Abdominal adipose tissue predicts major cardiovascular events in systemic necrotising vasculitides

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ABSTRACT

Objective. *Cardiovascular (CV) events are highly prevalent in systemic necrotising vasculitides (SNV). Visceral/subcutaneous adipose tissue (VAT/SAT) ratio has been shown to be associated with CV events in various diseases. We aimed to assess the relevance of abdominal adipose tissue measurement to predict major CV events (MCVEs) in SNV.*

Methods. *Patients with SNV were successively included in a longitudinal study assessing MCVEs and other sequelae. Dual x-ray absorptiometry was performed to evaluate abdominal adipose tissue. Patients were prospectively followed for MCVEs, defined as myocardial infarction, unstable angina, stroke, arterial revascularisation and/or hospitalisation for or death from CV causes.*

Results. *One hundred and twenty consecutive SNV patients were included and analysed (54 males, mean age 53±18 years). High CV risk was found in 28 (23.3%) patients. In univariate analysis, age, male gender, VDI, VAT/SAT ratio and serum troponin level were significantly associated with high CV risk, whereas age and VAT/SAT ratio remained independently associated with high CV risk. Variables associated with high tertile of VAT/SAT ratio included age and metabolic risk factors. After median follow-up of 42 months, 19 (16%) patients experienced MCVEs. Hazard ratios for incident MCVEs compared with 1st tertile of VAT/SAT ratio were 7.22 (1.02–51.3; p=0.048) and 9.90 (3.15–31.2; p=0.0002) in the 2nd and 3rd tertile, respectively.*

Conclusion. *Abdominal visceral adipose tissue is a reliable surrogate marker of CV risk and predicts incident MCVEs in SNV patients. Abdominal adipose tissue should be probably evaluated routinely in these patients to assess CV risk.*

Introduction

Systemic vasculitides are a group of diseases characterised by inflammation of large, medium- or small-sized blood vessels, leading to multi-organ involvement (1). Among vasculitides, systemic necrotising vasculitides (SNV) may be individualised and include polyarteritis nodosa (PAN) and antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV). Improved therapeutic strategies have transformed most of these acute and life-threatening diseases into chronic ones associated with relapses, organ damage accumulation and long-term treatment toxicity, especially cardiovascular (CV) diseases.

AAV have a significantly increased risk of mortality, ischaemic stroke, and coronary artery disease (2, 3), cardiovascular disease being the leading cause of death after the first year from diagnosis, representing roughly 25–30% of cases (4, 5). This long-term CV-related morbidity and mortality may be the consequence of premature atherosclerosis. Experimental data showed that arterial inflammation attributable to Th1 and Th17 cell infiltration and systemic inflammation were associated with accelerated subclinical atherosclerosis (6, 7). Also, epidemiological studies showed higher frequency of subclinical atherosclerosis in patients with SNV with higher frequency of plaque in the carotid artery and aorta compared to controls, independently of CV risk factors and systemic inflammation (8-10). Presence of other CV risk factors such as diabetes, hypertension, dyslipidemia and abdominal obesity (metabolic syndrome) are common in SNV patients (11). Furthermore, increased body mass index (BMI) was found to be associated with major CV events in SNV (10). However, there is no data about body composition abnormalities, *i.e.* increase

in fat mass and visceral abdominal adiposity, in SNV. In other chronic inflammatory diseases such as rheumatoid arthritis, decreased lean mass and increased fat mass were reported (12), and abdominal adiposity is emerging as a reliable cardiometabolic risk factor (13). Body fat tissue includes two compartments, *i.e.* subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT), with distinct metabolic characteristics. Visceral adipose tissue is associated with insulin resistance and CV disease, and releases various bioactive molecules and hormones, such as adiponectin, leptin, TNF-α and IL-6 (14). Dual energy x-ray absorptiometry (DXA) is a validated technique able to accurately determine body composition, less expensive and more accessible (15) than computed tomography and magnetic resonance imaging (16).
The aim of this study was to assess the relevance of abdominal adipose tissue measurement as potential surrogate markers for CV risk and a predictor of major CV events (MCVEs) in patients with SNV.

Methods

Participants.
Between January 2014 and May 2015, 120 consecutive patients with ANCA-associated vasculitides (AAV) and polyarteritis nodosa (PAN) seen in our Department were successively included in a longitudinal routine care study assessing CV complications and other sequelae, and were prospectively followed-up (OSTEOVAS cohort). Patients with systemic vasculitis fulfilled the American College of Rheumatology (ACR) criteria for PAN, granulomatosis with polyangiitis (GPA, formerly called Wegener's granulomatosis) and eosinophilic granulomatosis with polyangiitis (EGPA, formerly called Churg-Strauss syndrome), and/or the European Medicines Agency (EMA) algorithm and/or Chapel Hill definitions for all vasculitides including microscopic polyangiitis (MPA) (1, 17-20). Patient's informed consent was obtained from all patients.

Clinical variables and ongoing treatments
Clinical assessment included age, gender, disease duration defined as the time elapsed between the onset of first disease-related symptoms and enrolment. The activity of SNV was assessed by the Birmingham Vasculitis Activity Score (BVAS), version 3 (21) and the damage by the Vasculitis Damage Score (VDI) score (22). Glucocorticoid treatment (current dose, cumulative dose of prednisone equivalent), immunosuppressive or immunomodulatory agents, CV therapies (aspirin, statins) were collected using a predefined questionnaire filled by the physicians. Biological parameters including ANCA status and specificity [categorised as proteinase 3 (PR3)-ANCA or myeloperoxidase (MPO)-ANCA], C-reactive protein, glucose and lipids parameters, nutrition status and troponin were available at the time of the assessment.

Cardiovascular risk factor assessment
Hypertension was defined as blood pressure ≥140/90 mmHg or the use of antihypertensive drugs. Total cholesterol, high-density lipoprotein cholesterol after precipitation of low-density lipoprotein (LDL) and very LDL cholesterol, and triglycerides were measured enzymatically after overnight fasting. LDL cholesterol was calculated using the Friedewald formula. Hypercholesterolemia was defined as total cholesterol ≥5.18 mmol/L, LDL cholesterol ≥3.30 mmol/L, or use of lipid-lowering drugs. Current smoking was defined as at least 1 cigarette smoked within the month before inclusion. Blood glucose was measured enzymatically. Diabetes mellitus was defined as fasting blood glucose ≥7 mmol/L or use of drugs for diabetes.
High cardiovascular risk was defined according to the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATPIII) guidelines as: the presence of a known personal history of CV diseases, including all types of documented coronary, cerebrovascular, or peripheral arterial disease; diabetes mellitus; or a Framingham Risk Score ≥ 20% at 10 years (23).
During follow-up, MCVEs, defined as myocardial infarction, unstable angina, stroke, arterial revascularisation and/or hospitalisation for or death from CV causes, were recorded.

Body composition and abdominal adipose tissue measurements
Height (in cm) and weight (in kg) were measured per standardised protocols. BMI was calculated from weight/height^2 (kg/m^2). Obesity was defined by BMI value greater than 30. Body composition [fat mass (kg and %) and lean mass (kg)] was measured using DXA (Hologic®, QDR 4500A, Bedford, MA) from the whole-body scan. Adipose tissue was calculated in a region of interest, automatically placed by the software and limits were manually defined. Manual delineation is used to position the right and left heights limiting the skin as well as the outer and the inner muscle edges. This technique leads to separation of subcutaneous adipose tissue (SAT), intramuscular adipose tissue and visceral adipose tissue (VAT), respectively. The ratio of VAT/SAT was calculated. Images were analysed by one reader, following a standardised protocol. Interobserver reproducibility was previously assessed by the analysis of VAT on 30 DXA whole body scans with an Intra Class Correlation coefficient of 0.996 (CI 95% 0.992-0.998) (24).

Statistical analysis
Descriptive statistics were performed for baseline characteristics. For variables that were normally distributed, mean±SD was calculated. For categorical variables, counts and percentages were calculated. Univariate analysis and multivariate analysis using logistic regression were performed to identify factors associated with high cardiovascular risk (according to the NCEP-ATPIII guidelines). Due to the low number of patients with high CV risk, multivariate logistic regression analyses were also performed by backward selection, (removing variables that showed an association with the outcome measure with a *p*-value above 0.10) and by a model with the selection of 3 relevant variables (age, male gender and VAT/SAT ratio). Then, receiver operating characteristics (ROC) curves were plotted to assess the interest of VAT/SAT ra-

tio for the identification of patients with high CV risk. Variables associated with high tertile of VAT/SAT were assessed by univariate and multivariate logistic regression in the whole population and in men and women. Kaplan-Meier MCVEs-free survival curves were also plotted and compared with the log-rank test. A p-value <0.05 was considered statistically significant. All the analyses were performed on the SAS software (v. SAS 9.4).

Results

Patients' characteristics

One hundred and twenty consecutive patients with primary SNV were analysed (66 females and 54 males, mean age 53.2±18.0 years, with mean disease duration of 78.2±82.9 months). Patients' characteristics are summarised in Table I. Diagnoses included GPA in 61 patients, EGPA in 30, PAN in 14 and MPA in 13. For 2 patients, diagnosis of cryoglobulinaemia vasculitis was finally retained. One hundred and three (85.8%) patients were receiving glucocorticoids, with a median daily dose of prednisone of 8.5 (range, 0-80) mg/day and an estimated total cumulative dose of 14,999±10,014 mg at the time of assessment. Mean number of items from the VDI was 2.40±2.1, including disease-related items only in 53 (44%), treatment-related items only in 15 (13%), and both in 33 (28%). Main disease-related items were peripheral neuropathy, renal failure, nasal blockage/chronic discharge/crusting, chronic asthma and impaired lung function. Main treatment-related items were osteoporosis/vertebral collapse, significant muscle atrophy or weakness, angina or myocardial infarction and hypertension requiring antihypertensive drugs. Results of body composition and abdominal adipose tissue measurements are indicated in Supplementary Table SI.

Table I. Baseline characteristics of the 120 patients with primary SNV.

Variables	All patients (n=120)
Demography	
Age, yrs, mean (SD)	53.2 (18.0)
Male gender, n (%)	54 (45.0)
Disease duration, months, mean (SD)	78.2 (82.8)
Vasculitis characteristics	
BVAS, mean (SD)	4.45 (7.9)
VDI, mean (SD)	2.40 (2.1)
MPO-ANCA, n (%)	25 (20.8%)
PR3-ANCA, n (%)	44 (36.7%)
Current therapies	
Use of glucocorticoids, n (%)	103 (85.8)
Daily dose of glucocorticoids, mg/d, mean (SD)	18.6 (21.8)
Cumulative dose of glucocorticoids, mg, mean (SD)	14,999 (10,014)
Current immunosuppressive agents, n (%)	87 (72.5)
Statins, n (%)	18 (15.0)
Anti-platelets, n (%)	21 (17.5)
Cardiovascular risk factors	
Hypertension, n (%)	53 (44.2)
Total cholesterol, mmol/L, mean (SD)	2.18 (0.53)
LDL cholesterol, mmol/L, mean (SD)	1.20 (0.46)
HDL cholesterol, mmol/L, mean (SD)	0.72 (0.29)
Triglycerides, mmol/L, mean (SD)	1.36 (0.67)
Current smoking, n (%)	10 (8.3)
Diabetes, n (%)	11 (9.2)
BMI, kg/m^2, (mean ±SD)	25.4 (4.9)
BMI ≥30 kg/m^2, n (%)	21 (17.5)
Known history of cardiovascular disease, n (%)	16 (13.3)
10-year Framingham Risk Score ≥ 20%, n (%)	9 (7.5)
HBA1c, mean (SD)	5.70 (0.81)
Other biological parameters	
CRP, mg/L, mean (SD)	10.4 (19.9)
CRP ≥5 mg/L, n (%)	43 (37.4)
Troponin, pg/mL, mean (SD)	13.5 (19.6)

ANCA: antineutrophil cytoplasm antibodies; BMI: body mass index; BVAS: Birmingham Vasculitis Activity Score; CRP: C-reactive protein; MPO: myeloperoxidase; PR3: proteinase 3; SD: standard deviation; VDI: Vasculitis Damage Index.

Variables associated with high CV risk

High CV risk defined by the NCEP-ATPIII guidelines was found in 28 (23.3%) patients, including 16 (13.3%) patients with previous CV disease, 11 (9.2%) patients with diabetes and 9 patients (7.5%) with a Framingham cardiovascular risk score ≥20%.

Variables associated with high CV risk in univariate and multivariate analysis are indicated in Table II. In univariate analysis, age, male gender, VDI, VAT, VAT/SAT ratio, and serum troponin levels were significantly associated with high cardiovascular risk according to NCEP-ATPIII guidelines. High CV risk was not statistically different among the types of SNV. No variable remained independently associated with high CV risk in multivariate analysis, even if male gender and increased VAT/SAT ratio seemed to have the highest weights in the model. Using a backward stepwise selection model and a model with selection of the most relevant variables, VAT/SAT ratio was significantly associated with high CV risk in the first model, while age was independently associated with high CV risk with a tendency for VAT/SAT ratio in the second model (Table II). VAT/SAT ratio was significantly higher in patients with high CV risk (median 65.0 *vs*. 37.1% in those with low CV risk, p<0.0001), and especially in those with previous CV disease (median 76.4%) (Suppl. Fig. 1). Framingham CV risk score was also strongly correlated with VAT/SAT ratio (r^2=+0.36, p<0.0001), especially in men (r^2=+0.37, p<0.0001) rather than in women (r^2=+0.11, p=0.01) (Fig. 1). Receiver operating characteristic (ROC) curve analysis showed that area under the curve of VAT/SAT ratio for identification of high CV patients was statistically significant for men but not for women. Optimal cut-off values of VAT/SAT ratio to identify high CV patients in men were 56% with sensitiv-

Table II. Variables associated with high cardiovascular risk according to NCEP-ATPIII.

	Univariate analysis		Multivariate analysis	
Variables	OR (CI 95%)	*p* value	OR (CI 95%)	*p*-value
Demography				
Age	1.057 [1.025 – 1.090]	0.0004	1.04 [0.99 – 1.10]	0.1005
Male gender	4.265 [1.695 – 10.730]	0.002	2.41 [0.38 – 15.09]	0.3474
Disease duration	0.999 [0.994 – 1.004]	0.76		
Vasculitis characteristics				
BVAS	1.012 [0.961 – 1.065]	0.65		
VDI	1.376 [1.126 – 1.681]	0.002	1.03 [0.75 – 1.43]	0.8395
MPO-ANCA	1.000 [0.325 – 3.077]	0.84		
PR3-ANCA	0.814 [0.306 – 2.167]	0.66		
Current therapies				
Daily dose of GCs	1.007 [0.988 – 1.026]	0.46		
GCs cumulative dose	1.276 [0.830 – 1.962]	0.26		
Body composition				
BMI	1.015 [0.932 – 1.105]	0.73		
Waist perimeter	1.026 [0.991 – 1.062]	0.14		
VAT	1.009 [1.003 – 1.015]	0.005		
SAT	0.997 [0.993 – 1.001]	0.12		
VAT/SAT ratio	1.066 [1.037 – 1.095]	<0.0001	1.03 [0.99 – 1.09]	0.1595
Fat mass	0.986 [0.939 – 1.036]	0.57		
Appendicular lean mass	1.018 [0.974 – 1.064]	0.43		
Total Cholesterol	0.593 [0.248 – 1.417]	0.35		
LDL Cholesterol	0.559 [0.204 – 1.526]	0.26		
HDL Cholesterol	0.376 [0.072 – 1.954]	0.24		
Triglyceride	2.382 [1.244 – 4.563]	0.009	1.15 [0.49 – 2.73]	0.7454
Biological parameters				
CRP	1.017 [0.998 – 1.037]	0.09		
Troponin	1.040 [1.009 – 1.072]	0.01	1.00 [0.97 – 1.03]	0.9659
Backward stepwise selection				
Variables	OR (CI 95%)	*p*-value		
Demography				
Age	-	-		
Male gender	-	-		
VDI	-	-		
VAT/SAT ratio	1.07 [1.04 – 1.09]	<0.0001		
Triglyceride	-	-		
Troponin	-	-		
Relevant variables selection				
Variables	OR (CI 95%)	*p*-value		
Age	1.06 [1.01 – 1.11]	0.018		
Male gender	3.41 [0.60 – 19.33]	0.166		
VAT/SAT ratio	1.03 [0.99 – 1.08]	0.071		

ANCA: antineutrophil cytoplasm antibodies; BMI: body mass index; BVAS: Birmingham Vasculitis Activity Score; CRP: C-reactive protein; GCs: glucocorticoids; MPO: myeloperoxidase; PR3: proteinase 3; SD: standard deviation; SAT: subcutaneous adipose tissue; VAT: visceral adipose tissue; VDI: Vasculitis Damage Index.

ity and specificity of 94.4% (95% CI 72.7–99.9%) and 55.9% (95% CI 37.9–72.8%), respectively, and 70% with sensitivity and specificity of 61.1% (95% CI 35.8–82.7%) and 88.2% (95% CI 72.6–96.7%), respectively (Suppl. Fig. 2).

Variables associated with high tertile of VAT/SAT ratio

Because of the impact of gender on VAT/SAT value, analyses were performed separately in women and men. Frequency of specific conditions and serum levels according to each tertile are indicated in Figure 2. In women, variables associated with high tertile of VAT/SAT ratio (*i.e.* VAT/SAT ratio >34.7%) were age, VDI, BMI, hypertension and HbA1c in univariate analysis, and age, BMI and HbA1c in multivariate analysis (Suppl. Table S2 and Table III). In men, variables associated with high tertile of VAT/SAT ratio (*i.e.* VAT/SAT ratio >65.2%) were age, BVAS, VDI, diabetes, previous history of CV disease, serum troponin and triglyceride levels in univariate analysis, and age and VDI in multivariate analysis (Suppl. Table S3 and Table III).

Incident MCVEs and association with VAT/SAT ratio at baseline

After median follow-up of 42 months,

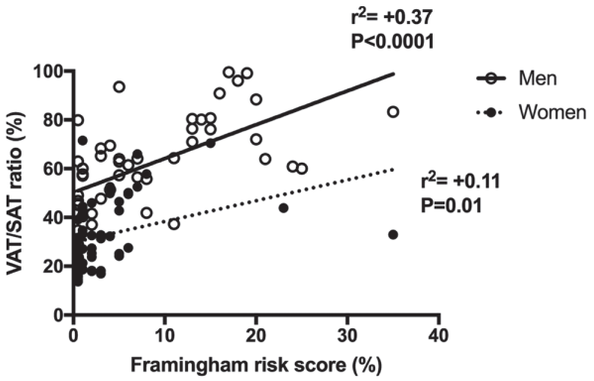

Fig. 1. Correlations between VAT/SAT ratio and 10-year cardiovascular Framingham risk score in men and women.

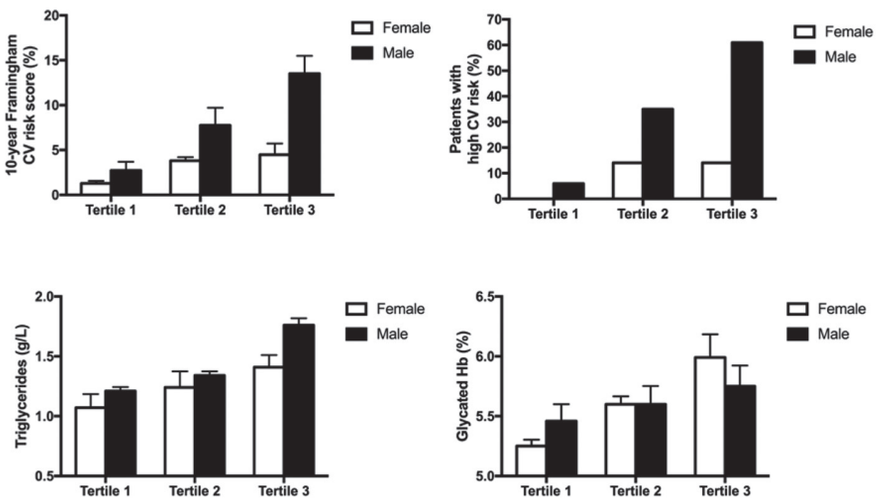

Fig. 2. Percentages and/or values of specific variables according to tertiles of VAT/SAT ratio. Females are indicated in white and males in black.

Table III. Multivariate analysis associated with high tertile of VAT/SAT in women (*i.e.* >34.7%) and in men (*i.e.* >65.2%).

Variables	OR (CI 95%)	*p*-value
Variables associated with high tertile of VAT/SAT (*i.e.*> 34.7%) in women		
Multivariate analysis		
Age (years)	1.041 [0.982 – 1.104]	0.1773
VDI score	1.357 [0.722 – 2.551]	0.3428
BMI (kg/m²)	**1.424 [1.112 – 1.825]**	**0.0052**
Hypertension	4.612 [0.694 – 30.633]	0.1136
HbA1c	**23.590 [1.127 – 493.557]**	**0.0416**
Backward selection		
Age (years)	1.067 [1.017 – 1.119]	**0.0080**
BMI (Kg/m²)	1.326 [1.108 – 1.585]	**0.0020**
Variables associated with high tertile of VAT/SAT (*i.e.*> 65.2%) in men		
Multivariate analysis		
Age (years)	1.110 [0.984 – 1.252]	0.0890
BVAS score	1.074 [0.872 – 1.324]	0.5016
VDI score	**1.791 [1.099 – 2.917]**	**0.0193**
Troponin	1.059 [0.950 – 1.181]	0.3042
Triglycerides	1.068 [0.299 – 3.813]	0.9191
Diabetes	33.975 [0.130 – 999]	0.2145
Previous history of CV disease	1.437 [0.087 – 23.604]	0.7996
Backward selection		
Age (years)	**1.145 [1.043 – 1.258]**	**0.0046**
VDI score	**1.782 [1.164 – 2.727]**	**0.0078**

19 (16%) patients experienced MCVEs: arterial revascularisation for 6 (including 4 with myocardial infarction or unstable angina), stroke for 5, hospitalisation for CV causes for 5 and 3 CV-caused deaths. Tertiles of VAT/SAT ratio in each gender were significantly associated with incident MCVEs (p<0.0001; logrank test and logrank test for trend). Hazard ratios (95% CI) for incident MCVEs compared with 1st tertile were 7.22 (1.02-51.3; p=0.048) and 9.90 (3.15-31.2; p=0.0002) in the 2nd and 3rd tertiles, respectively (Fig. 3). In contrast, age >65 years (HR 1.98 [0.72-5.43]; p=0.19) and body mass index >30 kg/m² (HR 1.37 [0.41-4.61]; p=0.61) were not associated with higher cumulative incident MCVEs (data not shown). VAT/SAT ratio remained associated with incident MCVEs even for only patients >65 years (p=0.07, logrank test; and p=0.03 logrank test for trend) (Fig. 3).

Discussion

Identification of reliable tools to predict the CV risk in patients with SNV is a therapeutic challenge, since CV disease has been shown to be the first cause of death (4). In the present study, we addressed for the first time the relevance of abdominal adipose tissue measurement as a potential surrogate marker for CV risk and predictor of MCVEs in SNV patients, and showed a significant association between a high DXA-assessed VAT/SAT ratio, CV risk and incident MCVEs in SNV patients.

We previously showed that increased BMI was associated with incident MCVEs in SNV patients (10). Even if BMI is the currently recommended adiposity-related biomarker for identifying individuals at increased risk of CV disease (25), BMI has several limitations, illustrating the need for new adiposity-related biomarkers (26, 27). DXA-assessed VAT/SAT ratio has been explored in various conditions but never so far in SNV. DXA is increasingly used to estimate VAT and SAT with the added benefits that it circumvents many of the limitations of CT and MRI, including prolonged scan time, high cost, and radiation (26). DXA also demonstrates excellent reproducibility

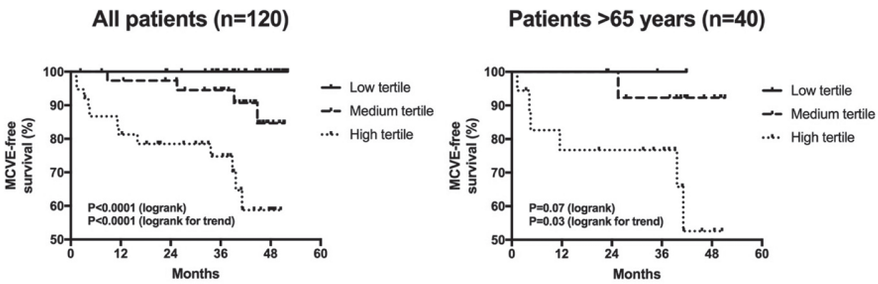

Fig. 3. MCVEs-relapse free survival curves according to tertiles of VAT/SAT ratio.
The highest VAT/SAT ratio in each gender was significantly associated with higher cumulative incidence of MCVEs (p<0.0001; logrank test and logrank test for trend). Hazard ratios (95% CI) for incident MCVE compared with 1st tertile were 7.22 (1.02-51.3; p=0.048) and 9.90 (3.15-31.2; p=0.0002) in the 2nd and 3rd tertile, respectively (left panel). The highest VAT/SAT ratio remained associated with incident MCVEs even for only patients >65 years (p=0.07, logrank test; and p=0.03 logrank test for trend) (right panel).

and repeatability in daily practice, especially in obese and diabetic populations (28, 29), and it has been shown that higher VAT mass was associated with increased risk of developing type 2 diabetes (30) and CV disease (31), independently of BMI. VAT/SAT ratio was also assessed in non-obese patients and patients with low CV risk. VAT/SAT ratio was positively related to arterial inflammation assessed by (18)F-fluorodeoxyglucose PET/CT and was an independent predictor of MCVEs (32).

Although our study was limited by the number of patients in comparison with large cardiovascular studies conducted in obese and diabetic populations, we were able to provide new insights into the relevance of VAT and SAT measurement in SNV. Age and increased VAT/SAT ratio were the main variables associated with high CV risk, suggesting that both variables could be reliably used to identify patients with the highest CV risk. This relationship tended to be independent of gender. However, correlation between Framingham CV risk score and VAT/SAT ratio was much stronger in men than in women. These results were supported by our ROC curve analyses showing that accuracy of VAT/SAT ratio to identify patients with high CV risk was significant for men, while bearing only a tendency for women. This discrepancy is probably related to our study population since performance of VAT/SAT ratio was shown to be powerful for both gender in non-vasculitides patients (33). Another major point could be that the Framingham CV risk score and the CV risk defined by the NCEP-ATPIII may not be accurate predictive scores in SNV patients.

Addressing the variables associated with high VAT/SAT ratio was another important goal of the study, to better identify comorbidities that could increase the CV risk. As in previous studies and because cut-off values for VAT/SAT ratio were different between genders, we analysed separately women and men. We observed that VAT/SAT ratio was significantly associated with hypertension, impaired fasting glucose, diabetes mellitus and metabolic syndrome. These findings are in accordance with data from the Framingham Heart Study which showed in a large population that abdominal visceral adipose tissue was associated with metabolic risk factors (33). We observed that VDI was also significantly associated with the highest tertile of VAT/SAT ratio. This finding could suggest that in SNV, CV risk factors such as hypertension and diabetes could be mainly related to vasculitis treatments. This hypothesis was supported by the long-term data from the European Vasculitis Study Group therapeutic trials, which showed that the most commonly reported items of treatment-related damage were hypertension (41.5%), osteoporosis (14.1%) and diabetes (10.4%) (34).

Glucocorticoid cumulative dose was not associated with high CV risk and VAT/SAT ratio, neither in univariate nor multivariate analyses. The negative impact of long-term glucocorticoids is admitted by all practitioners managing vasculitides, even if longer duration of glucocorticoids were associated with fewer relapses (35). This finding suggests that the benefit/risk balance of glucocorticoids regarding CV risk is probably more complicated to address, especially because controlling arterial and systemic inflammation could decrease inflammation-related atherosclerosis. However, we cannot exclude that the glucocorticoid cumulative dose was under-estimated because of potential self-medication by the patients.

Finally, to confirm the relevance of the VAT/SAT ratio to predict CV disease in SNV, we prospectively followed-up our study population for almost 4 years and analysed the occurrence of incident MCVEs. We observed a dose-effect relationship between tertiles of VAT/SAT ratio and cumulative incidence of MCVEs. Compared to the 1st tertile, the 2nd and 3rd tertiles of VAT/SAT ratio had a 7-fold and a 10-fold increase in the risk of incident MCVEs, respectively. Also, VAT/SAT ratio remained associated with incident MCVEs for patients >65 years. These findings strongly support the relevance of VAT/SAT ratio assessment in SNV patients, even in elderly patients.

In conclusion, measurement of abdominal visceral adipose tissue and especially VAT/SAT ratio seems to be a reliable surrogate marker of CV risk and predict incident MCVEs in SNV patients. Abdominal adipose tissue should be probably evaluated routinely in these patients to assess CV risk.

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