Clinical Rheumatology (2021) 40:2835–2841
https://doi.org/10.1007/s10067-021-05592-z

ORIGINAL ARTICLE

Visceral adipose tissue in granulomatosis with polyangiitis: association with disease activity parameters

Pedro L. Furlam[1] · Mariana O. Perez[1] · Andre S. Franco[1] · Valeria F. Caparbo[1] · Samuel K. Shinjo[1] · Rosa M. R. Pereira[1]

Received: 6 October 2020 / Revised: 21 December 2020 / Accepted: 13 January 2021 / Published online: 23 January 2021

Abstract

Objective To assess the body composition (BC) of patients with granulomatosis with polyangiitis (GPA) compared to healthy controls, emphasizing visceral adipose tissue (VAT) and associated BC parameters with disease activity, the damage index, and inflammatory parameters in patients with GPA.

Methods This study was conducted in 43 patients with GPA and 43 healthy controls matched by sex, age, and body mass index (BMI). BC was analyzed using dual-energy X-ray absorptiometry (DXA). The fat mass parameters evaluated were total fat mass (FM), adiposity (%), the fat mass index (FMI: fat mass/ht^2), and VAT (g, cm^2, cm^3). Disease activity was assessed by the Birmingham Vasculitis Activity Score (BVAS). Damage was assessed by the Vasculitis Damage Index (VDI). C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR) were measured.

Results Comparing patients with GPA with healthy controls, patients had a significantly greater VAT (VAT in g: 685.81 ± 306.10 vs. 581.21 ± 235.57, $p = 0.04$; VAT in cm^2: 142.23 ± 63.48 vs. 119.84 ± 49.54, $p = 0.03$; VAT in cm^3: 741.33 ± 330.97 vs. 628.44 ± 254.66, $p = 0.04$). Patients with higher VAT (≥ 768 g) had an increased value of ESR (22.77 ± 26.79 vs. 11.57 ± 11.30 mm/1st hour, $p = 0.04$) and an increased value of BVAS (3.18 ± 4.15 vs. 0.90 ± 1.70, $p = 0.01$) when compared to patients with less VAT (< 768 g).

Conclusion Patients with GPA have altered BC compared to healthy controls. Moreover, higher VAT was associated with disease activity and higher inflammatory markers, suggesting a relationship between GPA activity and adiposity parameters.

Key points
- *Granulomatosis with polyangiitis patients have increased visceral adipose tissue when compared to health controls;*
- *Granulomatosis with polyangiitis patients with higher values of visceral adipose tissue have worse disease activity and higher inflammatory markers;*
- *This paper represents important contribution to the well-studied association between vasculitis and inflammatory markers, adding the role of adipose visceral tissue in the disease physiopathology.*

Keywords Adipose tissue · ANCA vasculitis · Body composition · Granulomatosis with polyangiitis · Inflammatory markers

Introduction

Granulomatosis with polyangiitis (GPA) is an autoimmune systemic vasculitis that affects small vessels. It is recognized by the serological marker antineutrophil cytoplasmic antibody (ANCA) [1]. The main findings of GPA include necrotizing vasculitis, granulomatous inflammation, and necrotizing glomerulonephritis [2]. In addition to the main findings, it also has a very wide spectrum of clinical presentation; it may affect the kidneys, lungs, and upper respiratory tract, leading to non-specific symptoms and signs such as pulmonary infiltrates, sinusitis, arthralgia, fever, otitis, hemoptysis, ocular inflammation, and renal damage that can cause different failure degrees, including end stage renal failure [3, 4].

The association between immune-inflammatory diseases and increased cardiovascular risk is well known. In fact, in rheumatoid arthritis (RA), two recent metaanalyses [5, 6]

Pedro L. Furlam and Mariana O. Perez contributed equally to this work.

✉ Rosa M. R. Pereira
rosamariarp@yahoo.com

[1] Division of Rheumatology, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, Brazil

demonstrated a 48% increase in the risk of cardiovascular events in patients with RA compared to the general population. It was observed that patients with greater disease activity, assessed by acute phase inflammatory markers, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), had increased cardiovascular risk [7–9]. It has also been found that obese women with RA have higher CRP values and greater disease activity than nonobese women with RA [5].

Individuals with GPA have a higher prevalence of comorbidities. Furthermore, patients with GPA have both an increased cardiovascular risk and a higher risk for acute myocardial infarction in comparison to the overall population, mainly due to the higher prevalence of obesity, hypertension, and dyslipidemia [6, 10].

The role of adipose tissue as a producer of inflammation has been described in the literature. Interleukin-6 is the main cytokine produced by adipose tissue and acts directly on the liver, stimulating the production of CRP. There is also an increased level of TNF-α and leptin in obesity, which directly contribute to systemic inflammation [11]. Considering the different adipose tissue locations, the visceral adipose tissue (VAT) produces proinflammatory factors (TNF-α, IL-6, IL-1) in greater quantity when compared to subcutaneous and pericardium adipose tissue [12]. VAT is also the adipose tissue that mainly correlates with the pathogenesis of cardiovascular diseases [12, 13]. In the pathogenesis of GPA, TNF-α appears to have a fundamental role in the formation of granuloma, and high levels of IL-6 have been observed in the active phase of the disease [14].

There are several methods for calculating body composition, including VAT, such as computed tomography, magnetic resonance, and densitometry (dual X-ray absorptiometry [DXA]). Among them, DXA is the most interesting because it is cheaper and can be used more widely, in addition to exposing the patient to a lower dose of radiation.

Thus, considering that VAT produces proinflammatory factors that are involved in the genesis and worsening of the disease, the main objective of this study is to assess the body composition of patients with GPA, comparing it with healthy controls, with special emphasis on VAT. Second, we will evaluate disease activity, the damage index, and inflammatory parameters in patients with GPA.

Materials and methods

Patients

Forty-three patients with GPA diagnosis according to the American College of Rheumatology criteria [15] and the Chapel Hill Consensus (2012) were included in this study. The patients were followed up at the Vasculitis Outpatient Clinic of the Rheumatology Service of Clinics Hospital, University of Sao Paulo, School of Medicine. Patients with other associated autoimmune diseases or the presence of infections other than the airways at the time of analysis were excluded.

Clinical and demographic data

Clinical and demographic data were obtained by interviewing each patient and reviewing medical records, including race, age, disease duration, clinical manifestations, comorbidities, and treatment of GPA (glucocorticoid, immunosuppressant, immunobiological therapy, and prophylactic sulfamethoxazole-trimethoprim).

Body composition

All patients underwent total body densitometry (DXA) (Hologic, QDR 4500, Bedford, MA, USA). Fat mass parameters for the total body (except the head) and by region (arms, legs, and trunk) were obtained using APEX Software Version 4.0.2 (Bedford, MA, USA). Height (in cm) and weight (in kg) measurements were performed on all individuals by standardized protocols, standing, and wearing light clothes without shoes. BMI was calculated as weight (in kg) divided by height (in m^2). The fat mass parameters evaluated were total fat mass (FM), body fat percentage (adiposity), the fat mass index (FMI: fat mass/m^2), and visceral adipose tissue (VAT in g, cm^2, cm^3) [16, 17].

Laboratory evaluation

C-reactive protein (CRP) was assessed by the immunoturbidimetric method, and levels above 5 mg/L were considered high. The erythrocyte sedimentation rate (ESR) was measured by the Westergren method, with normal reference values in the first hour as follows: < 15 mm for men and < 20 mm for women. ANCA was assessed by indirect immunofluorescence.

Disease activity

Disease activity in GPA was assessed using the Birmingham Vasculitis Activity Score Modified for Wegener's Granulomatosis (BVAS/WG), a tool designed for clinical use and for research purposes to measure disease activity, vasculitis treatment outcomes, and prognosis. The BVAS/WG has 34 items divided into 9 groups, ranging from 0 to 63. Disease activity is defined as a BVAS ≥ 1, and remission is defined as a BVAS/WG of 0 [18]. We also considered the presence of ANCA positivity as an activity marker [19].

Damage score

The damage assessment by GPA and its treatment was done through the Vasculitis Damage Index (VDI). The VDI contains 64 items divided into 11 organ-based systems and a category "other", related to possible side effects of the treatment. A damage item is only considered if it occurred after the onset of vasculitis and if it lasts for more than 3 months. In the case of patients with established comorbidity before vasculitis, this will only be recorded if there has been significant clinical deterioration for at least 3 months since the onset of the disease [20].

Human Rights

This study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments and was approved by our Research Ethics Committee of Clinics Hospital, University of Sao Paulo, School of Medicine, under the following number: 2.723.911. All subjects of the study agreed in participate before their inclusion in the research protocol.

Statistical analysis

Statistical analyzes were performed using the Statistical Package for the Social Sciences (SPSS for Mac, 25.0, SPSS Inc). The results were presented as mean ± SD for continuous variables and as percentages for categorical variables. Quantitative variables were analyzed using Student's *t* test (normal distribution) or Mann–Whitney test (nonnormal distribution). Differences between categorical variables were assessed using the chi-square or Fisher's exact test. To establish correlation between the results, the Pearson correlation coefficient was used for data that conformed to normality and Spearman's correlation coefficient was adopted for nonnormal data. Statistical significance was considered for p values less than 0.05.

Results

A total of 43 patients with GPA (26 women and 17 men) were compared to 43 healthy controls, matched for age, sex, and BMI. The mean age of the patients was 46.9 ± 14.4 years. The mean age at diagnosis was 38.6 ± 14.4 years, and the mean disease duration was 7.4 ± 4.5 years.

Most patients (63%) had a generalized form of the disease, with a VDI of 4.8 ± 2.4 and BVAS of 2.7 ± 4.1. ANCA positivity was observed in 47%. The proportion of patients with BVAS ≥ 1 was 41.9%. Regarding therapy, 51% of patients received prednisone at doses of 10.8 ± 16.6 mg/day, 69% were using sulfamethoxazole-trimethoprim as a prophylactic approach, 74% were using immunosuppressants (methotrexate, sulfasalazine, azathioprine), and 14% were using biological treatment with rituximab. The rest of the patients (12%) were naive to treatment or using only trimethoprim-sulfamethoxazole.

The general characteristics of patients and heathy controls as well as treatment information are demonstrated in Table 1.

Regarding body composition, patients with GPA presented increased VAT compared to healthy controls (VAT in g: 685.8 ± 306.1 vs. 581.2 ± 235.6, p = 0.04; VAT in cm^2: 142.2 ± 63.5 vs. 119.8 ± 49.5, P = 0.03; VAT in cm^3: 741.3 ± 330.9 vs. 628.4 ± 254.6, P = 0.04); however, the total fat mass (26.8 ± 12.0 vs. 25.3 ± 10.2 kg, P = 0.26), adiposity tissue (33.7 ± 10.3 vs. 32.1 ± 9.6%, P = 0.23), and fat mass index (10.7 ± 5.0 vs. 9.8 ± 4.4 kg/m^2, P = 0.18) were not different between the two groups (Table 2).

We observed a significant correlation between CRP with total fat (0.379, P = 0.01), fat mass index (0.361, P = 0.01), and adiposity (0.337, P = 0.02). VAT was not significantly correlated with CRP (0.248, P = 0.10), ESR (0.129, p = 0.40), BVAS (0.171, P = 0.27) or cumulative glucocorticoid dose (0.01, P = 0.91).

Within the patient group, we divided them according to the value of VAT in grams. Due to the nonnormal distribution, we used the median value of 768 g, considering the higher group to be VAT ≥ 768 g, and the lower group to be VAT < 768 g. Patients with GPA with more VAT (> 768 g) had an increased value of ESR (22.8 ± 26.8 mm vs. 11.6 ± 11.3 mm, P = 0.04) and an increased value of BVAS (3.2 ± 4.1 vs. 0.9 ± 1.7, P = 0.01) than patients with GPA with less VAT, g. In addition, patients with less VAT, g had a longer disease duration compared to patients with GPA with more VAT, g (disease duration in years: 8.6 ± 4.8 vs. 6.3 ± 4.1, P = 0.049). No significant difference was observed when comparing other parameters between the GPA groups (Table 3).

Discussion

Inflammatory diseases are associated with changes in body composition [16, 21]. The relationship of visceral adipose tissue with cardiovascular disease and cerebrovascular disease in immune-inflammatory diseases has been the subject of several studies [22, 23], although this issue is not yet established in other rheumatic diseases, including vasculitis. To the best of our knowledge, the present study is the first to assess body composition in patients with GPA, comparing controls matched by age, sex and BMI.

Patients with GPA showed high VAT values when compared to controls, suggesting an active role of this adipose tissue in the inflammation caused by the disease. Since the patients and controls were matched by BMI, no difference in the total fat mass, adiposity, or fat mass index was observed.

Table 1 Characteristics of granulomatosis with polyangiitis (GPA) patients and matched healthy controls

	GPA patients (n = 43)	Healthy controls (n = 43)	P
Demographics	-	-	-
Female, n (%)	26 (40)	26 (40)	1.00
Caucasian race, n (%)	32 (74)	36 (83)	0.42
Current age, yrs	46.9 ± 14.4	46.4 ± 14.6	0.45
Body mass index, kg/m^2	30.7 ± 6.7	29.5 ± 5.6	0.18
GPA disease characteristics	-	-	-
Disease duration, yrs	7.4 ± 4.5	-	-
Generalized form, n (%)	27 (63)	-	-
Localized form, n (%)	16 (37)	-	-
BVAS	2.7 ± 4.1	-	-
VDI	4.8 ± 2.4	-	-
ANCA, n (%)	20 (47)	-	-
Obesity	23 (53)	16 (37)	0.19
Current GPA treatment	-	-	-
Prednisone, n (%)	22 (51)	-	-
Prednisone dose, mg/day	10.8 ± 16.6	-	-
Trimethoprim-sulfamethoxazole, n (%)	30 (69)	-	-
Immunosuppressive, n (%)	32 (74)	-	-
Rituximab, n (%)	6 (14)	-	-

*Values are expressed in mean SD and percentage unless otherwise indicated; *GPA* granulomatosis with polyangiitis; *BVAS* Birmingham Vasculitis Activity Score; *VDI* Vasculitis Damage Index

Importantly, VAT was differently suggesting that the location of visceral fat is a fundamental factor in defining its biological effects. Similarly, Özer Gökaslan et al. [24] evaluated that patients with mesenteric panniculitis, characterized by chronic inflammation, fat necrosis, and fibrosis, had higher VAT compared to healthy controls. VAT works as a proinflammatory environment, and adipocytes express cytokines such as TNF-α, IL-6, and IL-12 that produce acute phase proteins (CRP, ESR), in addition to producing other cytokines (MCP-1, MIF) that activate the cellular inflammatory response through macrophages [25]. The chronic use of glucocorticoids increases the BMI in most patients undergoing GPA treatment

Table 2 Anthropometric and dual x-ray absorptiometry–derived body composition characteristics for GPA patients and matched healthy controls

	GPA patients (n = 43)	Healthy controls (n = 43)	P
Body mass index, kg/m^2	30.7 ± 6.7	29.5 ± 5.6	0.18
Body mass index classification			0.22
Underweight, n (%)†	1 (2)	0	-
Normal weight, n (%)‡	8 (18)	9 (20)	-
Overweight, n (%)§	11 (25)	18 (41)	-
Obese, n (%)¶	23 (53)	16 (37)	-
Fat mass parameters	-	-	-
Total fat mass, kg	26.8 ± 12.0	25.3 ± 10.2	0.26
Adiposity, %	33.7 ± 10.3	32.1 ± 9.6	0.23
Fat mass index, kg/m^2	10.7 ± 5.0	9.8 ± 4.4	0.18
Android fat mass, g	2400.4 ± 1249.4	2152.8 ± 952.9	0.15
Visceral adipose tissue (VAT), g	685.8 ± 306.1	581.2 ± 235.6	0.04
Visceral adipose tissue (VAT), cm^2	142.2 ± 63.5	119.8 ± 49.5	0.03
Visceral adipose tissue (VAT), cm^3	741.3 ± 331.0	628.4 ± 254.6	0.04

*Values are expressed in mean SD and percentage unless otherwise indicated; *GPA* Granulomatosis with polyangiitis; †BMI < 18.50 kg/m^2 ; ‡BMI 18.50–24.99 kg/m^2 ; § BMI 25.00–29.99 kg/m^2 ; ¶BMI ≥ 30 kg/m^2

Table 3 Anthropometric dual x-ray absorptiometry–derived body composition characteristics, inflammatory markers and treatment for GPA patients with median VAT ≥ 768 g vs. VAT, < 768 g

	VAT ≥ 768 g (n = 22)	VAT < 768 g (n = 21)	P
Body mass index, kg/m^2	34.7 ± 5.2	26.6 ± 5.6	**< 0.01**
Body mass index classification			**< 0.001**
Underweight, n (%)†	0 (0)	1 (4)	-
Normal weight, n (%)‡	0 (0)	8 (38)	-
Overweight, n (%)§	4 (18)	7 (34)	-
Obese, n (%)¶	18 (82)	5 (24)	-
Inflammatory markers	-	-	-
CRP, mg/L	7.9 ± 12.3	4.3 ± 5.7	0.11
ESR, mm/1st hour	22.8 ± 26.8	11.6 ± 11.3	**0.04**
GPA disease characteristics	-	-	-
Disease duration, yrs	6.3 ± 4.1	8.6 ± 4.8	**0.049**
Generalized form, n (%)	13 (59)	14 (67)	0.75
Localized form, n (%)	9(41)	7 (33)	0.75
All GPA (n = 43), n (%)	22 (51)	21 (49)	**< 0.01**
ANCA, n (%)	11 (50)	9 (43)	0.76
BVAS	3.2 ± 4.1	0.9 ± 1.7	**0.01**
VDI	5.2 ± 2.5	4.5 ± 2.3	0.19
Current GPA treatment	-	-	-
Prednisone, n (%)	11 (50)	12 (57)	0.76
Prednisone dose,mg/day	12.2 ± 19.5	9.4 ± 13.4	0.30
Trimethoprim-sulfamethoxazole, n (%)	15 (68)	15 (71)	1.00
Immunosuppressive, n (%)	16 (73)	16 (76)	1.00
Rituximab, n (%)	2 (09)	4 (19)	0.41
Cumulative prednisone, last 3 yrs, mg	6178 ± 7196	6125 ± 9073	0.49

*Values are expressed in mean SD and percentage unless otherwise indicated; *VAT* visceral adipose tissue; *GPA* granulomatosis with polyangiitis; *BVAS* Birmingham Vasculitis Activity Score; *VDI* Vasculitis Damage Index; †BMI < 18.50 kg/m$^{2;}$ ‡BMI 18.50–24.99 kg/m^2 ; §BMI 25.00–29.99 kg/m^2 ; ¶BMI ≥ 30 kg/m^2

[25]. The exact gain in fat mass and VAT due to glucocorticoids is not well defined, nor is the extent to which this increase alters disease control. In our study, we did not find that patients with more VAT, g had significantly higher use of glucocorticoid cumulative dose or higher current glucocorticoid use.

Comparing the group of patients with GPA with higher values of VAT, with those with lower values, we observed that the first group had higher values of BVAS, reflecting greater disease activity. Ahn et al evaluated 117 patients with AAV, 28 of them with GPA, in relation to BC, using computed tomography. The authors observed that VAT was significantly correlated with age, BMI and BVAS in patients with AAV. In addition, high VAT was independently associated with all-cause mortality in these patients (OR, 7.13; 95% CI, 1.34–37.94; p = 0.02) [26].

In our patients, higher values of ESR were demonstrated in patients with GPA with higher VAT, suggesting that patients with more VAT produce a greater quantity of inflammatory mediators and consequently have greater disease activity. We also found that patients with longer disease had lower levels of VAT. One hypothesis for this finding is that the chronic metabolic stress induced by longer disease promoted lipolysis in VAT, since this visceral tissue is more sensitive to adrenergic stimulation, i.e., more susceptible to catecholamine-induced lipolysis [27].

The limitations of this study were mainly the small number of GPA patients analyzed, since this disease is rare even in a tertiary center.

Our study also demonstrated that the amount of VAT in patients with GPA is associated with disease duration, disease activity, and inflammatory markers. This finding shows new applicability of bone densitometry (DXA) in the assessment of body composition with VAT analysis in immune-inflammatory diseases, herein in patients with GPA. Longitudinal studies are necessary in relation to treatment with immunosuppressants, reduction of inflammatory parameters, and possible decrease in VAT values.

Funding Programa de Iniciação Científica e de Iniciação em Desenvolvimento Tecnológico e Inovação da USP (PIBIC) (P.L.F.); Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305556/2017-7 (R.M.R.P).

Data availability The data used in this study is available under considerations of patient privacy principles.

Compliance with ethical standards

Ethics approval The study was approved by the Research Ethics Committee of Clinics Hospital, University of Sao Paulo, School of Medicine, under the following number: 2.723.911.

Disclosures None.

Consent of participate All participants enrolled in the study signed a full consent form, previous approved by our local Ethics Committee.

Code availability Not applicable

References

1. Flossmann O, Berden A, de Groot K, Hagen C, Harper L, Heijl C, Höglund P, Jayne D, Luqmani R, Mahr A, Mukhtyar C, Pusey C, Rasmussen N, Stegeman C, Walsh M, Westman K, Group EVS (2011) Long-term patient survival in ANCA-associated vasculitis. Ann Rheum Dis 70(3):488–494. https://doi.org/10.1136/ard.2010.137778
2. Lutalo PM, D'Cruz DP (2014) Diagnosis and classification of granulomatosis with polyangiitis (aka Wegener's granulomatosis). J Autoimmun 48-49:94–98. https://doi.org/10.1016/j.jaut.2014.01.028
3. Blumberg MJ, Tung CI, May LA, Patel SP (2017, 2017) Granulomatosis with polyangiitis: seeing the diagnosis. BMJ Case Rep. https://doi.org/10.1136/bcr-2016-218030
4. Seo P, Stone JH (2004) The antineutrophil cytoplasmic antibody-associated vasculitides. Am J Med 117(1):39–50. https://doi.org/10.1016/j.amjmed.2004.02.030
5. George MD, Giles JT, Katz PP, England BR, Mikuls TR, Michaud K, Ogdie-Beatty AR, Ibrahim S, Cannon GW, Caplan L, Sauer BC, Baker JF (2017) Impact of obesity and adiposity on inflammatory markers in patients with rheumatoid arthritis. Arthritis Care Res (Hoboken) 69(12):1789–1798. https://doi.org/10.1002/acr.23229
6. Kuznetsova E, Novikov P, Moiseyev S (2013) SAT0180 Cardiovascular risk in granulomatosis with polyangiitis (Wegener'S) of different severity and duration. Ann Rheum Dis 72:A642–A6A642. https://doi.org/10.1136/annrheumdis-2013-eular.1906
7. Navarro-Millán I, Yang S, DuVall SL, Chen L, Baddley J, Cannon GW, Delzell ES, Zhang J, Safford MM, Patkar NM, Mikuls TR, Singh JA, Curtis JR (2016) Association of hyperlipidaemia, inflammation and serological status and coronary heart disease among patients with rheumatoid arthritis: data from the National Veterans Health Administration. Ann Rheum Dis 75(2):341–347. https://doi.org/10.1136/annrheumdis-2013-204987
8. Mantel Ä, Holmqvist M, Nyberg F, Tornling G, Frisell T, Alfredsson L, Askling J (2015) Risk factors for the rapid increase in risk of acute coronary events in patients with new-onset rheumatoid arthritis: a nested case-control study. Arthritis Rheumatol 67(11):2845–2854. https://doi.org/10.1002/art.39267
9. Zhang J, Chen L, Delzell E, Muntner P, Hillegass WB, Safford MM, Millan IY, Crowson CS, Curtis JR (2014) Republished: the association between inflammatory markers, serum lipids and the risk of cardiovascular events in patients with rheumatoid arthritis. Postgrad Med J 90(1070):722–729. https://doi.org/10.1136/postgradmedj-2013-204715rep
10. Luqmani R, Suppiah R, Edwards CJ, Phillip R, Maskell J, Culliford D, Jayne D, Morishita K, Arden N (2011) Mortality in Wegener's granulomatosis: a bimodal pattern. Rheumatology (Oxford) 50(4):697–702. https://doi.org/10.1093/rheumatology/keq351
11. Westhovens R, Nijs J, Taelman V, Dequeker J (1997) Body composition in rheumatoid arthritis. Br J Rheumatol 36(4):444–448. https://doi.org/10.1093/rheumatology/36.4.444
12. Alexopoulos N, Katritsis D, Raggi P (2014) Visceral adipose tissue as a source of inflammation and promoter of atherosclerosis. Atherosclerosis 233(1):104–112. https://doi.org/10.1016/j.atherosclerosis.2013.12.023
13. Nakamura T, Tokunaga K, Shimomura I, Nishida M, Yoshida S, Kotani K, Islam AH, Keno Y, Kobatake T, Nagai Y (1994) Contribution of visceral fat accumulation to the development of coronary artery disease in non-obese men. Atherosclerosis 107(2):239–246. https://doi.org/10.1016/0021-9150(94)90025-6
14. Grönhagen-Riska C, Teppo AM, Honkanen E, Ikäheimo R (1993) Alpha-1-antitrypsin, CRP and interleukin-6 in ANCA-positive vasculitis. Adv Exp Med Biol 336:337–340. https://doi.org/10.1007/978-1-4757-9182-2_55
15. Leavitt RY, Fauci AS, Bloch DA, Michel BA, Hunder GG, Arend WP, Calabrese LH, Fries JF, Lie JT, Lightfoot RW (1990) The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. Arthritis Rheum 33(8):1101–1107. https://doi.org/10.1002/art.1780330807
16. Giles JT, Ling SM, Ferrucci L, Bartlett SJ, Andersen RE, Towns M, Muller D, Fontaine KR, Bathon JM (2008) Abnormal body composition phenotypes in older rheumatoid arthritis patients: association with disease characteristics and pharmacotherapies. Arthritis Rheum 59(6):807–815. https://doi.org/10.1002/art.23719
17. Jensen MD, Kanaley JA, Reed JE, Sheedy PF (1995) Measurement of abdominal and visceral fat with computed tomography and dual-energy x-ray absorptiometry. Am J Clin Nutr 61(2):274–278. https://doi.org/10.1093/ajcn/61.2.274
18. Stone JH, Hoffman GS, Merkel PA, Min YI, Uhlfelder ML, Hellmann DB, Specks U, Allen NB, Davis JC, Spiera RF, Calabrese LH, Wigley FM, Maiden N, Valente RM, Niles JL, Fye KH, McCune JW, St Clair EW, Luqmani RA, (INSSYS) INftSotSV (2001) A disease-specific activity index for Wegener's granulomatosis: modification of the Birmingham Vasculitis Activity Score. International Network for the Study of the Systemic Vasculitides (INSSYS). Arthritis Rheum 44(4):912–920.
19. van der Woude FJ, Rasmussen N, Lobatto S, Wiik A, Permin H, van Es LA, van der Giessen M, van der Hem GK, The TH (1985) Autoantibodies against neutrophils and monocytes: tool for diagnosis and marker of disease activity in Wegener's granulomatosis. Lancet 1(8426):425–429. https://doi.org/10.1016/s0140-6736(85)91147-x
20. Exley AR, Bacon PA, Luqmani RA, Kitas GD, Gordon C, Savage CO, Adu D (1997) Development and initial validation of the Vasculitis Damage Index for the standardized clinical assessment of damage in the systemic vasculitides. Arthritis Rheum 40(2):371–380. https://doi.org/10.1002/art.1780400222
21. Giles JT, Bartlett SJ, Andersen R, Thompson R, Fontaine KR, Bathon JM (2008) Association of body fat with C-reactive protein in rheumatoid arthritis. Arthritis Rheum 58(9):2632–2641. https://doi.org/10.1002/art.23766
22. Le Jemtel TH, Samson R, Milligan G, Jaiswal A, Oparil S (2018) Visceral adipose tissue accumulation and residual cardiovascular risk. Curr Hypertens Rep 20(9):77. https://doi.org/10.1007/s11906-018-0880-0
23. Delgado-Frías E, González-Gay MA, Muñiz-Montes JR, Gómez Rodríguez-Bethencourt MA, González-Díaz A, Díaz-González F, Ferraz-Amaro I (2015) Relationship of abdominal adiposity and body composition with endothelial dysfunction in patients with rheumatoid arthritis. Clin Exp Rheumatol 33(4):516–523

24. Özer Gökaslan Ç, Aslan E, Demirel E, Yücel A (2020) Relationship of mesenteric panniculitis with visceral and subcutaneous adipose tissue. Turk J Med Sci 50(1):44–48
25. Wallace ZS, Miloslavsky EM, Cascino M, Unizony SH, Lu N, Hoffman GS, Kallenberg CGM, Langford CA, Merkel PA, Monach PA, Seo P, Spiera R, St Clair EW, Specks U, Brunetta P, Choi HK, Stone JH (2017) Effect of disease activity, glucocorticoid exposure, and rituximab on body composition during induction treatment of antineutrophil cytoplasmic antibody-associated vasculitis. Arthritis Care Res (Hoboken) 69(7):1004–1010. https://doi.org/10.1002/acr.23099
26. Ahn SS, Yoo BW, Kwon HC, Yoo J, Jung SM, Song JJ, Park YB, Lee SW (2020) Evaluation of body composition using computed tomography in patients with anti-neutrophil cytoplasmic antibody-associated vasculitis. Korean J Intern Med. https://doi.org/10.3904/kjim.2020.064
27. Ibrahim MM (2010) Subcutaneous and visceral adipose tissue: structural and functional differences. Obes Rev 11(1):11–18. https://doi.org/10.1111/j.1467-789X.2009.00623.x