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Influence of visceral adiposity on cardiovascular risk in patients with systemic sclerosis

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Abstract

Systemic sclerosis (SSc) is an autoimmune disease characterized by systemic inflammation, endothelial dysfunction, generalized fibrosis and high cardiovascular mortality. The evaluation of cardiovascular risk through the visceral adiposity index (VAI) has been helpful due to its direct relationship to the body and visceral fat percentage. We evaluated the influence of body composition and anthropometrics on cardiovascular risk as measured by VAI in healthy controls (HC) and SSc. An analytical cross-sectional study of 66 participants (33 SSc and 33 HC), mean age 52.7 ± 10, 95% women, was conducted from August 2020 to January 2021. Inclusion criteria in cases were consecutive patients with SSc (ACR/EULAR 2013), 63.6% were diffuse cutaneous (dcSS) subtype, and 36.4 were limited cutaneous (lcSS) subtype. HC was matched by age and gender. Serum lipid profiles and InBody anthropometrics were analyzed and compared. We performed descriptive statistics, bivariate analysis with Student's *t*, or Mann–Whitney *U*, correlation and chi-square according to the variable type and distribution. Total cholesterol was significantly higher in SSc than HC (345 vs 194, $p = < 0.001$). The BMI was higher in HC (26.2 vs 28.9, $p < 0.001$). Kilograms of muscle (19.8 vs 28.9, $p < 0.001$) and total fat (23.4 vs 28.9, $p < 0.001$) were lower in SSc patients compared to HC. VAI was similar when BMI < 25, but significantly higher when BMI > 25 in SSc than in HC (3 vs 1.9, $p = 0.030$). The increase in BMI at overweight or obese in SSc is associated with a significant increase in cardiovascular risk.

Keywords Systemic sclerosis · Cardiometabolic risk factor · Body composition · Visceral adipose tissue · Visceral adiposity index

Abbreviations

VAI	Visceral adiposity index
BMI	Body mass index
TG	Triglyceride
SSc	Systemic sclerosis
HC	Healthy controls
HDL	High-density lipoprotein-cholesterol
W	Waist
WHR	Waist-to-hip ratio

Introduction

Systemic sclerosis (SSc) is an autoimmune disease characterized by systemic inflammation, tissue fibrosis and endothelial dysfunction, which together have an impact on increased cardiovascular mortality [1]. A recent meta-analysis of 14,000 patients showed that SSc increases the risk of cardiovascular events by two to five times [2]. This appears to result from chronic inflammation, atherogenic lipid profile, endothelial injury, fibrosis, thrombosis as well as chronic and progressive organic ischemia [3, 4].

In general population, the increase in cardiometabolic risk has been directly associated with hyperuricemia, increased C-reactive protein, total fat percentage [5] and visceral fat, even in infants [6]. Multiple cardiovascular risk indexes coincide in their direct relationship with body mass index (BMI) and waist circumference. It is important to note this that the visceral adiposity index (VAI) includes

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anthropometric parameters and pro-atherogenic serum markers in its components [7].

VAI has been proposed as a surrogate method of visceral adiposity that assesses its quantity and function, but it is also associated with insulin resistance and cardiovascular risk [8, 9]. Additionally, the increase in fat mass is related to a decrease in the amount of fat in sedentary individuals or with musculoskeletal diseases such as SSc, where a low BMI and functional limitation are associated with sarcopenia and malnutrition predominate [10]. Therefore, the aim of our study was to compare the relationship of the VAI as a marker of cardiovascular risk, with the body composition between SSc and healthy controls (HC).

Methods

Compliance with ethical standards

Our study was carried out according to the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the Local Research Ethics Committee of our hospital (*Comité Local de Ética e Investigación en Salud* 3501 *IMSS*, No. R-2020-3501-077), on April 20, 2020. All patients gave full written informed consent. All authors had access to the study data.

Study population

An observational, descriptive, cross-sectional and analytical case–control study at a reference Hospital Center in Mexico City was conducted from August 2020 to January 2021. A total of 66 subjects, 33 with SSc and 33 HC, were included. The selection criteria of the *cases* in the study were consecutive patients with SSc (2013 ACR/EULAR), both genders, ≥ 18 years old, without comorbidities and signed informed consent. The selection criteria of the *controls* were voluntary healthy people, matched by age and sex, ≥ 18 years old, without comorbidities, with light or moderate physical activity according to International Physical Activity Questionnaire [11], and signed informed consent. We excluded those patients or HC who did not complete their clinical or biochemical evaluations; patients with metallic or electronic implants; pregnant women; subjects with fever or edema, individuals with diet restrictions or high protein or caloric intake; and patients who use diuretics, steroids or with any medical treatment used to modify intestinal motility or that could affect fat mass and those who did high-intensity exercise routinely or intermittently.

Clinical, body composition and laboratory data

Demographic and clinical variables related to the history of the disease were recorded. Dietary habits were evaluated by means of a 3-day, 24-h food record to determine an average of both macronutrients and micronutrients for each subject. Waist circumference was measured at the mid-axillary line level, at the midpoint between the lower costal margin and the upper edge of the iliac crests. For hip circumference, the tape was placed at the maximum protrusion of the buttocks at the level of the greater trochanter of the femur on each side.

The evaluation of body composition was carried out by electrical bioimpedance using a Body Composition Analyzer of the brand InBody CO. LTD, Lookin Body Basic ver p/120, year 2018, made in Korea, Model BPM040S12FXX. The patient was placed on the scale following the product instructions. The report of weight, BMI, fat and total body muscle was obtained by segments: trunk, abdomen, arms and legs in kilograms and percentage; visceral, protein, mineral and water percentages as well. Height was measured with a stadiometer. A blood sample was taken puncturing the basilic vein obtaining 10 ml of blood with 12-h fasting in the morning, and the sample was processed in the central laboratory of this unit using visible light spectrometry. We recommended not consuming high-fat foods, requesting that the last meal had not been rich in lipids prior to sampling. The sample evaluates glucose, total cholesterol, HDL (high-density lipoprotein), cholesterol and triglycerides.

The VAI was calculated according to sex using the following formulas [8]:

$$\text{VAI} = (\text{Waist circumference (cm)}/(39.68 + (1.88 \times \text{BMI}))) \times (\text{triglycerides}/1.03) \times (1.31/\text{HDL}) \text{ for men, expressed in mmol/L.}$$

$$\text{VAI} = (\text{Waist circumference (cm)}/(36.58 + (1.89 \times \text{BMI}))) \times (\text{triglycerides}/0.81) \times (1.52/\text{HDL}) \text{ for women, expressed in mmol/L.}$$

Statistical analysis

Quantitative variables were expressed firstly as mean and standard deviations and secondly as medians and ranges according to their distribution, which was determined using the Kolmogorov–Smirnov test. The qualitative variables were expressed in frequencies and percentages. Chi-square test and Fisher's exact test were used to compare proportions. Bivariate analyses were carried out with either

Table 1 Demographic characteristics and BMI classification of SSc and HC

Groups	SSc $N=33$ n (%)	HC $N=33$ n (%)	p
Age, μ ± SD, years	55 ± 10.50	50.55 ± 9.301	0.073[t]
Gender			
Female	32 (97)	31 (93.9)	0.500[x2]
Man	1 (3)	2 (6.1)	0.558[x2]
BMI			
Underweight	2 (6.1)	0 (0)	0.495[x2]
Normal	10 (30.3)	4 (12.1)	0.132[x2]
Overweight	13 (39.4)	25 (75.8)	0.003*,[x2]
Obese class I	7 (21.2)	1 (3)	0.338[x2]
Obese class II	1 (3)	2(6.1)	1.00[x2]
Obese class III	0 (0)	1 (3)	1.00[x2]
Type of sclerosis			
Limited cutaneous	12 (36.4)		
Diffuse cutaneous	21 (63.6)		

μ mean, *SSc* systemic sclerosis, *HC* healthy controls, *SD* standard deviation, *BMI* body mass index

[x2]Statistical analysis chi-square test; [t]Statistical analysis Student's t test, *$p=<0.05$

Student's *t* test or Mann–Whitney *U* test according to the information distribution. Spearman's correlation was analyzed for non-parametric quantitative variables. The power of the study $(1-Z_{\beta})$ for significant results of VAI in overweight and obesity (IBM ≥ 25) between SSc and HC was calculated by a two mean formula. A p value < 0.05 was considered statistically significant. All the data were processed in the statistical package IBM SPSS version 25.

Results

A total of 66 subjects, 33 with SSc and 33 HC, were included, 60 (90.9%) of which were women at an age 52.7 ± 10.0 (Table 1). Of the SSc patients, 21 (63.6%) had diffuse disease (dSSc) and 12 (36.4%) had limited disease (lSSc). Regarding metabolic parameters, we found an increase in total cholesterol (345 vs 194 mg/dL, $p<0.001$) and lower serum glucose (78 vs 91 mg/dL, $p=0.015$) in SSc patients compared to HC, respectively (Table 2).

Dietary habits

The median daily kilocalories consumed by patients with SSc was 1379 and those consumed by HC were 1437. In

Table 2 Comparison of biochemical parameters, anthropometry and VAI between SSc and controls

Variable	SSc	HC	p
Glucose, median IQR25-75, mg/dL	78 (66–95)	91 (84.4–95.5)	**0.015*,[u]**
Total cholesterol, median, IQR25-75 mg/dL	345 (196–467)	194 (173–208)	**< 0.001*,[u]**
HDL cholesterol median IQR25-75, mg/dL	45 (26.39–59.9)	51 (43.1–57.96)	0.207[u]
Triglycerides median, IQR25-75, mg/dL	123 (90.69–212)	108 (84.74–160)	0.213[u]
VAI median IQR25-75	2.63 (1.49–7.04)	1.91(1.37–3.02)	0.89[u]
Weight, μ ± SD, kg	60.5 ± 11.7	71.20 ± 11	**< 0.030*,[t]**
Height, median IQR25-75, m	1.52 (1.48–1.56)	1.56 (1.53–1.62)	**< 0.001*,[u]**
BMI, μ ± DE, kg/m^2	26.1696 ± 5.41	28.87 ± 4.42	**< 0. 001*,[t]**
Waist circumference, μ ± DE, cm	88.55 ± 11.3	90.74 ± 11.32	0.437[t]
WHR, median, IQR25-75, cm	0.92 (.82-.95)	0.95 (.90-.99)	**0.023*,[u]**
Arms fat %, median, IQR25-75	219 (120–305)	240 (202–309)	0.211*,[u]
Legs fat %, μ ± SD	169.85 ± 65.15	183.30 ± 49.54	0.349[t]
Abdominal fat % median, IQR25-75	274 (157–341)	282 (242–366)	0.116[u]
Total body fat %, median, IQR25-75	38.8 (30.9–44.5)	41.10 (36.4–44.9)	0.330[u]
Visceral fat %, μ ± SD	13 (6–15.50)	14 (12–17)	0.078[u]
Arm Muscle %, median, IQR25-75	108 (92.5- 126.90)	118 (105–134)	**0.048*,[u]**
Leg Muscle %, median, IQR25-75	85.6 (78.4–89.72)	85.4 (82.62–91.8)	0.330[u]
Abdominal muscle %, μ ± SD	91.33 ± 13.752	95.73 ± 7.65	0.113[t]
Total muscle %, median, IQR25-75	32.76 (29.42–36.20)	32.04 (29.62–34.48)	0.746[u]
Muscle mass kg, μ ± DE	19.79 ± 9.56	28.90 ± 3.61	**< 0.001*,[t]**
Total body fat kg, μ ± SD	23.38 ± 9.56	28.90 ± 7.84	**0.013*,[t]**

IQR25-35 interquartile range 25–75%, *mg/dL* milligrams/deciliter, *HDL* high-density lipoprotein cholesterol, *μ* mean, *SD* standard deviation, *BMI* body mass index, *WHR* waist–hip ratio, *kg* kilogram, *m* meters, *cm* centimeters

[t]Student's *t* test, [u]Mann–Whitney *U* test, *$p=<0.05$

the SSc group, the average carbohydrate intake was 173 g, representing 59% of the caloric intake, which consisted of an average of 14 g of fiber and 35 g of sugar, while the HC group had a carbohydrate intake of 221 g, 18 g of fiber and 23 g of sugar. In SSc patients, the average consumption of lipids was 34.9 g and 60 g of protein, whereas in HC it was 23 g and 71.6 g, respectively. In patients with SSc, the median micronutrient intake per day was the following: sodium 920 mg, calcium 522 mg and potassium 815 mg. In the HC, the median micronutrient intake per day was sodium 937 mg, calcium 588 mg and potassium 1178 mg.

Body composition

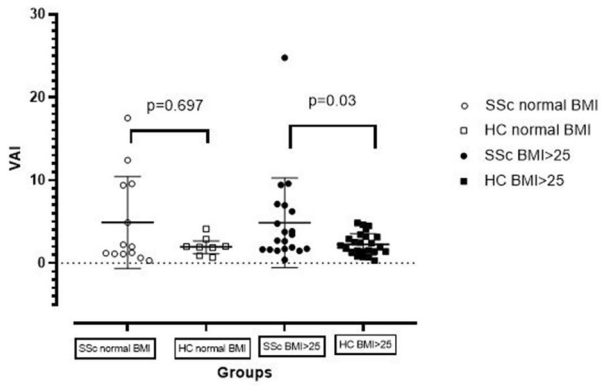
SSc patients showed a lower BMI compared to HC (26.2 vs 28.9, $p=0.001$). Both groups showed a higher percentage of body fat than that considered as healthy in the arms, legs, abdomen and visceral fat. The values of total body fat were 23.4 vs 28.9 kg, $p=0.013$. Also, the percentage of muscle was lower than expected in the legs, trunk, and total muscle in both groups. However, the percentage of muscle in the arms (SSc 108% vs HC 118%, $p=0.048$) and kilograms of lean mass (19.8 vs 28.9 kg, $p<0.001$) were found to be higher in the HC group compared to SSc patients (Table 2.) The waist–hip ratio (WHR) was significantly lower in the SSc group compared to HC (0.92 vs 0.95, $p=0.023$).

Visceral adiposity index

The overall median VAI was higher in patients with SSc compared with HC (2.63 vs 1.91, $p=0.089$); however, this difference was not statistically significant. Nevertheless, when comparing the VAI in subjects with overweight or obesity (BMI ≥ 25), this index was higher in patients with SSc compared to HC (3.0 vs 1.9, $p=0.03$, power $1-Z_{\beta}$ 88%) (Fig. 1). Elevated visceral fat (≥ 9%) was found in 84.8% of HC and 66.7% of SSc patients ($p=0.085$). Meanwhile, a high VAI (> 1) was found in 81.1% of the HC and in 90.9% of the patients with SSc ($p=0.282$).

Correlations

Considering each of the VAI components, where the result depends directly on triglycerides and waist circumference and indirectly on BMI and HDL, we confirmed a strong negative relationship with HDL similar to SSc and HC ($p<0.001$), and a strong positive relationship with triglycerides ($p<0.001$). Despite the aforementioned, changes in waist circumference and BMI did not have a significant influence on the VAI value. Additionally, body composition in percentages of fat and muscle by region did not show any significant relationship with VAI (Table 3).



VAI			
	SSc	HC	p
IMC > 25	3.0 (1.6-6.7)	1.91 (1.37-3.15)	.030[u]
IMC NORMAL	1.97 (1.1-9.4)	1.96 (1.13-2.67)	.697[u]

Fig. 1 VAI comparison into BMI > 25 and normal BMI between patients with SSc and HC. There was a significant difference in VAI between SSC and HC with elevated BMI ($p=0.03$). Normal BMI shows no difference between the groups. SSc shows higher levels of VAI. [u]Mann–Whitney *U* test

As expected, the proportion of total fat showed a marked correlation between visceral fat and WHR ($p<0.001$, Tables 3 and 4). In contrast, we found a strong negative correlation with the percentage of total muscle in both groups ($p<0.001$, Tables 3 and 4). The increase in WHR was moderately correlated with an inverse reduction in total muscle percentage in both groups ($p=0.0001$) and legs only for the SSc group ($r=-0.398$, $p=0.022$). However, it had a moderate positive relationship with the percentage of arm muscle in both groups ($p=0.002$) and abdomen only in HC ($p=0.001$) (Tables 3 and 4). In the case of total muscle, this had a strong negative relationship with fat in the abdomen ($p=<0.001$), legs ($p=<0.001$) and arms ($p<0.001$) (Tables 3 and 4).

Discussion

In this study, we found lower total levels of muscle and body fat in SSc than those in HC of the same age and gender. Body composition shows no relationship with normality or increased VAI in SSc or in HC, unlike BMI, which does show a relationship with VAI when it is greater than 25 in SSc, excluding HC. It is known that the percentage of body fat and dyslipidemia are directly related to increased cardiovascular risk. Cardiovascular risk has been assessed with multiple scales, one of which includes serum lipid parameters, VAI.

Table 3 Spearman correlation between variables of SSc

SSc	kgBFt	BFTotal	Kgmt	Mtotal	MAb	ML	MA	AbF	LF	AF	WHR	VF	TG	HDL
VAI	0.176	0.293	−0.239	−0.323	0.077	−0.058	0.136	0.247	0.255	0.244	−0.011	0.222	0.771***	−0.834***
GLU	0.154	0.239	−0.088	−0.242	0.036	0.093	0.067	0.186	0.261	0.162	0.242	0.183	−0.083	−0.564***
CL	−0.206	−0.192	0.061	0.224	−0.066	0.153	−0.147	−0.273	−0.194	−0.315	−0.370*	−0.208	0.083	0.348
HDL	−0.201	−0.288	0.124	0.305	−0.116	0.015	−0.193	−0.246	−0.283	−0.269	−0.062	−0.216	−0.370*	1
TG	0.2	0.269	−0.158	−0.285	0.053	−0.095	0.126	0.263	0.25	0.232	0.019	0.237	1	
VF	0.967***	0.958**	0.305	−0.931***	0.093	−0.494**	0.225	0.979***	0.931***	0.961***	0.743***	1		
WHR	0.743***	0.696***	0.365*	−0.662***	0.337	−0.398*	.443**	0.788***	0.695***	0.773***	1			
AF	0.960***	0.939***	0.316	−0.909**	0.164	−0.479**	0.303	0.980***	0.923***	1				
LF	0.958***	0.942****	0.314	−0.917**	0.11	−0.32	0.268	0.947***	1					
AbF	0.971**	0.950***	0.352*	−.914**	0.216	−0.430*	0.350*	1						
MA	0.269	0.176	0.504**	−0.104	0.891***	0.185	1							
ML	−0.408*	−0.527**	0.17	0.584***	0.249	1								
MAb	0.111	0.046	0.485**	0.021	1									
Mtotal	−0.886**	−0.989***	−0.038	1										
KgMtotal	0.417*	0.13	1											
BFTotal	0.926***	1												
KGBFTotal	1													

VAI visceral adiposity index, *Glu* glucose, *CL* cholesterol, *HDL* high-density lipoprotein, *TG* triglycerides, *VF* visceral fat, *WHR* waist–hip ratio, *AF* arms fat, *Lf* legs fat, *AbF* abdominal fat, *MA* muscle arms, *ML* muscle legs, *MAb* abdominal muscle, *Mtotal* percentage of total body muscle, *KgMtotal* kilograms of total body muscle, *BFtotal* percentage of total body fat, *KGBF* kilograms of total body fat

*$p < 0.05$, **$p < 0.01$, ***$p < 0.005$

Table 4 Spearman correlation between variables of HC

HC	kgBFt	%BFT	Kgmt	Mtotal	MAb	ML	MA	AbF	LF	AF	WHR	VF	TG	HDL
VAI	0.029	−0.072	0.398*	0.11	0.292	0.027	0.269	0.122	−0.129	0.026	0.222	0.032	0.750***	−0.812**
GLU	0.203	0.11	0.006	−0.116	0.118	0.02	−0.102	0.134	0.139	0.134	0.146	0.173	0.277	0.082
CL	0.104	0.214	−0.281	−0.227	0.12	−0.383*	0.157	0.244	0.059	0.192	0.231	0.179	0.135	−0.058
HDL	0.085	0.177	−0.371*	−0.223	−0.173	−0.048	−0.176	0.006	0.143	0.066	−0.037	0.117	−0.392*	1
TG	0.143	0.076	0.237	−0.03	0.332	−0.172	0.118	0.269	−0.062	0.139	0.358*	0.189	1	
VF	0.971***	0.947***	−0.165	−0.896***	0.174	−0.353*	0.201	0.933***	0.885***	0.974***	0.855***	1		
WHR	0.843***	0.710***	0.162	−0.611***	0.570**	−0.171	0.529**	0.932***	0.626***	0.848***	1			
AF	0.962***	0.930***	−0.131	−0.859**	0.185	−0.353*	0.188	0.963***	0.920**	1				
LF	0.895***	0.912***	−0.259	−0.868**	−0.074	−0.334	−0.019	0.827***	1					
AbF	0.928***	0.849***	−0.013	−0.757**	0.342	−0.318	0.33	1						
MA	0.269	0.016	0.489**	0.04	0.757**	0.502**	1							
ML	−0.192	−0.493**	0.696**	0.543**	0.332	1								
MAb	0.177	0.009	0.503**	0.081	1									
Mtotal	−0.815***	−0.979***	0.507**	1										
KgMtotal	−0.02	−0.391*	1											
BFTotal	0.887***	1												
KGBFTotal	1													

VAI visceral adiposity index, *Glu* glucose, *CL* cholesterol, *HDL* high-density lipoprotein, *TG* triglycerides, *VF* visceral fat, *WHR* waist–hip ratio, *AF* arms fat, *Lf* legs fat, *AbF* abdominal fat, *MA* muscle arms, *ML* muscle legs, *MAb* abdominal muscle, *Mtotal* percentage of total body muscle, *KgMtotal* kilograms of total body muscle, *BFtotal* percentage of total body fat, *KGBF* kilograms of total body fat

*$p < 0.05$, **$p < 0.01$, ***$P < 0.001$

The ATTICA study [8] showed that a high VAI was significantly and independently associated with a high incidence of adverse cardiovascular events after ten years, which was maintained even after adjusting for confounding variables such as lifestyle and certain laboratory parameters. The study also found that the predictive effect of VAI after ten years was better when compared with other anthropometric variables such as BMI and hip circumference, among others.

Few studies on patients with SSc have done research on the relationship between body composition and cardiovascular risk. In the present study, we decided to evaluate the relationship between VAI and anthropometric measures, including visceral fat, total fat and total muscle in SSc.

The VAI in a healthy population is expected to be less than 1.9 [12]; in our study, we found it to be elevated in both SSc and HC, although the highest values were in SSc. In relation to the lipid profile necessary to calculate the VAI, we found higher triglycerides and total cholesterol as well as lower HDL cholesterol more frequently in patients with SSc compared to HC. In this regard, an altered lipid profile in patients with SSc may be a consequence of oxidative stress derived from persistent systemic inflammation, where oxidative stress leads to oxidized LDL, reduction of HDL and conversion of anti-inflammatory HDL into proinflammatory HDL [13]. Ferraz-Amaro and Borba [14, 15] have also found decreased HDL and higher triglyceridemia in SSc than in HC.

Regarding body composition, large series of cases describe patients with SSc at higher cardiovascular risk despite having a low BMI. In fact, a Canadian study [10] with 586 SSc patients found a prevalence of 64% with a BMI below 25 and 17% below 19.5. In this study aimed at analyzing body composition, we included patients with a higher range of BMI, including 40% of them with BMI > 25.

We chose HC randomly by age and gender, where 80% had obesity and overweight, which coincides with the high prevalence of such in our country reported in the National Health and Nutrition Survey 2021, comprised of 75% of the female population and 69.6% of the male population that had this health problem [16].

In SSc, both BMI, kilograms of body fat and total body muscle were found to be lower when compared to HC. Some authors have found that it derives from abnormalities of the gastrointestinal tract, such as gastroparesis, hypomotility, gastroesophageal reflux and malabsorption, resulting in malnutrition and weight loss [17]. Much is still unknown about the pathophysiological mechanism that explains muscle reduction and weakness in SSc. Nevertheless, it is associated with reduced ranges of motion, tissue malnutrition, vasculopathy or neuropathy [18, 19]. Histopathological studies have found necrosis, polymyositis, fibrosing myopathy and dermatomyositis in muscle biopsies, which indicates that there is also an inflammatory process involved in muscle loss [20].

The percentage of muscle in the arms was lower in SSc, similar to Petterson et al. study [21], which mentions a reduction in muscle mass of the upper extremities, reduction of shoulder–arm ranges of motion and lower muscle resistance in dSSc compared to lSSc.

An interesting point in our study was that despite the elevated BMI of HC, VAI was still higher in SSc. When stratifying VAI into BMI > 25 or normal BMI (19.5–24.9 kg/m^2), SSc patients with BMI > 25 had significantly higher VAI than HC.

Obesity with a high-fat percentage has been related to low-grade inflammation in HC, with an increase in proinflammatory adipokines, which could be in synergy with the inflammation caused by the rheumatic disease itself [22, 23]. In this regard, it has been found that SSc patients with high BMI show higher serum concentrations of lectin, IL-17A, IL-2 and IL-10 compared to patients with low BMI [24].

In our study, the visceral fat percentage was directly related to abdominal, arm and leg fat. It was also inversely related to total muscle percentage in both SSc patients and HC. Interestingly, a study conducted in China [25] showed that visceral fat is associated with skeletal muscle loss in adults.

On the other hand, different studies have associated WHR with increased cardiovascular risk, such as the meta-analysis performed by Qinqin Cao et al. [26], where WHR was a predictor of acute myocardial infarction, mainly in women. In this regard, we found no relationship between WHR and VAI in either group; however, it was strongly and significantly related to the percentages of fat in different body areas, as well as with a decrease in the percentage of muscle. A study that measured the relationship between abdominal fat and muscle strength found that by decreasing the waist circumference, strength increased [27].

As we have discussed, increased obesity results in chronic subclinical inflammation. A study by Roubenoff et al. [28] proposes the theory that this may help develop and worsen sarcopenia, as several adipokines derived from visceral adipose tissue, tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), leptin and adiponectin are involved in insulin resistance and also in growth hormone secretion, which have been linked to a catabolic effect on the muscles.

As mentioned above, VAI has been shown to be a predictor of cardiovascular risk. A cohort study [29] conducted in 220 Mexican patients with SSc reported that 14% of mortality in a 9-year period was due to cardiovascular causes, which is why VAI is proposed for patients with SSc as a preventive measure.

Our study has some limitations. First, we only included patients from a single center, so our results cannot be

generalized. Second, our sample was small compared to other studies that address VAI or composition in patients with SSc, due to the low prevalence of the disease. Third, we did not perform longitudinal assessments, so it is not possible to analyze changes in body composition. Finally, the calculation of body fat by impedance does not allow to differentiate brown fat from white fat.

Conclusions

In our study, we found that patients with SSc have a higher VAI when having a BMI over 25. It is important to maintain a BMI within normal ranges in SSc, which would contribute to maintain a lower cardiovascular risk for VAI similar to that of HC. In addition, it is important to try to normalize the lipid profile to obtain an increase in muscle mass and to control the disease in order to lower cardiovascular risk. Follow-up studies are needed to evaluate the impact of these interventions on mortality and cardiovascular events in patients with SSc.

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Author contributions All authors meet the ICMJE criteria for authorship. GMD, MCD, and BLZ contributed to methodology, validation, and formal analysis; GMD, MCD, JFR, and RMC were involved in investigation and writing—original draft; MSS and OFD contributed to visualization, resources, and review; APA MAC, and OVL were involved in editing, project administration, conceptualization, and critical review; and KGG contributed to resources and formal analysis of diet. The final manuscript has been revised critically and approved by all the authors, who are fully responsible for the integrity and accuracy of all aspects of the work.

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Data availability The datasets generated during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

Ethical approval Our study was carried out according to the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the Local Research Ethics Committee of our hospital (*Comité Local de Ética e Investigación en Salud* 3501 *IMSS*, No. R-2020-3501-077), on April 20, 2020. All patients gave full written informed consent. All authors had access to the study data.

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