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Association between myosteatosis or sarcopenia based on abdominal CT and hypertension in systemic lupus erythematosus patients

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Abstract

Background Hypertension and obesity are common in systemic lupus erythematosus (SLE) patients, with obesity-related changes potentially driving hypertension. However, the specific adiposity measures associated with hypertension in SLE patients remain unclear. This study assessed the association between myosteatosis and sarcopenia detected on abdominal CT and hypertension in SLE patients. Mediators of the association between myosteatosis and hypertension were also investigated.

Methods This was a retrospective study involving SLE patients enrolled from January 2017 to August 2023 and who underwent abdominal CT at the L3 level to track myosteatosis and sarcopenia based on the skeletal muscle mean radiodensity (SMD) and skeletal muscle index considered as binary and continuous variables. The association between these body composition measures and hypertension was tested using logistic regression analyses, while mediation modeling was used to assess the mediators.

Results A total of 279 adult SLE patients (median age, 41.00 [30.00, 51.00] years; 245 women) were included in this study. Hypertension was associated with myosteatosis (adjusted OR: 3.54; 95% CI: 1.18–10.61 for the binary variable and 1.31; 95% CI: 1.02–1.68 for the continuous variable). No statistically significant association was observed between hypertension and sarcopenia (adjusted OR: 0.48; 95%CI: 0.23–1.01 for the binary variable and 0.95; 95%CI: 0.78–1.16 for the continuous variable). Mediation analyses revealed eGFR could mediate the association between myosteatosis (considered as a continuous variable) and hypertension in SLE patients when taken alone (95% CI: 0.0177–0.2765) or in combination with the TyG index (95% CI: 0.0032–0.0614).

Conclusions Myosteatosis was associated with hypertension in SLE patients. eGFR alone or in combination with the TyG index may mediate this association.

Keywords Systemic lupus erythematosus, Myosteatosis, Sarcopenia, Body composition, Hypertension

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Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease [1, 2]. Hypertension is common in patients with SLE and is associated with high cardiovascular disease burden [3, 4]. The use of corticosteroids and immunosuppressants to control inflammation may elevate blood pressure or exacerbate pre-existing essential hypertension. Lupus-associated kidney disease can also lead to secondary arterial hypertension [3]. Notably, patients with SLE have a high prevalence of obesity, estimated at 30–40% [5]. Alterations in hormones, inflammation, and endothelial cell levels that accompany obesity may contribute to hypertension and an increased incidence of cardiovascular disease through various mechanisms [6]. Moreover, obesity has been shown to be associated with both renal disease risk and hypertension in the general population [7]. However, few studies have investigated the effects of obesity on hypertension in patients with SLE.

Obesity is characterized by an excessive body fat accumulation and obesity is most commonly linked to hypertension based on the body mass index (BMI) [8]. However, the body mass index (BMI) fails to accurately quantify the body fat composition [9, 10]. Accordingly, abdominal Computed Tomography (CT) was developed as a standard method of assessment of body fat composition, with visceral adipose tissue (VAT) being the commonest body fat measure on abdominal CT [10, 11]. In both general and SLE populations, VAT has been linked with hypertension [6, 12]. Furthermore, muscle adiposity (myosteatossis) and sarcopenia (low skeletal muscle mass and function) which interplays with adiposity under certain circumstances, have also been linked with hypertension in the general population [10, 13–16]. However, to our knowledge, myosteatosis and sarcopenia have not been associated with hypertension in patients with SLE.

We previously found insulin resistance mediating an association between intermuscular adipose tissue (IMAT) area and renal impairment in patients with SLE [17]. This suggests a potential link between insulin resistance and body fat composition. Given the central role of kidneys in blood pressure regulation and hypertension pathogenesis as well as the established role of insulin resistance as an independent risk factor for cardiovascular disease, we hypothesized that insulin resistance and renal function may act as potential mediators in the relationship between abdominal fat-muscle composition and hypertension in patients with SLE [18–20].

Therefore, this study aimed [1] to investigate whether there is an epidemiological association between hypertension and abdominal CT-based measures of fat-muscle composition including mainly myosteatosis and sarcopenia in patients with SLE; and [2] to explore whether eventually insulin resistance renal impairment are mediators of the relationship between hypertension and abdominal CT-based measures of fat-muscle composition.

Methods

Study design

A retrospective, cross-sectional study was conducted. Findings were reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines to improve scientific rigor [21]. As this was a retrospective study, the ethics committee waived the requirement for written consent from all patients (KYLL-2021[KS]-226).

Study setting and population

The study was conducted at Qilu Hospital, Shandong University, China. We retrospectively reviewed the electronic medical records of patients hospitalized for SLE between January 2017 and August 2023. SLE classification was based on the ICD-10 (International Statistical Classification of Diseases and Related Health Problems, Tenth Revision) code M32 which indicates that these patients met either the 1997 American College of Rheumatology (ACR) revised SLE classification criteria, either the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria or the 2019 European Alliance of Associations for Rheumatology (EULAR)/ACR SLE classification criteria [22]. The other inclusion criteria for participants were an age ≥ 18 years and the availability of L3 cross-sectional images of abdominal CT scans. The exclusion criteria encompassed a pregnancy or puerperium state and factors that could lead to an erroneous interpretation of abdominal CT images such as a history of malignancy before the abdominal CT scan, low-quality CT images, distortion of anatomical structures, significant edema of adipose tissues, or severe ascites interfering with body composition measurements.

Data collection

A team of two trained resident doctors conducted the data collection process using a preconceived data sheet. We collected data on blood pressure levels, kidney function, other traditional cardiovascular/obesity risk factors, abdominal CT images, demographic parameters, and SLE clinical and therapeutic characteristics. The demographic information collected included age, sex and BMI (BMI = weight (in kg)/height^2 (in m^2)). The SLE clinical and therapeutic characteristics collected included SLE disease duration, regular treatment regimens, disease activity and white blood cell (neutrophils, lymphocytes and monocytes) counts upon admission. The regular treatment regimens assessed involved glucocorticoids and immunosuppressants. Disease activity was assessed using the systemic lupus erythematosus disease

activity index (SLEDAI)-2000 scores available in patients' electronic medical records [23]. Traditional cardiovascular/obesity risk factors recorded included the albumin-globulin (A/G; which could be viewed as a reflect of the body's nutritional and inflammatory status [24]) ratio, blood glucose (referred to here as GLU), triglyceride levels, low-density lipoprotein cholesterol (LDLc) levels, and high-density lipoprotein cholesterol (HDLc) levels. Insulin resistance was subsequently assessed using the triglyceride glucose (TyG) index calculated based on the formula:

TyG index = Ln [fasting blood glucose (mg/dL) × fasting triglyceride (mg/dL)/2] [25].

In addition, we evaluated patients' renal functions using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation for the estimated glomerular filtration rate (eGFR) [26].

Abdominal CT measurements of body fat-muscle composition

A single axial CT image with a 5-mm slice thickness at the L3 level was analyzed using SliceOmatic software (version 5.0; Tomovision, Montreal, Quebec, Canada) to quantify fat and muscle distribution for each participant, as this level demonstrates the highest correlation with overall body tissue mass [27, 28]. SliceOmatic was first used to semi-automatically outline the body composition of each region based on radiological radiodensity thresholds. A trained radiologist (Wang B.W) examined and adjusted the regions of interest, which were then reviewed by an abdominal radiologist with > 30 years of experience (Yu D.X). Neither radiologist knew the participants' clinical information. The skeletal muscle area (SMA) at the L3 level, encompassing the psoas, quadratus lumborum, erector spinae, transversus abdominis, external and internal obliques, and rectus abdominis muscles, was quantified by thresholding using attenuation values of − 29 to 150 HU [29]. The skeletal muscle index (SMI) was calculated to normalize SMA by height using the equation: SMI (cm^2/m^2) = SMA (cm^2) / height^2 (m^2) [29]. VAT was quantified using attenuation values of − 150 to − 50 HU, while SAT and IMAT were identified using − 190 to − 30 HU [29] (Fig. 1). Finally, the area and mean radiodensity of the skeletal muscle, SAT, VAT, and IMAT were recorded.

Definition of operational terms

Hypertension was defined as either a prior clinical diagnosis of hypertension, current use of antihypertensive medications, or newly identified hypertension during hospitalization based on the average of three consecutive blood pressure measurements showing systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg [30].

The definitions of myosteatosis and sarcopenia as binary variables were based on SMD and SMI cut-off values, respectively (see Fig. 1). Accordingly, myosteatosis was defined as SMD values < 41 HU (BMI values < 25 kg/m^2) or < 33 HU (BMI values ≥ 25 kg/m^2) [31], while sarcopenia was defined as SMI value < 50 cm^2/m^2 (males) or < 39 cm^2/m^2 (females) [29]. The definitions of myosteatosis and sarcopenia as continuous variables were based on linear reductions of SMD and SMI values, respectively.

Statistical analysis

Categorical variables were expressed as frequencies and percentages, and continuous variables were described by means and standard deviations or median with the interquartile range (IQR) (Q25, Q75). We compared the demographic and clinical characteristics between the SLE- non-hypertension group and the SLE-hypertension group using the Pearson χ^2 test for categorical variables, the test Independent Samples t test for normally distributed continuous variables, and the Mann–Whitney U test for non-normally distributed continuous variables.

We first compared the differences in body fat-muscle composition variables between SLE patients with and those without hypertension. We then used multivariate logistic regression to analyze the association between hypertension and fat-muscle metrics including myosteatosis, sarcopenia, IMAT, VAT, SAT, VAT/SAT, and BMI. During this analysis, the odds ratios (OR) of these different variables were compared. We fitted three regression models with incremental adjustments for potential confounders. The model 1 adjusted for demographic covariates (age, sex). The model 2 further adjusted for SLE-related parameters including disease duration, SLEDAI, history of immunosuppressant and glucocorticoid use and white blood cell counts including neutrophils, lymphocytes and monocytes. The model 3 which was the priority model, adjusted for the A/G ratio, GLU, LDLc, and HDLc levels on top of covariates in models 1 and 2. Because myosteatosis and sarcopenia were the main body fat-muscle composition measures of this study, they were both treated as binary (yes or no) and continuous (linear reductions of SMD and SMI values, respectively) variables. SMD, SMI, and BMI values were divided into 5 units, and VAT and SAT were divided into 20 units to make the results easily interpretable. To ensure that the SMD and SMI thresholds of myosteatosis and sarcopenia identified in other populations were relevant to our study population, we also estimated the nonlinear risk of hypertension in patients with SLE based on SMD and SMI using 3-knotted restricted cubic spline regression [29, 31].

Next, we exploratively analyzed the factors potentially underlying the association of myosteatosis with hypertension. To quantify the association between

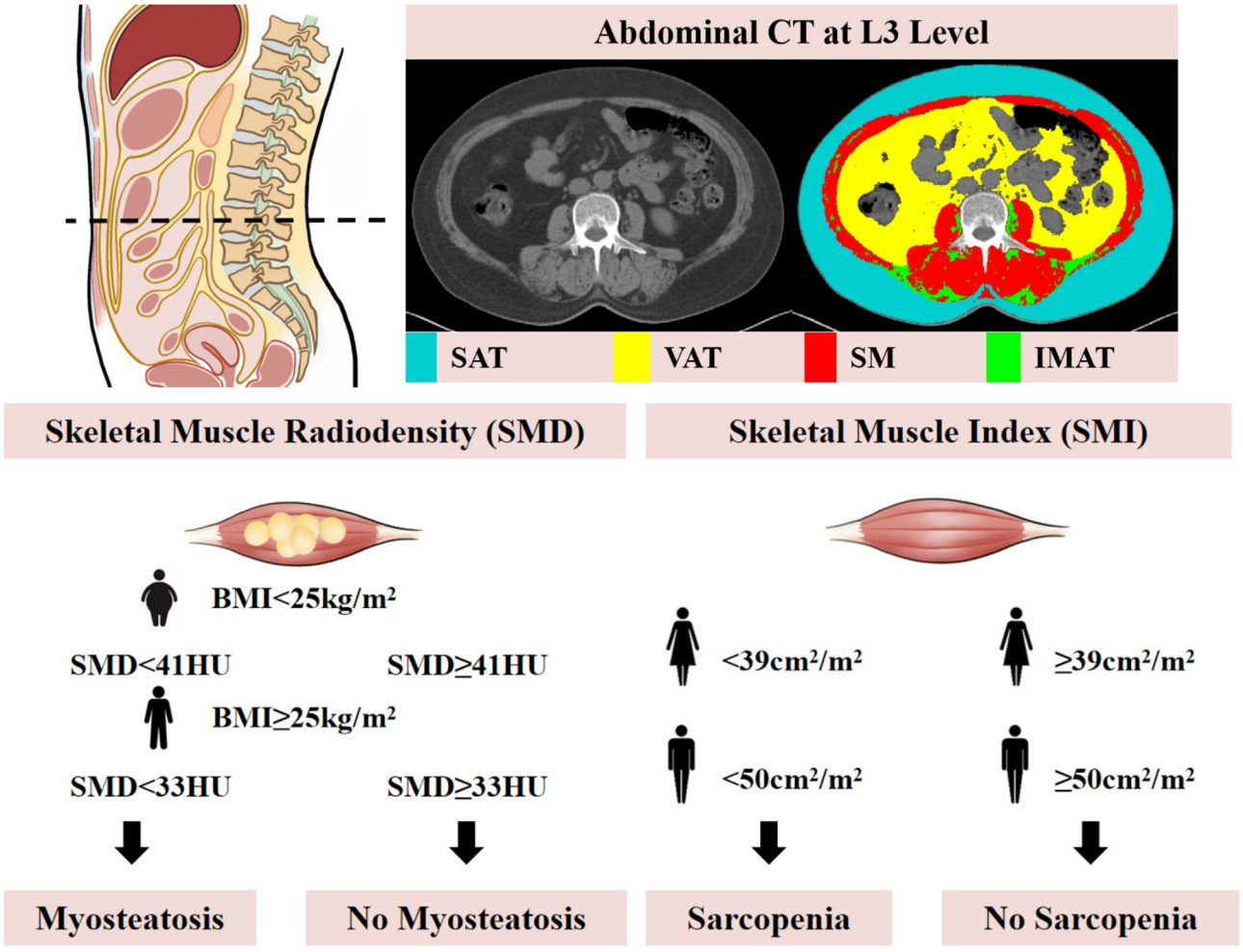

Fig. 1 Measurement of Body Composition and Definition of Myosteatosis and Sarcopenia. Cross-sectional axial CT images at the L3 level in patients with SLE were analyzed using semi-automated software (SliceOmatic version 5.0, Tomovision Inc., Montreal, Quebec, Canada). Blue, subcutaneous adipose tissue (SAT); yellow, visceral adipose tissue; red, skeletal muscle (SM); green, intermuscular adipose tissue (IMAT). Skeletal muscle area (SMA) was normalized by dividing by the square of height: SMI (cm^2/m^2) = SMA (cm^2) / height^2 (m^2). Phenotypic classification of skeletal muscle abnormalities in patients with SLE according to SMD and SMI

myosteatosis and those factors, myosteatosis was only considered as a continuous variable using SMD values in this analysis. Specifically, in this analysis, we first used Pearson and Spearman tests to determine whether there was a correlation between hypertension, SMD, TyG, and eGFR values. We then employed a Hayes' SPSS Process Macro Model 6 to quantify potential serial multiple mediation effects of TyG index and eGFR [32]. Given that the renal function is a variable of the SLEDAI tool, only covariates other than SLEDAI were adjusted for in the mediation model.

All statistical analyses were performed using the IBM SPSS 26.0 software (Chicago, Illinois, United States) and R statistical (version 4.3.2, The R Foundation for statistical computing, Vienna, Austria) softwares. A two-tailed p-value of less than 0.05 was used to define statistical significance for hypothesis testing, except for mediation effects, where statistical significance was determined based on 95% bootstrap CI not including zero, with 5000 bootstrap samples obtained.

Results

Demographic and clinical characteristics of the SLE patients

Of the 2,174 patients with SLE who received inpatient care between January 2017 and August 2023, we ultimately included 279 patients with SLE of China who met the inclusion and exclusion criteria (Fig. 2). A total of 79 (28.3%, 95%CI: 21.5-35.17%) SLE patients were diagnosed with comorbid hypertension. The median age of these patients was 41.00 (IQR 30.00, 51.00) years. The SLE-hypertension group showed significantly higher age (Z=-3.30, $P=0.001$), BMI (Z=-2.22, $P=0.026$), and disease duration (Z=-1.98, $P=0.047$) but lower eGFR (Z=-7.48,

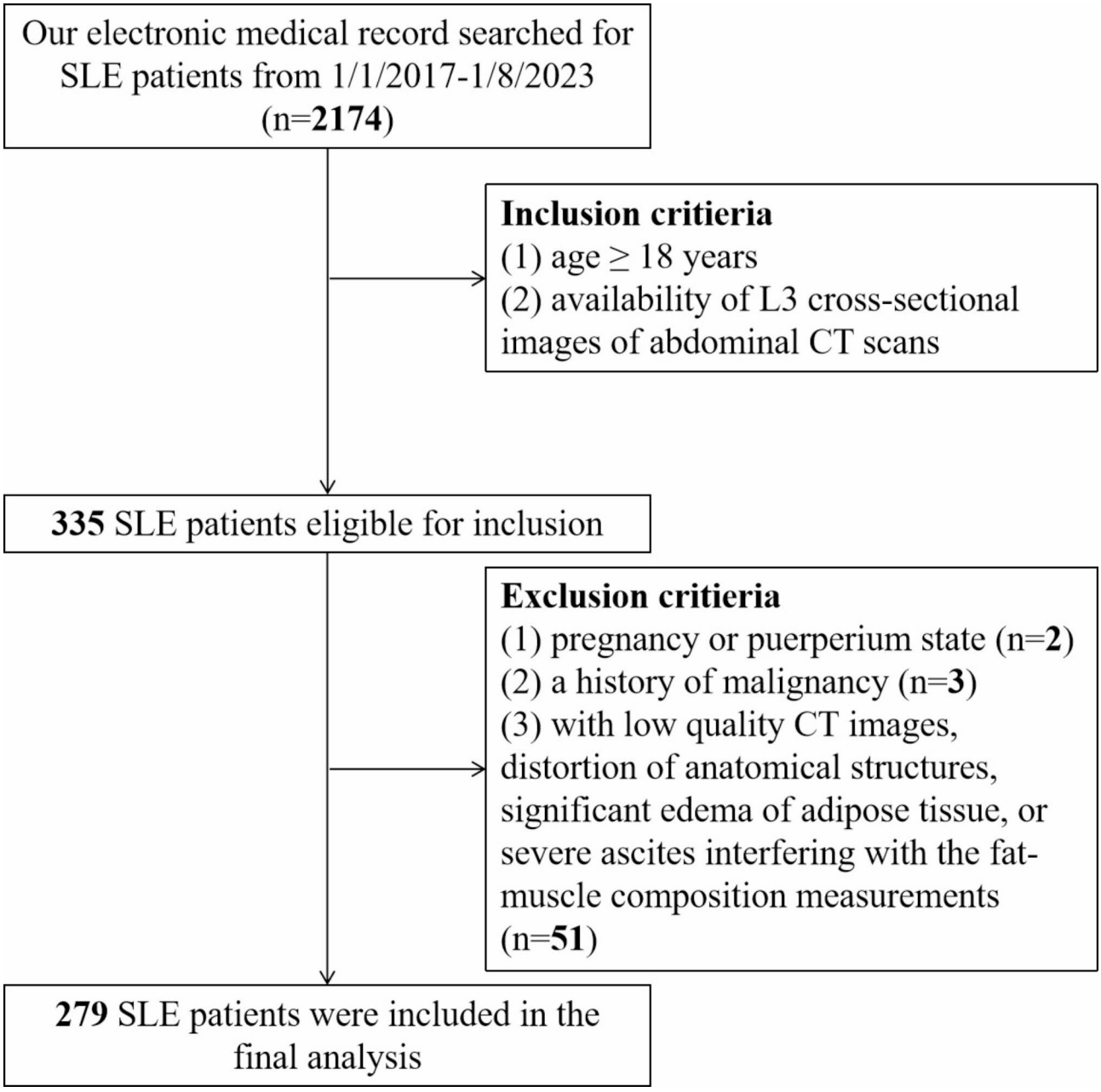

Fig. 2 Flowchart highlighting the selection of included SLE Patients

$P<0.001$) compared to the SLE-non-hypertension group. The detailed characteristics of the participants are shown in Table 1.

Association between body fat-muscle composition measures and hypertension: focus on myosteatosis and sarcopenia

Overall, 203 (72.8%, 95%CI: 66.03-79.57%) as having myosteatosis and 79 (58.8%, 95%CI: 51.3-66.3%) patients were defined as having sarcopenia (Table 2). We found that the proportion of myosteatosis in the SLE-hypertension group (68 of 79 [86.1%]) was significantly higher than in the SLE-non-hypertension group (135 of 200 [67.5%]) (χ^2=9.86, $P=0.002$). Correspondingly, SMD was lower in the SLE-hypertension group than in the SLE-non-hypertension group (31.31 [26.03, 35.74] vs. 34.45 [29.33, 40.39], t = 3.52, $P<0.001$). However, no significant differences were observed between the two groups in terms of the proportion of sarcopenia (χ^2=3.02 $P=0.082$) and SMI (Z=-0.31, $P=0.759$). A detailed comparison of the body fat-muscle composition measures can be found in Table 2. Furthermore, we found that in patients with SLE, SMD values were linearly and negatively associated

Table 1 Overall characteristics of participants with SLE

Parameter	Overall (*n* = 279)	SLE-non-hypertension group (*n* = 200)	SLE -hypertension group (*n* = 79)	Statistic Test performed	*P* Value
Age, years	41.00 (30.00, 51.00)	38.00 (29.00, 49.75)	47.00 (34.00, 56.00)	Z=-3.30	0.001
Sex				χ^2=1.14	0.286
Female, n (%)	245 (87.8)	173 (86.5)	72 (91.1)		
Male, n (%)	34 (12.2)	27 (13.5)	7 (8.9)		
BMI, kg/m^2	22.29 (20.03, 25.39)	22.03 (19.94, 24.84)	23.62 (20.47, 26.27)	Z=-2.22	0.026
Disease duration, years	1.00 (0.00, 8.00)	0.50 (0.00, 7.00)	5.00 (0.00, 10.00)	Z=-1.98	0.047
SLEDAI score	8.00 (4.00, 14.00)	8.00 (4.00, 14.00)	8.00 (3.00, 13.00)	Z=-0.73	0.463
Immunosuppressant drug treatment				χ^2=3.22	0.073
Yes, n (%)	108 (38.7)	116 (58.0)	55 (69.6)		
No, n (%)	171 (61.3)	84 (42.0)	24 (30.4)		
Glucocorticoid				χ^2=3.91	0.048
Yes, n (%)	191 (68.5)	130 (65.0)	61 (77.2)		
No, n (%)	88 (31.5)	70 (35.0)	18 (22.8)		
Neutrophil count, 10^{9}g/L	3.61 (2.11, 6.06)	3.15 (1.90, 5.82)	4.81 (2.91, 6.50)	Z=-3.49	< 0.001
Lymphocyte count, 10^{9}g/L	1.04 (0.61, 1.66)	0.98 (0.58, 1.56)	1.15 (0.76, 1.78)	Z=-1.78	0.075
Monocyte count, 10^{9}g/L	0.36 (0.24, 0.56)	0.32 (0.22, 0.48)	0.47 (0.26, 0.65)	Z=-3.18	0.001
A/G ratio	1.19 (0.96, 1.52)	1.11 (0.92, 1.48)	1.34 (1.11, 1.79)	Z=-4.26	< 0.001
GLU, mmol/L	4.63 (4.05, 5.70)	4.66 (4.13, 5.72)	4.53 (4.01, 5.62)	Z=-0.61	0.541
TyG index	8.67 ± 0.66	8.60 (8.20, 8.98)	8.66 (8.18, 9.13)	Z=-1.03	0.303
LDL-C level, mmol/L	2.39 (1.93, 3.13)	2.30 (1.87, 3.11)	2.55 (1.96, 3.14)	Z=-1.05	0.296
HDL-C level, mmol/L	1.13 (0.89. 1.40)	1.10 (0.85, 1.40)	1.13 (0.91, 1.45)	Z=-1.02	0.309
eGFR, mL/min/1.73m^2	107.62 (78.08, 120.36)	113.50 (96.91, 124.68)	77.48 (33.50, 102.88)	Z=-7.48	< 0.001

Abbreviation: SLE, systemic lupus erythematosus; BMI, body mass index; SLEDAI, systemic lupus erythematosus disease activity index; A/G, albumin-globulin ratio; GLU, blood glucose; TyG index, triglyceride-glucose index; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate

Table 2 Abdominal CT-Based body fat-muscle composition measures and BMI in SLE patients with hypertension and SLE patients without hypertension

Parameter	Overall (*n* = 279)	Absence of hypertension (*n* = 200)	Presence of hypertension (*n* = 79)	Statistic	*P* Value
Myosteatosis				χ^2=9.86	0.002
No, n (%)	76 (27.2)	65 (32.5)	11(13.9)		
Yes, n (%)[#]	203 (72.8)	135 (67.5)	68 (86.1)		
SMD, HU	33.64 ± 8.11	34.69 ± 8.12	30.98 ± 7.50	t = 3.52	< 0.001
Sarcopenia				χ^2=3.02	0.082
No, n (%)	115 (41.2)	76 (38.0)	39 (49.4)		
Yes, n (%)[§]	164 (58.8)	124 (62.0)	40 (50.6)		
SMI, cm^2/m^2	38.13 (33.12, 43.22)	37.92 (32.97, 43.84)	39.13 (33.37, 43.14)	Z=-0.31	0.759
IMAT, cm^2	7.95 (4.96, 12.81)	7.59 (4.71, 11.96)	10.87 (6.07, 14.72)	Z=-2.61	0.009
VAT, cm^2	73.25 (44.78, 125.5)	65.28 (43.39, 106.00)	114.20 (64.12, 150.60)	Z=-4.19	< 0.001
SAT, cm^2	122.00 (85.65, 178.90)	115.35 (81.23, 166.18)	147.50 (99.62, 198.50)	Z=-2.78	0.005
VAT/SAT	0.61 (0.42, 0.88)	0.57 (0.40, 0.81)	0.68 (0.47, 1.09)	Z=-2.85	0.004

[§]Sarcopenia was considered as a binary variable

[#]Myosteatosis was considered as a binary variable

Abbreviation: SLE, systemic lupus erythematosus; BMI, body mass index; SMD, skeletal muscle radiodensity; SMI, skeletal muscle index; IMAT, intramuscular adipose tissue; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue

with hypertension (Fig. 3A) while SMI was not associated with hypertension (Fig. 3B).

When considered as a binary variable, myosteatosis was independently associated with a higher odds for hypertension in SLE patients (adjusted OR: 3.54; 95%CI: 1.18–10.61). We did not find any association between hypertension and sarcopenia as a binary variable (adjusted OR: 0.48; 95%CI: 0.23–1.01). When myosteatosis and sarcopenia were considered as continuous variables, the adjusted ORs for their association with hypertension were 1.31 (95%CI: 1.02–1.68) per 5-HU of SMD reduction for myosteatosis, and 0.95

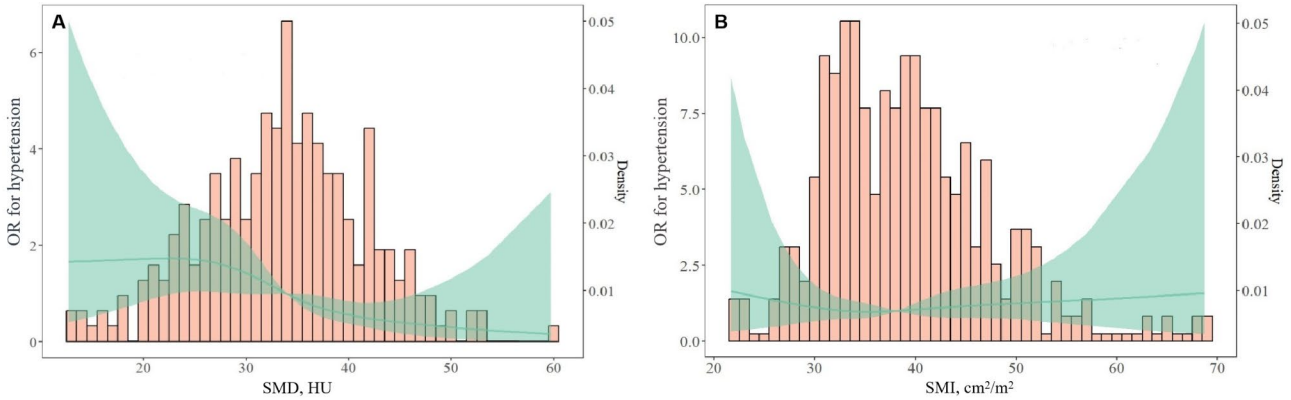

Fig. 3 Nonlinear Associations of CT-Based SMD and SMI with Hypertension in SLE Patients. Histograms and line graphs show unadjusted, nonlinear associations between abdominal CT-based (**A**) skeletal muscle radiodensity (SMD) and (**B**) skeletal muscle index (SMI) and hypertension among SLE patients

Table 3 Univariate and multivariate logistic regression analysis for the association between abdominal CT-Based body composition measures, BMI and hypertension in patients with SLE

Parameter	Crude OR (95%CI)	Adjusted[1] OR (95%CI)	Adjusted[2] OR (95%CI)	Adjusted[3] OR (95%CI)
Myosteatosis				
No	Reference	Reference	Reference	Reference
Yes	2.98 (1.48, 6.01) *	2.15 (1.00, 4.63) *	2.42 (1.03, 5.67) *	3.54 (1.18, 10.61) *
SMD, per 5-HU reduction	1.34 (1.13, 1.59) *	1.23 (1.01, 1.50) *	1.25 (1.02, 1.55) *	1.31 (1.02, 1.68) *
Sarcopenia				
No	Reference	Reference	Reference	Reference
Yes	0.63 (0.37, 1.06)	0.61 (0.36, 1.04)	0.51 (0.28, 0.93) *	0.48 (0.23, 1.01
SMI, per 5-cm^2/m^2 reduction	1.00 (0.87, 1.16)	0.97 (0.83, 1.12)	0.95 (0.81, 1.12)	0.95 (0.78, 1.16)
IMAT, per 5-cm^2 increase	1.12 (0.95, 1.32)	1.02 (0.86, 1.22)	1.02 (0.84, 1.24)	1.04 (0.82, 1.30)
VAT, per 20-cm^2 increase	1.19 (1.10, 1.30) *	1.16 (1.06, 1.27) *	1.14 (1.04, 1.25) *	1.14 (1.02, 1.28) *
SAT, per 20-cm^2 increase	1.09 (1.02, 1.16) *	1.09 (1.02, 1.16) *	1.09 (1.02, 1.16) *	1.08 (1.00, 1.16)
VAT/SAT	2.76 (1.46, 5.22) *	2.26 (1.10, 4.64) *	1.84 (0.85, 4.00)	1.91 (0.68, 5.37)
BMI, per 5-kg/m^2 increase	1.27 (0.94, 1.71)	1.28 (0.94, 1.73)	1.26 (0.91, 1.74)	1.33 (0.91, 1.94)

Crude ORs and adjusted ORs with 95% CIs are presented from unadjusted and adjusted Logistic models, respectively

[1] Adjusted for age, sex

[2] Adjusted for age, sex, disease duration, SLEDAI, immunosuppressant, glucocorticoid, neutrophil, lymphocyte, monocyte

[3] Adjusted for age, sex, disease duration, SLEDAI, immunosuppressant, glucocorticoid, neutrophil, lymphocyte, monocyte, A/G, GLU, LDL-C, HDL-C

* Association is significant at $P<0.05$

Abbreviation: SLE, systemic lupus erythematosus; BMI, body mass index; SMD, skeletal muscle radiodensity; SMI, skeletal muscle index; IMAT, intramuscular adipose tissue; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; SLEDAI, systemic lupus erythematosus disease activity index; A/G, albumin-globulin ratio; GLU, blood glucose; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol

(95%CI: 0.78–1.16) per 5-cm^2/m of SMI reduction. In addition, the VAT was also associated with hypertension in patients with SLE (adjusted OR: 1.14; 95%CI: 1.02–1.28). There was no association between hypertension and IMAT (adjusted OR: 1.04; 95%CI: 0.82–1.30), SAT (adjusted OR: 1.08; 95%CI: 1.00-1.16), VAT/SAT (adjusted OR: 1.91; 95%CI: 0.68–5.37), and BMI (adjusted OR: 1.33; 95%CI: 0.91–1.94) values (Table 3).

Correlation between SMD, TyG index, eGFR, and hypertension

A correlation analysis between SMD, TyG index, eGFR, and hypertension is shown in Table S1. SMD values were correlated with TyG index ($r=0.196$, $P=0.003$) and hypertension ($r=0.216$, $P<0.001$), and inversely correlated with eGFR (r=-0.356, $P<0.001$). In contrast, eGFR was negatively correlated with TyG (r=-0.189, $P=0.003$) and hypertension (r=-0.457, $P<0.001$).

Mediating effect of TyG index and eGFR in the relationship between myosteatosis and hypertension

Table 4 shows the mediating effect values of TyG index and eGFR between SMD and hypertension in patients with SLE. The bootstrap 95% of CI (0.0354, 0.3272) for the total indirect effect (0.1403) of TyG index and eGFR had a significant mediating effect on the association between SMD and hypertension. The total indirect effect results from the sum of three indirect effects: [1]

Table 4 Mediating effect of TyG index and eGFR in the relationship between SMD and hypertension in patients with SLE

Model Pathways	Effect size	Boot SE	Boot CI	
			Lower	Upper
Direct effect	0.1886	0.1358	-0.0797	0.4528
Total indirect effect	0.1403	0.0750	0.0354	0.3272
Indirect 1	0.0071	0.0322	-0.0576	0.0759
Indirect 2	0.1121	0.0666	0.0177	0.2765
Indirect 3	0.0211	0.0150	0.0032	0.0614

Adjusted for age, sex, disease duration, immunosuppressant, glucocorticoid, neutrophil, lymphocyte, monocyte, A/G, GLU, LDLc, HDLc

Note. SMD in per 5-HU reduction. Indirect effect 1: SMD–TyG index–hypertension; Indirect effect 1: SMD–eGFR–hypertension; Indirect effect 1: SMD–TyG index–eGFR–hypertension

Abbreviation: SLE, systemic lupus erythematosus; SMD, skeletal muscle radiodensity; eGFR, estimated glomerular filtration rate; TyG index, triglyceride-glucose index; A/G, albumin-globulin ratio; GLU, blood glucose; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol

indirect effects of TyG index (SMD–TyG index–hypertension; effect size = 0.0071); [2] indirect effect of eGFR (SMD–eGFR–hypertension; effect size = 0.1121); and [3] indirect effect of both TyG index and eGFR (SMD–TyG index–eGFR-hypertension; effect size = 0.0211). The indirect effect 1 (95% CI: -0.0576, 0.0759) was not significant. In contrast, the indirect effects 2 (95% CI: 0.0177, 0.2765) and 3 (95% CI: 0.0032, 0.0614) were statistically significant (Table 4). Based on the above analysis, the chain intermediary model is shown in Figure S1.

Discussion

In this study, we found that myosteatosis as a binary and a continuous variable was significantly associated with high odds of hypertension in patients with SLE. Furthermore, our findings suggest that the relationship between myosteatosis and hypertension may be mediated by the eGFR either alone or in combination with the TyG index. By contrast, sarcopenia as a binary and a continuous variable was not statistically associated with hypertension in participants with SLE.

The finding of a strong association between myosteatosis and hypertension in patients with SLE is consistent with findings from studies on the general population. For example, an analysis from the Framingham Heart Study [33] reported that lower SMD values in the two paraspinal muscles was correlated with a higher prevalence of hypertension. In a cross-sectional study conducted in Korea, researchers segmented SMA from abdominal CT scans at the L3 level into normal attenuated muscle area and low attenuated muscle area based on SMD [14]. The results demonstrated that individuals with hypertension exhibited more advanced profiles of myosteatosis compared to normotensive counterparts, and a lower normal attenuated muscle area/BMI ratio was significantly associated with a higher risk of hypertension [14]. Compared to the general population, patients with SLE are more prone to developing muscle-related complications, including myositis (an inflammatory muscle disease) and drug-induced myopathy (a complication associated with long-term steroid use) [34]. These conditions can lead to type II muscle fiber atrophy and increased intramuscular fat infiltration [34, 35]. Therefore, the association between myosteatosis and hypertension may hold greater clinical significance in the context of SLE.

The chain-mediation model identified renal impairment, either alone or combined with insulin resistance, as a potential mediator in the association between myosteatosis and hypertension in SLE patients, though underlying mechanisms remain unexplored. Myosteatosis, characterized by ectopic fat accumulation in skeletal muscle due to exceeded adipocyte storage capacity, may share mechanisms with adiposity-induced hypertension, including insulin resistance, inflammation, leptin-mediated arterial stiffness, sympathetic nervous system activation, and renin-angiotensin-aldosterone system stimulation with increased sodium reabsorption [8, 36]. Further research is needed to explore the roles of adipokines and oxidative stress, particularly their interactions with renal impairment and insulin resistance, to better elucidate the mechanisms linking myosteatosis to hypertension. Current research indicates that increased adipokines can stimulate renal interstitial cell proliferation, thickening of the basement membrane, and expansion of the extracellular matrix, leading to glomerulosclerosis, loss of nephron function, and elevated arterial pressure [37–39]. Furthermore, increasing evidence indicates that when lipids and their derivatives accumulate in skeletal muscle, it induces mitochondrial dysfunction, and interferes with fatty acid β-oxidation, thereby leading to impaired insulin signaling. Intramuscular fat accumulation also induces changes in muscle metabolism and insulin sensitivity through secretion of inflammatory adipokines [40, 41]. The consequent hyperinsulinemia exerts direct effects on multiple segments of the renal tubule, enhancing sodium reabsorption while suppressing urinary sodium excretion which play an important role in initiating hypertension associated with obesity [42]. While our study highlights these associations in SLE patients, these mechanistic insights informed by existing research require further exploration to establish causality.

However, no statistically significant association between sarcopenia and hypertension was found in patients with SLE. A cross-sectional study using data from the Fourth and Fifth Korean National Health and Nutrition Examination Survey found that elderly individuals with sarcopenia had a significantly higher prevalence of hypertension compared to those without sarcopenia [43]. In contrast, another cohort study based on a Chinese middle-aged and elderly community population showed that sarcopenia was not associated with hypertension [44]. Thus, the association between sarcopenia and hypertension may vary in different countries. Han et al. [35] conducted a large prospective cohort study that demonstrated low relative skeletal muscle mass was independently associated with the prevalence of hypertension in Korean males, but this association was not significant in females, suggesting that there may be a sex-dependent relationship between muscle mass and hypertension [35]. Notably, these studies were conducted in general populations, whereas our study specifically focused on SLE patients, a population predominantly comprising young women (nearly 90% of our participants were female) [45]. This distinct demographic characteristic may contribute to the observed differences. Future studies incorporating gender-stratified analyses could provide further insights into the relationship between sarcopenia and hypertension in SLE patients.

This study had several limitations. First, it included a population receiving care in a tertiary referral center, which is therefore less representative of the community's SLE population. Second, we did not assess the Chinese Visceral Adiposity Index, which is increasingly recognized as an important tool for predicting cardiovascular disease in China, notably when combined with the insulin resistance marker TyG index [46, 47]. However, we used VAT measures that may also apply to SLE patients from other parts of the world [27,28]. Third, there is currently no internationally standardized SMD cut-off value for defining myosteatosis based on abdominal CT, and the SMD cut-off value we employed was developed in studies involving cancer patients [10, 31, 48]. These limitations call for large multicenter prospective cohorts or case-control studies to further assess the association between hypertension and both myosteatosis and sarcopenia given that prospective cohorts are the gold standard for demonstrating causality among observational primary studies, whereas case-control studies may be the most efficient observational primary studies for assessing causality in relatively uncommon diseases such as SLE [49].

Conclusions

Among all abdominal CT–based body fat-muscle composition variables measured in this cross-sectional study, myosteatosis is the one that was statistically significantly associated with hypertension in patients with SLE. This association may be indirectly mediated by eGFR isolated or combined with the TyG index. Sarcopenia was not linked to hypertension. Timely identification of muscle adiposity in patients with SLE using abdominal CT could be a useful tool for hypertension prevention in patients with SLE if future diagnostic test accuracy and cost-effectiveness studies prove it to be useful for measuring myosteatosis in SLE patients and if future case-control/cohort studies confirm the epidemiological association between myosteatosis and hypertension in SLE. Future well-designed large-scale case control/cohort studies are warranted to further assess whether there is an epidemiological link between hypertension and other adiposity measures or sarcopenia in SLE patients.

Abbreviations

A/G	Albumin-globulin ratio
BMI	Body mass index
CI	Confidence interval
CT	Computed Tomography
eGFR	Estimated glomerular filtration rate
GLU	Blood glucose
HDLc	High-density lipoprotein cholesterol
HU	Hounsfield units
IMAT	Intermuscular adipose tissue
IQR	Interquartile range
LDLc	Low-density lipoprotein cholesterol
OR	Odds ratio
SAT	Subcutaneous adipose tissue
SLE	Systemic lupus erythematosus
SLEDAI	Systemic lupus erythematosus disease activity index
SMA	Skeletal muscle area
SMI	Skeletal muscle index
TyG index	Triglyceride-glucose index
VAT	Visceral adipose tissue

Supplementary Information

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Supplementary Material 1

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Author contributions

W.B. and Z.L. performed the majority of the research and they analyzed the data; W.B, F.J. and Z.W. wrote the manuscript; A.Y and C.W. were involved in revising the paper. Y.D. supervised and organized the study and contributed to the critical revision. All authors approved the final version of the manuscript.

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Data availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This retrospective study was approved by our Ethics Committee and the requirement for informed consent was waived (KYLL-202307-043).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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