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ORIGINAL ARTICLE

Altered body composition and increased visceral adipose tissue in premenopausal and late postmenopausal patients with SLE

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Abstract

Objective Visceral adipose tissue (VAT) is becoming a recognized cardiovascular (CV) risk factor. This study aimed to evaluate body composition, especially VAT, in systemic lupus erythematosus (SLE) and to explore the association between VAT and SLE disease-related factors.

Method Ninety-eight inpatients with SLE and 108 age- and body mass index (BMI)–matched healthy controls were included. Demographic and clinical parameters were recorded. The VAT was measured by dual-energy x-ray absorptiometry.

Result The mean age and disease duration of patients were 46.4 ± 13.0 years and 8.0 ± 7.0 years, respectively. Patients with SLE had higher VAT volume ($p = 0.0015$) and mass ($p = 0.0017$) than controls, especially in premenopausal and postmenopausal groups. The subanalysis of subjects with BMI less than 25 kg/m^2 indicated that patients had lower lean mass ($p = 0.0005$), fat-free mass ($p = 0.0005$), and fat-free mass index ($p = 0.0001$), but increased adiposity distribution than controls, including VAT volume and mass. However, overweight/obese patients had similar body composition with controls. The VAT volume correlated with BMI, age, menopausal status, hypertension, uric acid, creatinine, non-high-density lipoprotein cholesterol, and triglyceride in both groups. In the patient group, the VAT volume correlated with disease duration, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR-DI), and low serum complement, but not with SLEDAI and glucocorticoid dose.

Conclusion This study suggested that SLE patients had some traditional CV risk factors such as altered body composition and increased VAT. The higher VAT in patients with SLE was associated with traditional cardiometabolic risks, which may contribute to CV events in SLE populations.

Key Points

- *Patients with SLE had increased VAT volume and mass than controls.*
- *The VAT volume correlated with traditional cardiometabolic risk factors.*
- *In SLE patient group, the VAT volume correlated with disease duration, SLICC/ACR-DI, and low serum complementC3/C4, but not with SLEDAI and glucocorticoid dose.*

Keywords Body composition · Cardiovascular risk factors · DXA · Systemic lupus erythematosus · Visceral adipose tissue

Introduction

Systemic lupus erythematosus (SLE) is one of the most complicated autoimmune diseases, and it can affect any organ and present with diverse phenotypes. It affects women more frequently than men at a ratio of nearly 9 to 1. The prognosis of SLE patients has markedly improved due to the introduction of immunosuppressive regimens over the last decades. The 5-year survival rate of SLE has exceeded 90% in recent years [1].

However, as life expectancy increases, subsequent complications such as cardiovascular disease (CVD) are becoming a more and more serious clinical problem

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[1]. Manzi et al. [2] demonstrated that women with SLE (most of them were Caucasian, the rest were African American, American Indian, Asian American, and Eastern Indian.) in the 35–44-year age group were over 50 times more likely to have a myocardial infarction (MI) than age-matched controls. Another southern Sweden prospective study found that the incidence of MI in patients with SLE was nine times higher than that in a control population [3]. Recently, a Danish nationwide study showed that patients with SLE without lupus nephritis (LN) were more than twice as likely to have a MI as the control subjects, and the hazard ratio was 18.3 in patients with LN [4]. The mechanism of CVD in SLE is multifactorial. Traditional CV risk factors, such as age, hypertension, dyslipidemia, and smoking, cannot fully explain the increased CVD occurrence in SLE [5–7], and disease-related risk factors, such as disease activity, cumulative damage, renal involvement, inflammatory mediators, and medications, have been implicated in increasing the CV risk in SLE [8]. Recently, Seguro et al. showed that SLE was associated with altered adiposity distribution and increased visceral adipose tissues (VAT) in premenopausal SLE patients, and that VAT was correlated with traditional risk factors for CVD [9].

Prospective studies identifying risk factors for incident coronary heart disease had shown that VAT was a predictive factor of coronary heart disease independently of age and body mass index (BMI) [10]. The possible mechanism was justified by more and more studies, which related it to highly lipolytic visceral deposits releasing fatty acids into the portal vein that subsequently travel to the liver. Here, they cause hepatic insulin resistance and lead to hyperinsulinemia and accelerated synthesis of glucose by the liver [11]. Moreover, potential protective factors for CVD and diabetes, such as leptin, adiponectin, and peroxisome proliferator-activated receptor-gamma, were expressed at lower levels in visceral than in subcutaneous adipose tissue [12]. Thus, an assessment of VAT may be necessary for the evaluation of CVD risk in SLE patients.

Unfortunately, there were only two studies examining VAT and its determinants among patients with SLE [9, 13], and the changes of VAT in postmenopausal patients with SLE and in Chinese patients have never been reported. Since the prevalence and disease activity of SLE were found to have geographical variations, SLE patients in Asia may be different from those on other continents. Our study aimed to examine body composition, especially VAT, in a population of Chinese women with SLE, and compare it with age-, sex-, and BMI-matched controls, and then to explore the association between VAT and other clinical parameters in patients with SLE.

Subjects and methods

Subjects recruitment

Patient group

Ninety-eight women who fulfilled the 1997 revised American College of Rheumatology classification criteria for SLE were enrolled from the Department of Rheumatology, the First Affiliated Hospital of Jinan University since October 2016. Our research was approved by the Medical Ethics Committee of the First Affiliated Hospital of Jinan University. Patients with accompanying rheumatoid arthritis, mixed connective tissue disease, thyroid diseases, malabsorption, and other chronic inflammatory diseases were excluded. Pregnant and breastfeeding women were also excluded. Data including demographic, anthropometric, and clinical parameters were assessed by medical records review. The latest 5-year cumulative corticosteroid dose was calculated from medical records. The disease activity and severity were assessed using the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR-DI) at the time of recruitment.

Healthy controls

The healthy control group consisted of 108 subjects recruited from hospital staff matched to the patient group by age, gender, and BMI. The same exclusion criteria were used for both groups. Their medical history and laboratory results were reassessed to exclude autoimmune, thyroid diseases, and other metabolic disorders.

Menopausal status

Menopausal status was assessed via a self-reported questionnaire including menstrual bleeding and its regularity. Premenopause was identified as menses in the 12 months prior to study entry without change in regularity [14, 15]. Late postmenopause was defined as no menstrual period for 5 years or more [16, 17]. From the beginning of women's loss of menstrual cycle until the fifth year after no menstruation, this period is collectively referred to as perimenopause. Because of the complex changes in endocrine and body composition during this period, it is too difficult to further divide into subgroups.

Laboratory evaluation

All the tests were undertaken in a clinical laboratory and performed according to standard protocol. Laboratory evaluation

data included complete blood count, urinalysis, fasting plasma glucose, serum creatinine, uric acid, high-sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate (ESR), lipid profile (i.e., triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C)), complement fragments C3 and C4, anti-nuclear antibody (ANA) (including anti-dsDNA), and anti-extractable nuclear antigen (ENA) profile (i.e., anti-Sm, anti-La, and anti-Ro).

Dual-energy X-ray absorptiometry analysis

The anthropometric and dual-energy X-ray absorptiometry (DXA) measurements were obtained for patients during the same visit. Weight was measured using a platform digital scale with a precision of 0.1 kg, and height was recorded with a stadiometer to the nearest 0.1 cm. BMI was calculated as body mass (weight) divided by height squared (kg/m^2). Body composition including fat mass (FM), lean mass (LM), bone mineral content (BMC), VAT volume, and VAT mass was measured with a Lunar iDXA bone densitometer (GE Healthcare, Madison, WI), and data were analyzed using enCORE software (ver. 16.0, standard-array mode). Indices of body fat distribution including android (abdominal) fat (%), gynoid (peripheral depot) fat (%), and android/gynoid fat were also measured using the software. From these measurements, the following derivative values were calculated: fat mass index (FMI, total fat mass/height [2]) and fat-free mass (FFM, the sum of LM and BMC). The precision error (% CV) was less than 2% for total LM and total FM and less than 3% for regional (trunk, appendicular, android, gynoid) LM and FM, as determined by duplicate scans with repositioning between each measurement among 30 volunteer subjects. A daily quality assurance scan was conducted by scanning an aluminum spine phantom according to the manufacturer's instructions. The same well-trained technologist performed all DXA measurements throughout the study and was blind to the clinical situation of the subjects (Fig. 1).

Statistical analysis

The descriptive results are expressed as either mean (standard deviation (SD)) or median (interquartile range), depending on the data distribution. Qualitative data were shown as percentages. Patients and controls were compared using the unpaired *t* test or chi-square test. Subgroup analysis was performed by the menopause state and VAT mass distribution. The associations between body composition and disease or treatment-related parameters among patients were tested using Spearmen correlations. A $p < 0.05$ indicated a statistically significant difference. All data analyses were performed by STATA 12.0.

Results

Clinical and demographic characteristics

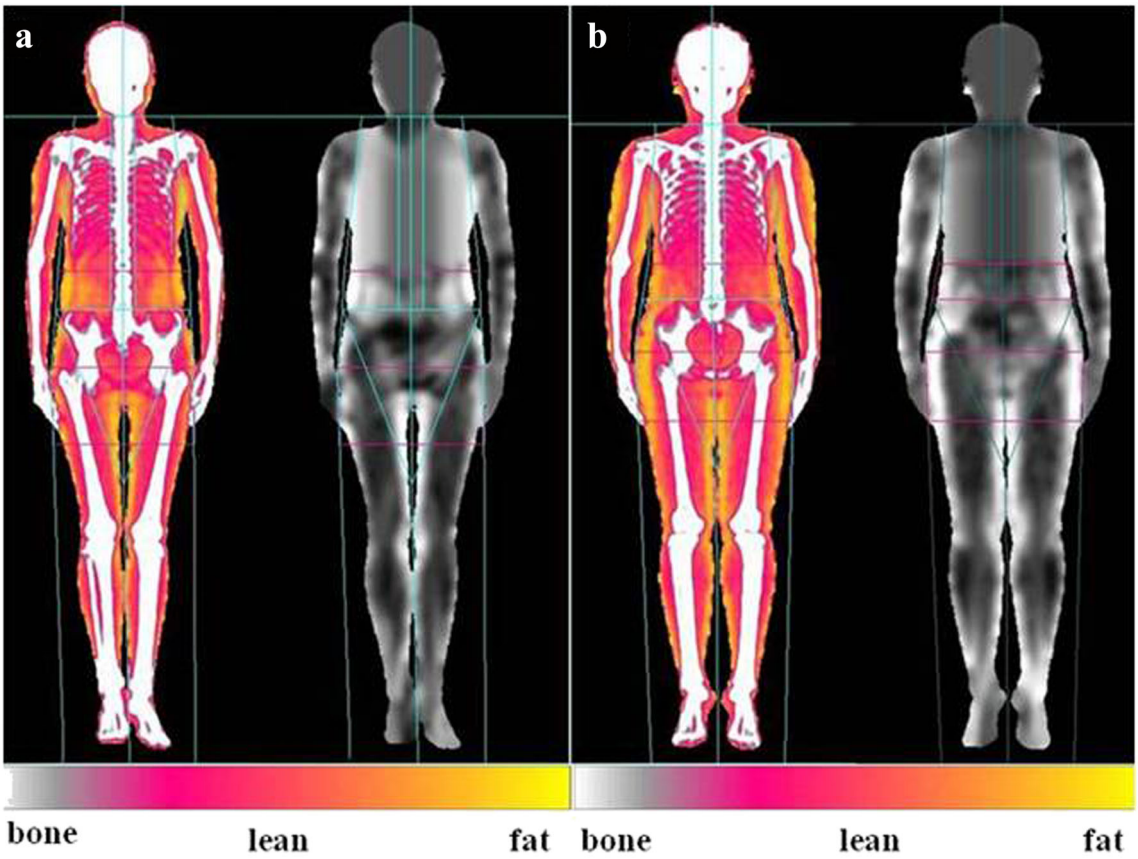
Demographic and clinical characteristics of the patients and healthy controls are shown in Table 1. No significant difference was noticed between groups regarding age, menopausal status, height, weight, and BMI. With respect to complication, 28.57% of patients with SLE had hypertension ($n = 28$), 4.08% ($n = 4$) diabetes, 2.04% ($n = 2$) coronary heart disease, and 8.16% ($n = 8$) cerebrovascular disease. The prevalence of dyslipidemia was not different between the patients with SLE and controls (21.4% vs. 30.8%, $p = 0.132$). The mean disease duration of all the patients was 8.0 ± 7.0 years. The average SLEDAI-2K and SLICC/ACR-DI scores were 2.5 ± 4.0 and 0.6 ± 1.0, respectively. The mainly affected organ systems were (in descending order of prevalence) hematologic, musculoskeletal, mucocutaneous, and renal. Most of the patients were currently receiving systemic glucocorticoid ($n = 79$, average prednisone dose 6.9 ± 8.3 mg) and immunosuppressant therapy ($n = 82$, mainly cyclophosphamide, mycophenolate mofetil, and hydroxychloroquine). Only 9 patients in SLE groups used statins because they had cardiovascular or/and cerebrovascular diseases while none of the controls used anti-dyslipidemic agents.

Laboratory characteristics

The laboratory findings of the patients and healthy controls are shown in Table 2. The SLE patients had a lower level of serum TC ($p = 0.0005$), HDL-C ($p = 0.0009$), and LDL-C ($p = 0.0001$), but higher level of serum creatinine ($p = 0.0256$), TG ($p = 0.0435$), and TG/HDL-C ($p = 0.0019$) than controls. The majority of the patients were ANA positive, and the most common ENA antibody was anti-Ro. Thirty patients had low serum complement C3/C4.

Body composition

With regard to the body composition parameters (Table 3), patients with SLE had lower lean mass ($p = 0.0009$), FFM ($p = 0.0010$), and FFMI ($p = 0.0007$) than controls. However, the android fat% ($p = 0.0010$), A/G ($p = 0.0345$), VAT volume ($p = 0.0015$), and VAT mass ($p = 0.0017$) was higher in the patient group. The subanalysis of premenopausal SLE patients and controls showed only that SLE patients had a lower FFMI ($p = 0.0288$). The subanalysis of perimenopausal and late postmenopausal patients with SLE and controls demonstrated that patients with SLE were younger than controls. The late postmenopausal patients had an altered adiposity distribution, namely higher android fat% ($p = 0.0223$), gynoid fat% ($p =$



Measure	result
Total body% fat (kg)	12.6
Fat mass/height²(kg/m²)	5.2
Android/Gynoid Ratio	1.3
LM(kg)	29.7
BMC(kg)	2.2
Est.VAT mass(g)	484
Est.VAT Volume(cm³)	457

Measure	result
Total body% fat (kg)	15.7
Fat mass/height²(kg/m²)	6.3
Android/Gynoid Ratio	1.3
LM(kg)	37.2
BMC(kg)	2.2
Est.VAT mass(g)	186
Est.VAT Volume(cm³)	157

Fig. 1 Visceral adipose tissue analysis of SLE patient and control. Adipose indices from body composition analysis including VAT by Lunar iDXA bone densitometer (GE Healthcare, Madison, WI) with enCORE software (ver. 16.0, standard-array mode). VAT is measured over the android region, a portion of the abdomen extending from the iliac crest toward the head for 20% of the distance from the iliac crest to the base of the skull. **a** Scan of a 34-year-old SLE patient with BMI = 19.0 kg/m^2. **b** Scan of a 32-year-old control with BMI = 21.0 kg/m^2. BMI, body mass index; DXA, dual X-ray absorptiometry; SLE, systemic lupus erythematosus; VAT, visceral adipose tissue

0.0367), VAT volume ($p = 0.0113$), and VAT mass ($p = 0.0112$).

The subgroup analysis of subjects with a BMI less than 25 kg/m^2 indicated that patients had lower lean mass ($p = 0.0005$), FFM ($p = 0.0005$), and FFMI ($p = 0.0001$), especially premenopausal and late postmenopausal patients. Moreover, premenopausal and late postmenopausal patients with a BMI less than 25 kg/m^2 had a higher value of adiposity distribution than controls: FMI, android fat%, gynoid fat%, VAT volume, and VAT mass (Table 4).

However, the subanalysis of subjects with BMI of 25 kg/m^2 or higher showed that they had similar age ($p = 0.5143$), weight ($p = 0.7629$), height ($p = 0.5411$), body composition, and VAT characteristics ($p > 0.05$) (data not shown).

Associations of VAT with cardiometabolic risk factors by SLE status

In patients with SLE and healthy controls, VAT volume correlated strongly with BMI ($r = 0.6819$, $p < 0.0001$), correlated moderately with age ($r = 0.4759$, $p < 0.0001$), and correlated

Table 1 Demographic and clinical characteristics of the patients with systemic lupus erythematosus and the control subjects

Characteristics	SLE patients (n = 98)	Controls (n = 108)	p value
Age, years[a]	46.4 ± 13.0	47.5 ± 13.2	0.5537
Premenopause, n, %	44 (44.9%)	55 (50.96%)	0.129
Perimenopause, n, %	19 (19.39%)	28 (25.96%)	
Postmenopause, n, %	35 (35.71%)	25 (23.08%)	
Height	1.56 ± 0.05	1.57 ± 0.05	0.254
Weight	54.2 ± 7.4	54.8 ± 6.6	0.5329
BMI,kg/m^2	22.1 ± 2.6	22.2 ± 2.4	0.9119
Disease duration, years[a]	8.0 ± 7.0	–	–
SLEDAI[a]	2.5 ± 4.0	–	–
SLICC/ACR-DI[a]	0.6 ± 1.0	–	–
Clinical manifestation, n, %			
Mucocutaneous	51 (52.0%)	–	–
Renal	42 (43.3%)	–	–
Musculoskeletal	58 (59.2%)	–	–
Hematologic	60 (61.2%)	–	–
NPSLE	9 (9.2%)	–	–
Serositis	13 (13.3%)	–	–
Lung involvement	9 (9.2%)	–	–
Gastrointestinal involvement	6 (6.12%)	–	–
Current prednisone dose, mg[a]		–	–
Prednisone (< 10 mg/day)	70 (71.4%)		
Prednisone (10–15 mg/day)	21 (21.4%)		
Prednisone (> 15 mg/day)	7 (7.1%)		
Cumulative prednisone dose, g[a]	10.3 ± 6.7	–	–
Immunosuppressant use, n, %		–	
Hydroxychloroquine	77 (78.6%)	–	–
Cyclophosphamide	40 (40.8%)	–	–
Mycophenolate mofetil	9 (9.3%)	–	–
Hypertension, n, %	28 (28.57%)	–	–
Diabetes, n, %	4 (4.08%)	–	–
Coronary heart disease, n, %	2 (2.04%)	–	–
Cerebrovascular disease, n, %	8 (8.16%)	–	–
Dyslipidemia, n, %	21 (21.4%)	32 (30.8%)	0.132

[a] Mean (standard deviation)

Mucocutaneous = new rash, alopecia, or mucositis; musculoskeletal = arthritis or myositis; renal = casts, hematuria, proteinuria, pyuria, or lupus nephritis; serositis = pleurisy or pericarditis; hematologic = leukopenia or thrombocytopenia; NPSLE = neuropsychiatric systemic lupus erythematosus

weakly with serum uric acid (r = 0.3332, p < 0.0001), serum creatinine (r = 0.2661, p = 0.0002), non-HDL-C level (r = 0.2209, p = 0.0016), and serum TG level (r = 0.2254, p = 0.0018).

Subgroup analysis

The subanalysis of SLE patients and controls with different menopausal status showed that the subjects in perimenopausal (672.0 ± 53.0 vs. 445.7 ± 28.8, p = 0.0001) and late postmenopausal status (893.5 ± 54.6 vs. 445.7 ± 28.8, p < 0.0001) had higher VAT volume than those in premenopausal status. The subanalysis of SLE patients with hypertension showed that they had higher VAT volume than those without hypertension (1015.8 ± 70.3 vs. 598.3 ± 46.0, p < 0.0001). Regardless of the use of statins, there was no significant difference in VAT volume in patients with SLE.

Association of SLE characteristics with VAT

In patients with SLE, VAT volume positively correlated with disease duration (r = 0.3573, p = 0.0003) and SLICC/ACR-DI score (r = 0.2499, p = 0.0131), and negatively correlated with low serum complement C3/C4 (r = −0.2667, p = 0.0079), whereas VAT volume did not correlate with SLEDAI-2K

Table 2 Laboratory characteristics of the patients with systemic lupus erythematosus and the control subjects

Characteristics	SLE patients $n = 98$	Healthy control $n = 108$	p value
TG, mmol/L	1.5 ± 0.9	1.2 ± 0.7	*0.0435*
TC, mmol/L	4.6 ± 1.3	5.2 ± 1.0	*0.0005*
HDL-C, mmol/L	1.2 ± 0.4	1.4 ± 0.3	*0.0009*
LDL-C, mmol/L	2.6 ± 0.9	3.1 ± 0.8	*0.0001*
Non-HDL-C	3.4 ± 1.1	3.4 ± 1.5	0.8686
TG/HDL-C	1.4 ± 1.1	1.0 ± 0.7	*0.0019*
Uric acid, umol/L	331.6 ± 126.7	305.7 ± 59.3	0.0808
Creatinine, umol/L	68.7 ± 44.8	57.8 ± 8.9	*0.0256*
ANA positive, *n* (%)	89 (94.7%)	–	–
Anti-Ro positive, *n* (%)	58 (61.7%)	–	–
Anti-dsDNA positive, *n* (%)	21 (22.3%)	–	–
Anti-La positive, *n* (%)	15 (16.0%)	–	–
Anti-Smith positive, *n* (%)	8 (0.5%)	–	–
Complement C3	933.8 ± 259.0	–	–
Complement C4	206.7 ± 94.8	–	–
ESR, mm/h	42.5 ± 32.9	–	–
HsCRP, mg/L	9.9 ± 21.5	–	–

score, hsCRP, ESR, serum antibody level (ANA, anti-dsDNA, Anti-Smith, anti-Ro, Anti-La), and current or cumulative glucocorticoid dose ($p > 0.05$).

Compared with SLE patients with the lower thirds of VAT, the ones with the upper third were more likely to be older, have a higher BMI, and have longer disease duration. In addition, they had a higher prevalence of hypertension and a higher level of serum uric acid, TC, TG, serum creatinine, and non-HDL-C. The SLICC/ACR-DI was also higher in the upper third group (Table 5).

Discussion

Although past studies observed that patients with SLE had increased CV risk, the specific mechanism was still unknown. Here, we focused on body composition, especially VAT, which may have an effect on the CV risk in SLE patients. The significant findings of the present study were that the patients with SLE did have higher VAT volume and mass in both premenopausal and late postmenopausal patients. Moreover, we also found that some disease-related factors correlate with VAT mass, which could be concluded as patients with longer disease duration, poor disease control, and organ damage may have a higher VAT mass. Other CV risk factors, such as hypertension, higher serum uric acid, TC, and TG level, were also related to higher VAT volume.

In most cases, the VAT measurements are performed by computed tomography (CT) or magnetic resonance tomography (MRI). However, because these imaging techniques are expensive, their use is limited in large-scale studies. Recently, some investigators used DXA to provide accurate quantitative assessments of both total and regional adiposity [18, 19]. The comparing study has shown that DXA correlated well with gold standard MRI and CT, and provides a low radiation, efficient, cost-effective option despite its underestimation of VAT to some extent [20, 21]; therefore, we used DXA to evaluate the VAT in this study.

Similar to other studies, we found that our patients had some traditional risk factors for CVD, such as higher serum creatinine and uric acid, and lower HDL-C. Wang et al. [-22]reported that the frequency of CVD was high in Chinese patients with SLE, and higher serum creatinine levels and lower HDL-C were the risk factors for CVD. Yang et al. [-23]also found that elevated serum creatinine was an independent risk factor for CVD. Daniele Machado et al. [22]reported that the most significant difference of lipid profile between adolescent females with juvenile SLE and healthy controls was lower HDL-C, whereas TC, LDL-C, TG, and non-HDL-C were not different between the two groups, and also suggested low HDL-C might contribute to an increased atherosclerotic risk. Studies demonstrated that the TG/HDL-C ratio was more useful than isolated lipid values, as it more closely reflects the complex interactions of lipoprotein metabolism [24]. Recent studies indicated a high level of the TG/HDL-C ratio had been associated with insulin resistance, obesity, and metabolic syndrome [25, 26]. We actually found that the TG/HDL-C ratio of our patients was higher than that of the control group, which may be associated with higher CVD risk. In 2018, a Brazilian cross-sectional study demonstrated that the TG/HDL-C ratio was higher in dyslipidemic SLE patients than the others and it was correlated with disease activity [27]. Our group of SLE patients had lower serum TC and LDL-C level than controls, which was not consistent with previous studies [23]. The possible reason was that most of our patients had a well-controlled disease and were under minimal glucocorticoid therapy and long-term hydroxychloroquine treatment. A longitudinal study demonstrated that antimalarials could significantly decrease TC and LDL-C in SLE patients [28].

According to our study, SLE patients likely had lower BMC and LM compared with the control group, especially in premenopausal patients. Accelerated rates of bone and muscle loss have reported before in patients with SLE [29, 30]. The inflammatory nature of SLE, decreased physical exercise, malnutrition, vitamin D supplementation, and glucocorticoid therapy have been found to be associated with this phenomenon [31].

So far, only two studies have examined the relationship between visceral fat and SLE. In 2013, Shields et al. [13] used

Table 3 Body composition parameters, including VAT of all SLE patients and control

Parameter	SLE ($n = 98$)	HC ($n = 108$)	p value	Premenopausal			Perimenopausal			Late postmenopausal		
				SLE ($n = 44$)	HC ($n = 53$)	p value	SLE ($n = 19$)	HC ($n = 27$)	p value	SLE ($n = 35$)	HC ($n = 24$)	p value
BMI, kg/m^2	22.1 ± 2.6	22.2 ± 2.4	0.9119	21.6 ± 2.4	22.0 ± 2.5	0.4293	21.9 ± 2.9	22.4 ± 2.4	0.5203	22.2 ± 2.2	22.9 ± 2.6	0.2914
Age	46.4 ± 13.2	46.4 ± 13.2	0.5537	36.4 ± 8.9	38.3 ± 9.1	0.3031	45.1 ± 1.0	50.8 ± 4.4	*0.0001*	59.7 ± 8.5	64.1 ± 7.3	*0.0387*
Height, m	1.56 ± 0.05	1.57 ± 0.05	0.2540	1.58 ± 0.05	1.58 ± 0.05	0.9200	1.56 ± 0.04	1.58 ± 0.04	0.4597	1.54 ± 0.05	1.55 ± 0.05	0.7126
Weight, kg	54.2 ± 7.5	54.8 ± 6.6	0.5329	54.0 ± 7.3	55.0 ± 6.4	0.5050	53.8 ± 7.2	55.9 ± 7.0	0.3432	54.5 ± 7.1	53.2 ± 6.7	0.4867
FM, kg	19.3 ± 5.0	18.3 ± 4.4	0.1255	18.4 ± 4.4	17.8 ± 4.3	0.5197	18.9 ± 5.9	19.3 ± 4.6	0.8183	20.7 ± 5.2	18.2 ± 4.3	0.0513
FMI, kg/m^2	7.9 ± 2.0	7.4 ± 1.7	0.0664	7.3 ± 1.6	7.1 ± 1.7	0.5584	7.7 ± 2.5	7.8 ± 1.8	0.9686	8.7 ± 2.0	7.6 ± 1.6	0.0280
Lean mass, kg	32.8 ± 4.1	34.7 ± 3.5	*0.0009*	33.7 ± 4.6	35.3 ± 3.3	0.0570	32.8 ± 3.0	34.7 ± 3.9	0.0748	31.8 ± 3.9	33.2 ± 3.0	0.1221
FFM, kg	34.8 ± 4.3	36.7 ± 3.7	*0.0010*	35.8 ± 4.7	37.5 ± 3.5	0.0527	34.9 ± 3.3	36.8 ± 4.2	0.0889	33.5 ± 4.2	33.9 ± 3.2	0.1592
FFMI, kg/m^2	14.2 ± 1.4	14.8 ± 1.2	*0.0007*	14.3 ± 1.6	15.0 ± 1.3	*0.0288*	14.2 ± 1.0	14.8 ± 1.3	0.0893	14.1 ± 1.3	14.6 ± 1.0	0.0925
BMC, kg	2.0 ± 0.3	2.1 ± 0.3	0.0757	2.1 ± 0.3	2.2 ± 0.2	0.0822	2.1 ± 0.3	2.1 ± 0.4	0.6162	1.8 ± 0.3	1.7 ± 0.3	0.5677
Android fat%	40.6 ± 9.2	36.8 ± 7.7	*0.0021*	37.2 ± 7.7	34.3 ± 7.5	0.0586	39.9 ± 11.2	38.7 ± 7.3	0.6792	45.1 ± 8.2	40.5 ± 7.9	*0.0223*
Gynoid fat%	37.9 ± 5.1	36.7 ± 5.2	0.0855	37.7 ± 5.2	36.4 ± 5.0	0.2298	36.6 ± 4.4	37.7 ± 5.9	0.4572	39.0 ± 5.4	36.1 ± 5.0	*0.0367*
A/G	1.1 ± 0.2	1.0 ± 0.2	*0.0345*	1.0 ± 0.2	0.9 ± 0.2	0.2072	1.1 ± 0.2	1.0 ± 0.2	0.4153	1.2 ± 0.2	1.1 ± 0.03	0.5448
VAT volume,cm^3	717.6 ± 424.4	543.6 ± 344.5	*0.0015*	502.6 ± 218.6	398.4 ± 322.4	0.0624	696.3 ± 445.2	654.9 ± 292.7	0.7254	999.6 ± 453.7	738.8 ± 310.9	*0.0113*
VAT mass, g	675.0 ± 399.5	512.8 ± 324.9	*0.0017*	469.7 ± 198.7	375.9 ± 304.0	0.0712	656.7 ± 420.1	617.9 ± 276.2	0.7268	999.6 ± 453.7	738.8 ± 326.8	*0.0112*

FM, fat mass; *BMC*, bone mineral content; *FFM*, fat-free mass; *VAT*, visceral adipose tissue; fat mass index (FMI) was calculated by dividing body fat mass by the square of the height (kg/m^2) and fat-free mass index (FFMI) by dividing fat-free mass by the square of the height (kg/m^2); A/G was calculated by dividing android fat by gynoid

Table 4 Body composition parameters, including VAT of SLE patients and controls with BMI < 25 kg/m^2

Parameter	SLE (n = 86)	HC (n = 90)	p value	Premenopausal			Perimenopausal			Late postmenopausal		
				SLE (n = 42)	HC (n = 47)	p value	SLE (n = 17)	HC (n = 22)	p value	SLE (n = 27)	HC (n = 21)	p value
BMI, kg/m^2	21.4 ± 1.8	21.5 ± 1.7	0.8098	21.3 ± 1.8	21.3 ± 1.7	0.8887	21.1 ± 1.8	21.6 ± 1.7	0.4172	21.8 ± 1.8	21.7 ± 1.9	0.8323
Age, year	45.9 ± 13.1	46.7 ± 13.4	0.7081	36.9 ± 8.7	37.2 ± 8.9	0.8406	45.4 ± 3.8	50.0 ± 4.2	*0.0009*	60.2 ± 9.2	64.1 ± 7.8	0.1226
Height, m	1.56 ± 0.05	1.57 ± 0.06	0.3283	1.58 ± 0.05	1.58 ± 0.05	0.6255	1.57 ± 0.04	1.57 ± 0.04	0.6516	1.54 ± 0.05	1.54 ± 0.06	0.8730
Weight, kg	52.4 ± 5.7	53.0 ± 5.0	0.4412	53.1 ± 5.6	53.5 ± 4.9	0.7048	52.0 ± 5.1	53.6 ± 5.4	0.3478	51.6 ± 6.2	51.3 ± 4.6	0.8571
FM, kg	18.2 ± 3.9	17.1 ± 3.2	0.0534	17.9 ± 3.7	16.7 ± 2.0	0.0963	17.5 ± 4.1	18.0 ± 3.9	0.6608	19.0 ± 4.0	17.1 ± 2.9	0.0611
FMI, kg/m^2	7.4 ± 1.5	7.0 ± 1.3	*0.0265*	7.2 ± 1.4	6.7 ± 1.2	0.0729	7.1 ± 1.7	7.3 ± 1.5	0.7689	8.0 ± 1.5	7.2 ± 1.3	0.0606
Lean mass, kg	32.2 ± 3.7	34.1 ± 3.1	*0.0005*	33.2 ± 4.1	34.9 ± 3.2	*0.0411*	32.5 ± 3.1	33.9 ± 3.0	0.1637	30.5 ± 3.0	32.6 ± 2.5	*0.0136*
FFM, kg	34.2 ± 3.9	36.1 ± 3.3	*0.0005*	35.2 ± 4.1	37.0 ± 3.3	*0.0356*	34.6 ± 3.3	36.0 ± 3.2	0.1890	32.2 ± 3.2	34.3 ± 2.7	*0.0206*
FFMI, kg/m^2	14.0 ± 1.2	14.6 ± 1.0	*0.0001*	14.1 ± 1.5	14.7 ± 1.0	*0.0320*	14.0 ± 0.9	14.5 ± 1.0	0.1352	13.6 ± 0.9	14.5 ± 0.9	*0.0025*
BMC, kg	1.9 ± 0.3	2.0 ± 0.3	0.0652	2.0 ± 0.2	2.2 ± 0.2	*0.0372*	2.0 ± 0.3	2.1 ± 0.3	0.8359	1.7 ± 0.3	1.7 ± 0.3	0.9604
Android fat%	39.2 ± 8.7	35.2 ± 6.7	*0.0008*	37.0 ± 7.7	32.8 ± 6.3	*0.0060*	37.7 ± 9.7	36.9 ± 6.4	0.7676	43.6 ± 8.3	39.0 ± 5.8	*0.0263*
Gynoid fat%	37.6 ± 4.9	36.1 ± 4.7	*0.0364*	37.7 ± 5.3	35.8 ± 4.6	0.0780	36.0 ± 4.3	37.1 ± 5.3	0.4851	38.5 ± 4.6	35.6 ± 4.5	*0.0333*
A/G	1.0 ± 0.2	0.9 ± 0.2	*0.0352*	1.0 ± 0.2	0.9 ± 0.2	0.0866	1.0 ± 0.2	1.0 ± 0.2	0.4936	1.1 ± 0.2	1.1 ± 0.03	0.5763
VAT volume,cm^3	636.5 ± 347.2	465.0 ± 267.7	*0.0003*	493.8 ± 212.1	326.5 ± 208.1	*0.0003*	612.9 ± 385.6	571.9 ± 241.3	0.7039	873.2 ± 374.5	663.0 ± 243.7	*0.0234*
VAT mass, g	600.4 ± 327.6	438.7 ± 252.5	*0.0003*	465.9 ± 200.1	308 ± 196.0	*0.0003*	578.0 ± 363.8	539.6 ± 227.7	0.7061	823.8 ± 353.3	625.5 ± 229.9	*0.0234*

FM, fat mass; *BMC*, bone mineral content; *FFM*, fat-free mass; *VAT*, visceral adipose tissue; fat mass index (FMI) was calculated by dividing body fat mass by the square of the height (kg/m^2) and fat-free mass index (FFMI) by dividing fat-free mass by the square of the height (kg/m^2); A/G was calculated by dividing android fat by gynoid fat

Table 5 Comparison of the demographic, clinical, and laboratory data between SLE patients with the lower thirds and upper third of VAT

Parameters	Lower thirds ($n = 65$)	Upper third ($n = 33$)	p value
Age, year	42.0 ± 10.5	55.0 ± 13.8	< 0.0001
Weight, kg	51.7 ± 5.6	59.0 ± 8.3	< 0.0001
Premenopausal	39(60.00%)	5(15.15%)	0.0001
BMI, kg/m^2	21.0 ± 1.8	24.3 ± 2.7	< 0.0001
Disease duration, year	6.4 ± 5.2	10.9 ± 8.9	0.0021
Hypertension, n, %	7 (10.8%)	21 (63.64%)	< 0.0001
Serum uric acid, umol/L	292.0 ± 98.0	408.4 ± 141.6	< 0.0001
Creatinine, umol/L	55.7 ± 18.1	94.3 ± 66.5	< 0.0001
TC, mmol/L	4.4 ± 1.0	5.2 ± 1.5	0.0027
TG, mmol/L	1.3 ± 0.7	1.8 ± 1.2	0.0082
Non-HDL-C, mmol/L	3.2 ± 0.9	3.8 ± 1.3	0.0100
LDL-C, mmol/L	2.5 ± 0.7	2.9 ± 1.1	0.0158
SLICC/ACR-DI	0.3 ± 0.6	1.0 ± 1.3	< 0.001

electron beam computed tomography to evaluate descending thoracic aortic perivascular adipose tissue (PVAT) solely, which is a visceral adipose deposit in close proximity to blood vessels. They concluded that the volume of PVAT was greater in female SLE patients than in age- and race-matched controls and associated with calcification in different vascular beds, which could influence CVD. LPC Seguro et al. [9] used DXA to evaluate VAT in premenopausal patients with SLE, and they found that SLE was associated with increased VAT, and the latter was correlated with traditional CV risks. Our result was partly consistent with their result that premenopausal SLE patients with BMI less than 25 had a higher VAT parameter than controls. Furthermore, we found the same change in late postmenopausal SLE patients, but not in perimenopausal patients. The possible reason was that patients with SLE were much younger than controls in the perimenopausal group, and the age factor may offset the effect of the disease itself on VAT. In addition, perimenopausal women have significant individual differences in hormone secretion, which may be another confounding factor affecting VAT.

Our results showed that VAT was related to traditional CV risks, such as age, BMI, menopausal status, hypertension, serum uric acid, serum creatinine, non-HDL-C level, and serum TG level, in both patients and controls. Many studies had verified that the amount of VAT increased with age in both genders and both lean and overweight/obese people [12]. Indeed, the visceral deposit was increasing with BMI increase, whereas the correlation between BMI and adipose distribution was different among individuals [12]. Thus, it was necessary to identify a VAT parameter other than BMI to assess the CV risk. The association between VAT and serum TC, non-HDL-C, LDL-C, and TG levels in the general population was reported before, and was due to higher lipolytic activity and weaker antilipolytic effect of insulin in visceral adipocytes. The mechanism of this phenomenon was complicated, but the different expression and sensitivity of the receptors in visceral and subcutaneous adipocytes was the key factor [12].

In addition, LPC Seguro et al. [9] failed to find that VAT was related to disease duration, SLEDAI score, SLICC/ACR-DI, or current glucocorticoid use. In the present study, we identified several SLE disease-related factors positively associated with increased VAT: SLE disease duration and SLICC/ACR-DI score, whereas low complement C3/C4 was negatively associated. Kravvariti et al. [32] found that disease duration was a determinant of subclinical atherosclerosis progression in SLE patients, whose mechanism was multifactorial and possibly it may have been associated with increased VAT. The basis of the association of complement with VAT was not clear. Because there was no known biologic link between compliment and adipose accumulation, the association may relate to compliment as a disease severity marker.

The previous study demonstrated that long-term low-dose prednisone exposure was associated with increased visceral fat in patients with rheumatoid arthritis [33]. Glucocorticoid could preferentially upgrade lipoprotein lipase expression and activity in visceral adipose tissue, but not subcutaneous adipose tissue. Thereby, a higher rate of free fatty acid delivery from triglyceride-rich lipoproteins might contribute to the visceral fat accumulation [34]. We failed to find glucocorticoid exposure in SLE patients related to VAT; the possible reason was that the majority of patients were under long-term glucocorticoid therapy. And, because the dose of glucocorticoid varied in different periods among individuals, it was difficult to distinguish the influence of glucocorticoid on VAT in a cross-sectional study. According to the related studies, it is still safe to say that clinicians should minimize glucocorticoid use to the possible minimum dose to prevent underlying VAT-associated CV events.

There were some confounding factors that may have association with VAT which we did not explore in this study. A large community-based cross-sectional study demonstrated that participants who adhered to recommended dietary guidelines and physical activity (PA) had lower VAT volumes in White people [35]. Other studies also showed that PA intervention was negatively correlated with VAT in obese/overweight population [36–38]. Ethnicity was another confounding factor affecting VAT accumulation [39]. Iris A. Lesser et al. [40] found that when ethnic differences in PA were taken into account, there were no longer any differences in VAT between the Chinese and European groups, while VAT remained higher in South Asians than Europeans. Due to this was a preliminary study, we did not take all these factors into account. In the further study, an exercise intervention study is necessary to further elucidate the effects of PA on VAT in ethnic patients with SLE.

Some limitations of our study are the following: First, the sample size of our study was relatively small, and it was a single-center study. Second, the study was cross-sectional in nature, which made it difficult to explain the cause-and-effect correlation. Third, most of our patients had well-controlled disease and low glucocorticoid dose, which could not reflect the diversity of SLE disease. In addition, DXA was not the most accurate method to measure VAT, which may have some influence on the results. Besides, there were some confounders, such as PA and dietary quality, which affected VAT that we could not control. Notwithstanding its limitations, this study does suggest that patients with SLE in China have increased VAT, and it was associated with traditional CV risk factors and related to the disease itself. To fully identify the associations between SLE and VAT distribution, large-scale, long-term cohort studies should be performed to exclude other confounding factors, such as diet and exercise.

Conclusion

We actually found some traditional CV risk factors in SLE patients, such as low HDL-C, high TG/HDL-C, high serum creatinine, and high uric acid. Furthermore, this study suggested the VAT increases significantly in SLE patients, especially in a premenopausal and late postmenopausal period. The increased VAT in patients with SLE was associated with traditional cardiometabolic risk factors, which may contribute to CV risk in SLE populations. Cohort studies are necessary to validate the long-term effect of VAT on CV complications in SLE. Some other confounding factors, such as PA, dietary quality, and ethnicity, should also take into account in the further study.

Compliance with ethical standards

Our research was approved by the Medical Ethics Committee of the First Affiliated Hospital of Jinan University.

Disclosure None.

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