and synovitis were analysed using multiple regression models.

Results

The patients had a mean age of 50.5±9.3 years, BMI of 28.2±5.6 kg/m², and median disease duration of 8 years. The highest VAT tertile was associated with a higher prevalence of synovitis (75.7% vs. 51.5%; p=0.041), lower handgrip strength (p=0.025), and higher HAQ scores (p<0.001). VAT mass was significantly correlated with obesity (p<0.001), functional disability (p=0.002), and ESSPRI (p=0.01). Postmenopausal patients had significantly higher VAT levels than premenopausal patients (p=0.005). There were no significant correlations between VAT and inflammation.

Conclusion

Elevated VAT levels in SjD are associated with increased disease activity, a higher prevalence of synovitis, and greater functional disability, suggesting that VAT may contribute to the functional impairment observed in SjD.

Key words

Sjögren's disease, adipose tissue, body composition, inflammatory markers, ESSDAI, SSDI

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Introduction

Systemic inflammatory diseases, through the activation of the immune system and inflammatory cytokines, contribute to accelerated atherosclerosis and an increased risk of cardiovascular events (1-5). Visceral adipose tissue (VAT) plays a key role as a major source of inflammatory cytokines, further promoting atherosclerosis and cardiovascular complications (6-9). Body composition assessment using dual-energy x-ray absorptiometry (DXA) is a cost-effective, widely accessible method with low radiation exposure, commonly used to measure VAT (10).

Sjögren's disease (SjD) is a chronic multisystemic autoimmune condition, primarily characterised by *sicca* syndrome, and is more prevalent in women (11). SjD is marked by dysregulation of both the innate and adaptive immune systems, leading to a proinflammatory cytokine profile with elevated levels of interferon-gamma, tumour necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6). As a result of this immune activation, inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and gamma globulins are often elevated (12-14). Moreover, patients with SjD are more likely to have metabolic syndrome and altered adipokine profiles, particularly higher resistin levels, which further exacerbate the inflammatory milieu (12).

Despite these associations, limited research has explored the role of VAT in the context of SjD. Given that VAT is a primary source of inflammatory mediators involved in SjD pathogenesis, its relationship with disease activity, inflammatory markers, and functional impairment remains underexplored. This study aims to fill this gap by stratifying VAT levels in women with SjD and investigating their association with inflammatory markers, disease activity, and functional impairment, thereby seeking to shed light on the potential interplay between metabolic health and autoimmune inflammation in this population.

Methods

This was a *post-hoc* analysis of a study originally designed to investigate the associations between bone erosions, disease activity, damage, and functional disability in patients with SjD (15). This cross-sectional study included patients undergoing regular follow-up care at the Sjögren's Disease outpatient clinic of the Rheumatology Service at the Hospital das Clinicas of the School of Medicine of the University of São Paulo, Brazil, a tertiary public hospital of high complexity. The study was approved by the local ethics committee (#57726522.6.0000.0068), and all patients provided written informed consent before participation.

Participants

Patients regularly followed at the outpatient clinic were evaluated. The study included patients aged 18 to 65 years who met the classification criteria for SjD established by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) (16). Exclusion criteria consisted of patients with osteoporosis or other osteometabolic diseases, those receiving medications for osteoporosis treatment, individuals with other autoimmune diseases, and those with a history of cancer. Control participants were enrolled in a 1:2 ratio, resulting in 200 healthy individuals matched for age, weight, and sex, who served as a reference group for VAT levels. Cardiovascular risk factors were also reported for the control group.

Outcomes

- Clinical and laboratory assessments

Demographic and clinical data were collected through patient interviews and chart reviews, including age, disease duration, self-reported race/ethnicity (categorised into four fixed groups: White, Black, Asian, and Pardo, the latter referring to individuals of mixed ethnicity), comorbidities, and SjD treatment information. Disease activity was assessed using the standardised EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) (17). The primary symptoms of SjD, including ocular and oral dryness, fatigue, and pain, were evaluated using the EULAR Sjögren's Syndrome Reported Index (ESSPRI) (18). In addition, damage index was as-

sessed using the Sjögren's Syndrome Disease Damage Index (SSDDI) (19). These assessments were performed by the same trained physician.

Inflammation-related markers included C-reactive protein (CRP), measured using the immunoturbidimetric method, with levels above 5 mg/L considered high. Erythrocyte sedimentation rate (ESR) was determined using the Westergren method, with normal reference values in the first hour as follows: <15 mm for men and <20 mm for women. IL-1b and IL-6 levels (pg/mL) were assessed by Luminex® multiple analyte profiling.

Disease-specific parameters, assessed as part of routine care, consisted of protein electrophoresis, immunoglobulin G (IgG), rheumatoid factor (RF), anti-citrullinated peptide antibody (anti-CCP), indirect immunofluorescence assay on HEp-2 cells (HEp-2 IFA), anti-Ro/SS-A, and anti-La/SS-B.

Health-related markers comprised glucose, glycated haemoglobin, cholesterol, HDL-cholesterol, LDL-cholesterol, and triglycerides.

- Body composition

All patients underwent total body densitometry (GE Lunar iDXA, GE Healthcare, Bucks, United Kingdom). Fat mass parameters for the total body (except the head) and by region (arms, legs, and trunk) were obtained using APEX Software version 4.0.2 (Bedford, MA, USA). Height (in cm) and weight (in kg) measurements were performed on all individuals by standardised protocols, standing, and wearing light clothes without shoes. Body mass index (BMI) was calculated as weight (in kg) divided by height (in m^2). The fat mass parameters evaluated were total fat mass (FM), body fat percentage (adiposity), and visceral adipose tissue (VAT in g and cm^3) (20, 21).

- Assessment of synovitis

Joint assessment was performed using high-resolution ultrasound of the hands and wrists, focusing on 36 joints and 36 tendon areas. This objective assessment designed to evaluate disease activity and synovitis. The equipment used was the MyLab 70 XVG (Esaote SPA, Genova, Italy) with a high-frequency linear transducer (6–18 MHz), Power Doppler frequency of 9.1–11.1 MHz, and a pulse repetition frequency of 750 Hz, according to the EULAR recommendations for musculoskeletal ultrasound in rheumatology (22). The ultrasound findings were interpreted using OMERACT definitions, focusing on key parameters of joint inflammation including synovitis, and tenosynovitis (23). The ultrasound was performed by the same experienced ultrasonographer.

- Assessment of menopausal status

Menopausal status was self-reported based on the participant's menstrual history, including the number of peri-

Table I. Demographic and clinical data of the female patients with Sjogrën's disease included in the study.

Characteristics	Patients with SjD (n=100)
Age, years	50.5 ± 9.3
BMI, kg/m^2	28.2 ± 5.6
Self-reported skin colour, n (%)	
White	48 (48)
Black	15 (15)
Disease duration, years	8 [5-14.8]
Disease indices	
ESSDAI	1 [0 - 3]
ESSPRI	5.5 [3.4 - 7.0]
SSDDI	3 [2 – 4.8]
HAQ	0.375 [0.0 – 0.75]
Physical activity (Baecke)	7.5 [6.4 – 8.4]
Non-dominant handgrip, kg.f	17.2 ± 6.6
Comorbidities, n (%)	
Obesity	32 (32)
Hypertension	18 (18)
Type 2 diabetes	6 (6)
Smoking, n (%)	22 (22)
Menopause	49 (49)
Hormonal therapy	0 (0)
Treatment history, n (%)	
Hydroxychloroquine	88 (88)
Synthetic disease-modifying antirheumatic drugs	63 (63)
Oral glucocorticoid	64 (64)
Current usage, n (%)	33 (33)
Current average dose, prednisone mg	8.39 ± 5.42
Cumulative dose, prednisone mg	3,540 [0 – 12,265]
Hep-2 IFA, n(%)	94 (94)
Anti-Ro/SS-A, n(%)	91 (91)
Anti-La/SS-B, n(%)	42 (42)
Positive RF, n(%)	59 (59)
Complement C3, mg/dL	122.2 ± 23.9
Complement C4, mg/dL	22.6 ± 8.3
Fasting glucose, mg/dL	91.6 ± 21.5
Glycated haemoglobin, %	5.5 ± 0.7
Cholesterol, mg/dL	182.5 ± 36.4
HDL-cholesterol, mg/dL	52.6 ± 13.8
LDL-cholesterol, mg/dL	109.1 ± 30.3
Triglycerides, mg/dL	108.2 ± 74.4
Gamma globulin electrophoresis, g/dL	1.51± 0.42
CRP, mg/L	3.5 ± 4.3
ESR, mm first hour	21.3 ± 19.4
IL-1b, pg/mL	53.4 [15.2 – 198.2]
IL-6, pg/mL	10.3 [3.2 – 45.2]
VAT, cm^3	947.4 ± 661.4
VAT, g	882.6 ± 629.8

Data are expressed as mean ± SD, median [interquartile range], and No. of patients (%).
SjD: Sjögren's disease; BMI: body mass index; ESSDAI: EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI: EULAR Sjögren's Syndrome Reported Index; SSDDI: Sjögren's Syndrome Disease Damage Index; HAQ: Health Assessment Questionnaire; RF: Rheumatoid factor; HDL-cholesterol: high-density lipoproteins; LDL-cholesterol: low-density lipoproteins; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

ods in the last 12 months and the age at which menstruation ceased. Postmenopausal status was defined as the absence of menstruation in the last 12 months.

- Assessment of physical activity

Physical activity was assessed using the standardised Baecke score (24), which assesses habitual physical activity over the past 12 months. This questionnaire consists of 16 items covering different aspects of physical activity, including occupational activity, physical exercise, leisure time activities, and transportation.

- Assessment of functional disability

Functional disability was assessed using the standardised Health Assessment Questionnaire (HAQ), which includes functional capacity and pain level (25). The questionnaire was completed based on the patient's experiences during the past week prior to the interview.

- Evaluation of handgrip strength

Handgrip strength of the dominant and non-dominant hand was assessed using the Saehan SH5001 Hydraulic Hand Dynamometer (Changwon-si, Gyeongsangnam-do 51342, South Korea), measured in kg.f. The test was performed with the patient seated and the elbow flexed at 90° relative to the torso. The average of three measurements was used for each hand.

Statistical analysis

Data are presented as mean ± SD or median [IQR], and as percentages for categorical variables. Patients with SjD were compared with healthy controls using either Student's t-test or the Mann-Whitney U-test, depending on the results of the normality test. Parameters that showed correlations with VAT mass but without high collinearity, as well as parameters for which VAT mass was statistically different between categories in bivariate analyses, were selected for inclusion in the multivariable model using multiple linear regression. Stepwise backward selection method was used to determine the final model variables, with entry and exit criteria set at 5%. The frequency of synovitis across tertiles of VAT mass in SjD patients was assessed using the chi-square test, and the correlation between VAT mass and synovitis was assessed using the point-biserial correlation coefficient. All tests were two-sided, and the significance level was set at α=0.05. Statistical analyses were performed using R version 4.3.1 (2023-06-16) and IBM SPSS Statistics for Windows, version 22.0.

Table II. Body composition data measured by total body densitometry in patients with SjD and healthy controls.

Body composition	Patients with SjD (n=100)	Healthy controls* (n=200)	*p*
Total fat, %	41.8 ± 7.4	36.0 ± 6.0	**<0.001**
Lean mass, kg	39.1 ± 5.8	41.6 ± 5	**<0.001**
Fat mass, kg	29.5 ± 10.8	25.1 ± 7	**0.001**
VAT, cm^3	947.4 ± 661.4	592.7 ± 328.0	**<0.001**
VAT, g	882.6 ± 629.8	544.6 ± 279.2	**<0.001**

Data are expressed as mean ± standard-deviation.
SjD: Sjögren's disease; VAT: visceral adipose tissue. *Healthy controls age-, sex-, and BMI-matched.

Table III. Summary of multivariate linear regression results for predictors of VAT mass.

Variable	beta coefficient	95% confidence interval	*p*
Mean ESSPRI	47.8	11.3-84.3	<0.001
Postmenopausal	213.3	21.0-405.6	0.033
BMI, kg/m^2	76.2	59.1-93.3	<0.001

This model has a R^2 = 0.577. VAT: visceral adipose tissue; ESSPRI: EULAR Sjögren's Syndrome Reported Index; BMI: body mass index.

Results

Patients

Of 378 patients assessed for eligibility, 100 patients were included in the study. The mean age was 50.5±9.3 years, and the mean BMI was 28.2±5.6 kg/m^2. The majority of patients self-identified as White (48%). The median disease duration was 8 [5–14.8] years. The median disease-related scores were ESSDAI: 1 [0–3], ESSPRI: 5.3 [3.4–7.0], and SSDDI: 3 [2–4.8]. Functional disability had a median score of 0.375 [0.0–0.8], while physical activity had a median value of 7.5 [6.4–8.4].

Regarding treatment, 88% of patients were receiving hydroxychloroquine, 63% were on synthetic immunosuppressants, 14% were treated with rituximab, and 33% were currently taking prednisone, with a cumulative dose of 3,540 mg [0–12, 265 mg] (Table I). According to the ESSDAI, synovitis within the joint domain was identified in 14 patients (14%), with 3 classified as having moderate arthritis and none with severe activity. Ultrasound assessment revealed synovitis in 58 patients (58%), distributed as 45 cases of grade 1, 29 of grade 2, and 9 of grade 3 synovitis. Additionally, 43 patients (43%) showed joint power Doppler activity, predominantly grade 1 (87.6%). Regarding other ESSDAI domains, lymphadenopathy was observed in 5 patients, glandular involvement in 6, cutaneous manifestations in 2, respiratory involvement in 3, renal involvement in 2, peripheral nervous system involvement in 1, and no cases of central nervous system or muscle involvement. Haematological abnormalities were present in 13 patients, and biological domain activity was present in 33 patients. No patients had a history of lymphomatous transformation.

In the control group, nearly half (49.3%) of women were postmenopausal. Only a small proportion had comorbidities, including type 2 diabetes mellitus (1.2%) and hypertension (2.5%). Regarding lifestyle factors, 13.8% reported alcohol consumption, and 22% were smokers.

Body composition

VAT levels were significantly higher in patients with SjD compared to the control group. VAT volume in cm^3

Table IV. Demographic and clinical data of the patients according to menopause status.

Characteristics	Premenopausal SjD patients (n = 51)	Postmenopausal SjD patients (n = 49)	*p*
Age, years	43.9 ± 7.2	57.4 ± 5.4	**<0.001**
BMI, kg/m^2	27.4 ± 5.2	29.0 ± 5.9	0.139
Self-reported skin color, n (%)			0.370
White	21 (41.2)	27 (55.1)	
Black	9 (17.6)	6 (12.2)	
Disease duration, years	8.4 ± 5.2	12.1 ± 8.3	**0.009**
Disease indices			
ESSDAI	2.8 ± 4.1	1.9 ± 3.8	0.296
ESSPRI	5.3 ± 2.5	5.3 ± 2.7	0.941
SSDDI	2.5 ± 1.8	3.9 ± 2.0	**<0.001**
HAQ	0.4 ± 0.5	0.6 ± 0.6	0.083
HAQ > 1	5 (10.0)	11 (22.4)	0.092
Physical activity (Baecke)	7.3 ± 1.4	7.4 ± 1.6	0.616
Non-dominant handgrip, kg.f	17.7 ± 6.1	16.7 ± 7.0	0.448
Comorbidities, n (%)			
Obesity	14 (27.5)	18 (36.7)	0.320
Hypertension	6 (11.1)	12 (23.1)	0.167
Type 2 diabetes	2 (3.9)	4 (8.2)	0.432
Treatment history, n (%)			
Hydroxychloroquine	49 (90.7)	45 (86.5)	0.707
Synthetic disease-modifying antirheumatic drugs	37 (68.5)	31 (59.6)	0.451
Oral glucocorticoid			
Current usage, n (%)	24 (47.1)	9 (18.4)	**0.002**
Current average dose, prednisone mg	8.8 ± 5.3	7.5 ± 5.9	0.569
Cumulative dose, prednisone mg	8019.2 ± 9530.6	7965.7 ± 12987.8	0.981
Fasting glucose, mg/dL	86.0 ± 15.0	96.9 ± 25.2	**0.019**
Glycated haemoglobin, %	5.3 ± 0.5	5.7 ± 0.8	**0.016**
Cholesterol, mg/dL	171.3 ± 34.7	193.8 ± 34.9	**0.002**
HDL-cholesterol, mg/dL	51.3 ± 13.3	54.0 ± 14.2	0.332
LDL-cholesterol, mg/dL	100.2 ± 29.2	117.9 ± 29.0	**0.004**
Triglycerides, mg/dL	102.3 ± 90.8	114.2 ± 53.6	0.444
CRP, mg/L	4.1 ± 5.3	2.9 ± 2.8	0.156
ESR, mm first hour	22.7 ± 20.5	19.9 ± 18.2	0.478
IL-1b, pg/mL	64.6 [15.2 – 198.9]	38.0 [14.3 – 204.5]	0.462
IL-6, pg/mL	11.6 [2.6 – 45.2]	9.6 [3.3 – 44.9]	0.790
VAT, cm^3	768.3 ± 550.6	1133.9 ± 718.9	**0.005**
VAT, g	725.1 ± 519.3	1046.6 ± 695.2	**0.011**

Data are expressed as mean ± SD and No. of patients (%).
SjD: Sjögren's disease; BMI: body mass index; ESSDAI: EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI: EULAR Sjögren's Syndrome Reported Index; SSDDI: Sjögren's Syndrome Disease Damage Index; HAQ: Health Assessment Questionnaire; HDL-cholesterol: high-density lipoproteins; LDL-cholesterol: low-density lipoproteins; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

was 947.4±661.4 in the SjD group and 592.7±328.0 in the control group (p<0.001), while VAT mass in grams was 882.6±629.8 *versus* 544.6±279.2 (p<0.001). Patients with SjD exhibited a higher total body fat percentage (41.8±7.4% *vs*. 36.0±6.0%, p<0.001), lower lean mass (39.1±5.8 kg *vs*. 41.6±5.0 kg, p<0.001), and higher fat mass (29.5±10.8 kg *vs*. 25.1±7.0 kg, p=0.001) compared to healthy controls (Table II).

Associations of VAT levels with disease activity, clinical and laboratory parameters

Linear correlation analysis was performed between variables of interest and VAT mass values in the group of women with SjD. A significant positive correlation was found between VAT mass and several variables: Age (r=0.337, p=0.001), BMI (r=0.743, p<0.001), ESSPRI (r=0.261, p=0.009), HAQ (r=0.478, p<0.001), fasting glucose (r=0.446, p<0.001), glycated haemoglobin (r=0.380, p=0.001), total cholesterol (r=0.213, p=0.039), LDL-cholesterol (r=0.246, p=0.017), and triglycerides (r=0.469, p<0.001). In contrast, non-dominant handgrip strength (r=-0.256, p=0.010) and HDL-cholesterol levels (r=-0.213, p=0.039) showed a significant negative correlation with VAT mass. The mean VAT mass was significantly higher in patients with a HAQ score >1 (1333.8±619.2 g *vs*. 800.4±600.2 g, p=0.002) and in patients with obesity (p<0.001). However, no significant differences in VAT mass were observed based on disease duration, physical activity score, or cumulative glucocorticoid dose.

In the multiple regression model, postmenopausal patients had a mean 213.3 g higher VAT mass than premenopausal patients, independent of other assessed characteristics. For each 1 kg/m^2 increase in BMI, VAT mass increased by 76.2 g, and for each 1-unit increase in the ESSPRI score, VAT mass increased by 47.8 g. The adjusted model explained 57.7% of the variability in VAT mass (Table III).

Associations of VAT levels with synovitis

The prevalence of synovitis, assessed by ultrasound, was significantly higher in patients in the upper VAT tertile compared to those in the lower (75.7% *vs*. 51.5%; p=0.041) and middle tertiles (75.7% *vs*. 47.0%; p=0.016). A significant positive correlation was also observed between VAT levels and the presence of synovitis (rpb=0.27; p=0.006).

Sub-analysis of menopausal status on clinical and laboratory parameters and VAT levels

A sub-analysis comparing menopausal status (Table IV) showed that postmenopausal patients were older (57.4±5.4 years *vs*. 43.9±7.2 years, p<0.001), had a longer disease duration (12.1±8.3 years *vs*. 8.4±5.2 years, p=0.009), higher SSDDI scores (3.9±2.0 *vs*. 2.5±1.8, p<0.001), fasting glucose levels (96.9±25.2 mg/dL *vs*. 86.0±15.0 mg/dL, p=0.019), and glycated haemoglobin (5.7±0.8% *vs*. 5.3±0.5%, p=0.016) compared to premenopausal patients. VAT volume (1133.9±718.9 cm^3 *vs*. 768.3±550.6 cm^3, p=0.005), mass (1046.6±695.2 g *vs*. 725.1±519.3 g, p=0.011), total cholesterol (193.8±34.9 mg/dL *vs*. 171.3±34.7 mg/dL, p=0.002), and LDL-cholesterol (117.9±29.0 mg/dL *vs*. 100.2±29.2 mg/dL, p=0.004) were significantly increased in postmenopausal patients compared to premenopausal patients. Interestingly, the current use of oral glucocorticoids was more common in premenopausal patients (47.1% *vs*. 18.4%, p=0.002).

Discussion

This study included a large cohort of patients with SjD and a long median disease duration. It emphasises the use of standardised assessments of disease activity and functional disability, including the ESSDAI, ESSPRI, SSDDI, HAQ, joint ultrasound, and handgrip strength. Compared to age-, sex-, and BMI-matched healthy individuals, patients with SjD had higher levels of VAT. Interestingly, VAT was found to be associated with disease activity scores, inflammatory markers, synovitis, reduced handgrip strength, and increased functional disability. To our knowledge, this is the first study to demonstrate these findings.

VAT is easy to measure and can be assessed by bioimpedance, densitometry, computed tomography, and magnetic resonance imaging (10). Recent studies have shown an association of VAT with cardiovascular disease (26) and the development of pancreatic cancer and squamous cell carcinoma of the lung (27). VAT is also associated with an increased risk of mortality (28).

A study comparing SjD patients with healthy controls have found higher levels of IL-1β, IL-6, and BAFF in patients (12). This study also showed that SjD patients with metabolic syndrome had higher levels of leptin, insulin, IL-1β, IL-6, and BAFF, suggesting that patients with metabolic syndrome have more inflammation (12). SjD has been identified as an independent risk factor for cardiovascular disease, highlighting its role as a novel model to study atherosclerosis in autoimmune diseases (26). Patients with SjD exhibit a higher prevalence of traditional cardiovascular risk factors such as hypertension and dyslipidaemia, which predispose to endothelial dysfunction and premature atherosclerosis (29, 30). However, the disease-specific mechanisms underlying this process remain poorly understood.

A study of patients with granulomatosis with polyangiitis, a systemic vasculitis, showed that patients had higher VAT values compared to healthy controls (31). Our analysis showed significantly higher VAT levels in patients with SjD compared to healthy controls. Both VAT, measured in cm^3 and grams, as well as fat mass and total body fat percentage, were significantly increased in the patient group, while lean mass was reduced. These differences may be attributed to the disease itself, glucocorticoid use, or decreased physical activity. However, VAT levels were not associated with disease duration, physical activity or cumulative glucocorticoid dose, suggesting that these factors may not directly influence VAT levels in this cohort. This finding contrasts with a study on patients with ANCA-associated vasculitis, which showed that higher glucocorticoid doses were associated with increased disease activity and could potentially impact VAT levels (32). The lack of association between VAT and cumulative glucocorticoid dose in our study may be explained by the relatively low disease activity observed in our cohort, which likely required lower cumulative glucocorticoid doses, thus reducing the potential impact of glucocorticoids on VAT accumulation.

While there were no significant differences in disease activity or damage across VAT tertiles, a notable difference was observed in the ESSPRI score, indicating that higher VAT is associated with increased symptom severity. These associations suggest that VAT may influence specific symptom domains in SjD, possibly through inflammatory or metabolic pathways. The prevalence of synovitis was also significantly higher in patients with elevated VAT, and a significant correlation between VAT and synovitis was observed. This association highlights the role of VAT in the inflammatory process and its potential impact on joint involvement. Functional capacity assessments revealed that patients with higher VAT had lower handgrip strength and higher HAQ scores, indicating greater functional impairment. Notably, patients with HAQ>1, reflecting functional disability, had significantly higher VAT levels compared to patients with HAQ≤1. This highlights the potential impact of VAT on functional disability in SjD patients. Indeed, obese female patients with rheumatoid arthritis tend to have higher CRP levels and greater disease activity compared to non-obese patients with rheumatoid arthritis (33). Similarly, in patients with granulomatosis with polyangiitis, a systemic vasculitis, those with higher VAT levels have greater disease activity and higher inflammatory markers (31). In addition, patients with radiographic axial spondyloarthritis, even when receiving immunobiologic therapy, showed that higher VAT correlates with greater disease activity, reduced mobility, and functional disability (31). In patients with enteropathic arthritis, higher VAT levels were associated with lower glucocorticoid-free remission and en-

doscopic remission (35). Studies in patients with cutaneous psoriasis and psoriatic arthritis show that higher VAT levels are associated with greater functional disability according to the HAQ and higher disease activity (36).

This study has several limitations that should be considered. First, its cross-sectional design precludes the establishment of causal relationships between VAT levels and disease activity or functional impairment. Additionally, patient inclusion was limited to a pre-existing larger project, which excluded individuals with osteoporosis and those of older age, potentially reducing the generalizability of our findings. The lack of dietary assessments is another notable limitation, as dietary habits can significantly influence body composition and inflammation. Furthermore, although our analysis included standardized assessments of disease activity and functional capacity, other potential confounders, such as physical activity levels beyond self-reported data and specific metabolic parameters, were not thoroughly explored. Future longitudinal studies with broader inclusion criteria and more comprehensive metabolic and lifestyle evaluations are needed to better understand the impact of VAT in SjD. Despite these limitations, our study provides valuable insights into the relationship between VAT and SjD. We demonstrate a significant association between VAT levels and ESSPRI, inflammatory biomarkers, and functional capacity, reinforcing the inflammatory role of VAT in this population. These findings underscore the potential relevance of VAT as a therapeutic target in SjD, warranting further investigation into its pathophysiological mechanisms and clinical implications.

Conclusions

In women with SjD, higher levels of VAT are associated with increased disease activity, a greater prevalence of synovitis, and functional disability. Menopause may be a contributing factor to elevated VAT levels. These findings reinforce the clinical perspective that VAT may play a detrimental role in disease outcomes in SjD. As such, evaluating VAT levels could serve as a valuable component in managing and potentially targeting therapeutic strategies for SjD.

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The authors used a large language model, such as ChatGPT, exclusively for improving text fluency and correcting grammatical errors.

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