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 complement C3/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.
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 at least 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/m²). 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 =
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/m² 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/m² 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/m² 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...
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 \( (672.0 \pm 53.0 \text{ vs. } 445.7 \pm 28.8, p = 0.0001) \) and late postmenopausal status \( (893.5 \pm 54.6 \text{ vs. } 445.7 \pm 28.8, p < 0.0001) \) 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 \( (1015.8 \pm 70.3 \text{ vs. } 598.3 \pm 46.0, p < 0.0001) \). 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  
|----------------|------------------|
|                | Healthy control |
|                | n = 98          | n = 108         |
| 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
| Parameter | SLE  
|-----------|-------|
|           | (n = 98) | HC  
|           | (n = 108) | p value | Premenopausal | Perimenopausal | Late postmenopausal | p value  
|           | 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/m² | 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 | 0.0187  
| 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/m² | 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/m²² | 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, cm³ | 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/m²); fat-free mass index (FFMI) by dividing fat-free mass by the square of the height (kg/m²²); 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 | 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    | 0.7765    | 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.
Comparison of the demographic, clinical, and laboratory data

| 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/m²            | 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 |

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 patients 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 menopause 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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