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Correlation between DXA and laboratory parameters in normal weight, overweight, and obese patients

Maria Pilar Aparisi Gómez [a,b], Federico Ponti [c], Daniele Mercatelli [c], Chiara Gasperini [d], Alessandro Napoli [e], Giuseppe Battista [d], Stefano Cariani [f], Giulio Marchesini [g], Alberto Bazzocchi [c,*]

[a] Department of Radiology, Auckland City Hospital, Auckland, New Zealand
[b] Department of Radiology, Hospital Nueve de Octubre, Valencia, Spain
[c] Diagnostic and Interventional Radiology, IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy
[d] Department of Specialized, Diagnostic, and Experimental Medicine, University of Bologna, Sant'Orsola - Malpighi Hospital, Bologna, Italy
[e] Radiology Section, Department of Radiological, Oncological and Anatomopathological Sciences, "Sapienza" University of Rome, Rome, Italy
[f] Obesity Surgery Center, Department of Emergency-Urgency, General Surgery and Transplantation, University of Bologna, Sant'Orsola - Malpighi Hospital, Bologna, Italy
[g] Unit of Metabolic Diseases & Clinical Dietetics, University of Bologna, Sant'Orsola - Malpighi Hospital, Bologna, Italy

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ABSTRACT

Objective: The aim of this study was to review the existence and types of correlations between body composition densitometric parameters and laboratory values associated to cardiometabolic risk.
Methods: We retrospectively analyzed data from 316 individuals in the weight range from normality to super-obesity, submitted to total body dual-energy x-ray absorptiometry (DXA) scans and routine biochemistry at S.Orsola-Malpighi Hospital from June 2010 to March 2014. The study included 182 women, 45.8 ± 13.4 y of age, with a body mass index (BMI) of 31.5 (± 11) kg/m^2 (group F) and 134 men, 45.4 ± 13.6 y of age, with a BMI of 27.6 (± 7.8) kg/m^2 (group M). All patients underwent whole-body scan (Lunar iDXA, GE Healthcare, Madison, WI, USA) and laboratory analysis (blood fasting glucose, total cholesterol, high-density lipoprotein cholesterol, tricylglycerides [TGs], aspartate aminotransferase, and alanine aminotransferase). Correlation between laboratory values and total body and regional fat mass (including visceral adipose tissue [VAT] and subcutaneous adipose tissue in the android region), and lean mass parameters were analyzed with linear and stepwise regressions analysis (significance limit, $P < 0.05$). Receiver operating characteristic curves were performed to assess the accuracy of the best-fit DXA parameter (VAT) to identify at least one laboratory risk factor.
Results: In both groups, BMI and densitometric parameters showed a linear correlation with fasting blood glucose and TG levels and an inverse correlation with high-density lipoprotein cholesterol ($P < 0.05$), whereas no correlation was observed with total cholesterol levels. The only densitometric parameter retained in the final model of stepwise multiple regression was VAT for fasting blood glucose (group F: $\beta = 0.4627$, $P < 0.0001$; group M: $\beta = 0.6221$, $P < 0.0001$) and TG levels (group F: $\beta = 0.4931$, $P < 0.0001$; group M: $\beta = 0.1990$, $P < 0.0261$) independently of BMI. The optimal cutoff points of VAT to identify the presence of at least one laboratory risk factor were >1395 g and >1479 cm^3 for men and >1281 g and >1357 cm^3 for women.
Conclusions: DXA analysis of VAT is associated with selected laboratory parameters used for the evaluation of cardiometabolic risk and could be per se a helpful parameter in the assessment of clinical risk.

Introduction

The number of people affected by obesity is increasing globally [1]. Body mass index (BMI) is widely used for the assessment and quantification of obesity, but is not useful to evaluate the degree of abdominal obesity, which is a risk factor for cardiometabolic pathologies (e.g., metabolic syndrome [MetS], hypertension and type 2 diabetes mellitus) [2–4]. Dual-energy x-ray absorptiometry

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* Corresponding author: Tel.: +39 051 636 6021; Fax: +39 051 636 6280.
E-mail address: abazzo@inwind.it (A. Bazzocchi).

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(DXA) is a valid technique for assessing body composition, as it is able to quantitate whole-body and regional fat mass (FM), lean mass (LM), and bone mineral content (BMC) [5–7].

A new DXA tool has been introduced for the analysis of visceral and subcutaneous adipose tissue (VAT and SAT, respectively) in the android region (a segment of the abdomen comprised between a lower demarcation line joining the superior limits of the iliac crests and an upper demarcation line drawn at a level representing 20% of the distance in between the iliac crests line and the chin). The new DXA tool allows the physician to estimate the SAT and then to subtract it from android total FM to obtain VAT (in grams and volume). DXA-assessed VAT measurement has been validated against computed tomography (CT) in a wide range of age (18–90 y old) and BMI (18–40 kg/m^2) [8], and a strong correlation exists between adipose tissue accumulation, in particular VAT, and the development of obesity-related comorbidities [9–11].

Impaired fasting glucose (IFG), that is, fasting plasma glucose levels in the range of 100 to −125 mg/dL, often is referred to as prediabetes, indicating the relatively high risk for the development of diabetes [12]. IFG should not be viewed as a clinical entity on its own but rather as a risk factor for diabetes as well as cardiovascular disease (CVD) [13]. Moreover, IFG is associated with obesity (especially abdominal or visceral obesity), high tricylglycerides (TGs) or low high-density lipoprotein cholesterol (HDL-C), and hypertension [14].

In the past, waist-to-hip ratio (WHR) was used as reference value to identify abdominal obesity, but in 2008, the World Health Organization (WHO) recognized that waist circumference (WC) per se had a higher predictive value of obesity-related disease risk. During the past years, different indexes based on imaging techniques such as ultrasound (US), CT, magnetic resonance imaging (MRI), and DXA were introduced to measure the severity of obesity [15–19]. However, the predictive value of these indexes to define the cardiometabolic risk compared with anthropometric parameters has not been fully evaluated. To date, only a few studies have analyzed the clinical significance of DXA parameters, and validated sex- and age-specific reference cutoff values for the increase of risk for obesity-related diseases are still lacking.

The primary aim of the present study was to evaluate the correlation among body composition DXA parameters and laboratory values associated with cardiometabolic risk. The secondary aim was to calculate the cutoff value of DXA parameter best predictive of laboratory data in order to define a DXA parameter threshold for cardiometabolic laboratory risk.

Materials and methods

Study design and population

We retrospectively analyzed 316 individuals in the BMI range from normal weight to severe obesity, submitted to total body DXA scans and routine biochemistry at S.Orsola-Malpighi Hospital from June 2010 to March 2014 (Table 1). All participants were white, living in Italy, and were free of symptomatic past or present obesity-related diseases (diabetes and endocrinological/metabolic diseases) and malignant tumors, as well as any additional systemic or organ-related disease.

Exclusion criteria were heavy smoking (>20 cigarettes/d) and risky drinking habits, the use of drugs potentially modifying body composition (BC) and the laboratory parameters (e.g., hormonal therapies), recent diagnostic tests with barium or radiopaque substances, known to alter BC, the presence of surgical hardware implantable devices or foreign bodies, and pregnant women.

All participants completed an informed consent before participation, and the studies were conducted after the approval of the local Institutional Review Board according to the Declaration of Helsinki.

Patients' height and weight were measured while they were barefoot and wearing underwear and a cloth gown, to the nearest 0.1 cm and 0.1 kg, respectively, using a mechanical balance with altimeter (Seca 711, Seca GmBH & Co Kg, Germany). BMI was calculated as weight/height (kg/m^2). All measurements (DXA analysis and laboratory tests) were performed on the same day.

Table 1
Characteristics of study population

	Total (N = 316)	Men (n = 134)	Women (n = 182)
Age (y)	45.6 ± 13.4	45.4 ± 13.6	45.8 ± 13.4
Weight (kg)	84.4 ± 27.4	87.3 ± 26.4	82.2 ± 28
Height (cm)	168.7 ± 10.3	177.7 ± 6.7	162.1 ± 6.9
BMI (kg/m^2)	29.7 ± 9.9	27.6 ± 7.8	31.5 ± 11
FM (kg)	32.4 ± 20.8	26.7 ± 19.7	36.7 ± 20.6
LM (kg)	49.6 ± 11.3	57.9 ± 8.7	43.5 ± 8.7
ALM (g)	23139.4 ± 6131.4	27616.3 ± 4764.9	19867.8 ± 4813.5
VAT (g)	1355.7 ± 1409.1	1543.5 ± 1621	1217.5 ± 1216.4
SAT (g)	1702.4 ± 1472.1	1200.2 ± 1213.5	2072.2 ± 1537.9
VAT/SAT	0.9 ± 0.8	1.3 ± 1	0.5 ± 0.4
VATI	0.5 ± 0.5	0.5 ± 0.5	0.5 ± 0.5
SATI	0.6 ± 0.5	0.4 ± 0.4	0.8 ± 0.6
LMI	17.3 ± 3	18.3 ± 2.3	16.6 ± 3.2
FMI	11.7 ± 7.7	8.4 ± 6	14.1 ± 7.9
ALMI	12 ± 2.9	14.0 ± 2.2	10.5 ± 2.3
%FM	35.8 ± 11.9	27.9 ± 9.9	41.6 ± 9.8
FM/LM	0.6 ± 0.3	0.4 ± 0.2	0.8 ± 0.3
T/L FM	1.6 ± 0.6	1.9 ± 0.6	1.4 ± 0.5
AFM/GFM	0.5 ± 0.3	0.6 ± 0.2	0.4 ± 0.3
Android FM/LM	0.8 ± 0.5	0.6 ± 0.4	0.9 ± 0.6
Fasting glucose (mg/dL)	86.5 ± 17	8616.7	86.9 ± 17.3
Tricylglycerides (mg/dL)	107.3 ± 62	115 ± 16.2	101.6 ± 54.6
HDL cholesterol (mg/dL)	58.8 ± 17.8	52.8 ± 14.1	62.1 ± 18.8
Total cholesterol (mg/dL)	195.1 ± 35.6	192.3 ± 34.2	197.3 ± 36.6
AST (mg/dL)	21.7 ± 8.6	24.1 ± 9.7	20.1 ± 7.3
ALT (mg/dL)	22.7 ± 13	25.8 ± 15.5	20.4 ± 10.1

AFM, android fat mass; AFM/ALM, android FM/LM; A/G FM, android/gynoid FM; ALM, appendicular lean mass; ALMI, appendicular lean mass index; ALT, alanine aminotransferase; AST, aspartate transaminase; BMI, body mass index; FM, fat mass; FMI, fat mass index; GFM, gynoid fat mass; HDL, high-density lipoprotein; LM, non-bone lean mass; LMI, non-bone lean mass index; SAT, subcutaneous adipose tissue; SATI subcutaneous adipose tissue index; T/L FM, trunk to leg fat mass ratio; VAT, visceral adipose tissue; VATI, visceral adipose tissue index

Biochemical analyses

Biochemical analyses included fasting glucose, total cholesterol (TC), TGs and HDL-C, measured in samples collected after a 12-hour fast. Parameters (intra- and interassay coefficient of variance [CV]) were measured in the Central Laboratory of S.Orsola-Malpighi Hospital by Modular analyzer (Roche Diagnostics, Mannheim, Germany): TGs (<1.5 and 1.8%), TC (<1 and 2.7%) and HDL-C (<0.95 and 1.3%); glucose was measured with a glucometer Breeze 2 (BAYER, Leverkusen, Germany, CV range 2–4.5%).

The presence of at least one altered laboratory parameter, according to the cut-offs of MetS [20] (fasting glucose ≥100 mg/dL, TGs ≥150 mg/dL, HDL-C ≤ 40 mg/dL, in men, or ≤50 mg/dL, in women) was used to define an impaired cardiometabolic profile.

Body composition parameters

An automatic whole-body scan was performed to measure total and regional BC using a new narrow-angle, fan-beam densitometer (GE Lunar iDXA 2005; Madison, WI, USA; enCORE 2011 software version 13.6 with CoreScan). The scanner was calibrated daily using a standard calibration block supplied by the manufacturer. All metal items were removed before densitometry. The participants, wearing only underwear and a cloth gown, were placed in a supine position with arms at sides slightly separated from the trunk and correctly centered on the scanning field. The scan duration was about 7 min in standard mode for total body scan (10 min in thick mode). The regions of interest (ROIs) were defined using the software provided by the manufacturer and included total body, trunk, upper limbs, lower limbs, android region (a segment of the abdomen comprised in between a lower demarcation line joining the superior ends of the iliac crests and an upper demarcation line drawn at a level representing 20% of the distance in between the iliac crests line and the chin), and gynoid region (a segment overlapping the trunk and legs region, including the hips and upper thighs, which extends caudally from an upper demarcation line placed at 1.5 times the android height below the level of the iliac crests, through two times the height of the android region). For each region, DXA scanned the weight (in g) of total mass, FM, LM, and BMC.

Visceral fat analysis was performed by CoreScan. This was indirectly obtained through the detection of the thickness of the SAT layer at the sides of the android region, which can be determined using x-ray attenuation. With this information, a software algorithm allowed the mapping and estimation of the total SAT compartment and the amount of VAT was indirectly derived by subtracting SAT from the total android FM (Fig. 1) [21–23].

We considered many densitometric measurements and indices following the latest International Society for Clinical Densitometry Official Position Guideline on Body Composition [24]. In particular, we analyzed total mass (weight), total LM, total FM, appendicular lean mass (lean mass arms + lean mass legs), VAT, SAT, and the corresponding indices standardized to height (ht) represented by BMI, lean mass index (LMI: total LM/ht^2), fat mass index (FMI: FM/ht^2), appendicular lean mass index (ALMI: ALM/ht^2), visceral adipose tissue index (VATI: visceral mass/ht^2), and subcutaneous adipose tissue index (SATI: subcutaneous mass/ht^2). In addition, we considered absolute indices considered as pivotal markers of body composition in terms of general balance of masses (percent FM — %FM; total body FM/LM — TFM/TLM), central/peripheral distribution of FM (trunk-to-leg fat mass ratio — T/L ratio; android/gynoid FM — AFM/GFM) and central or VAT compartment (android FM/LM — AFM/ALM and VAT/SAT).

Statistical analysis

The normal distribution of the present sample population was tested by skewness and excess kurtosis test; normal ranges were considered for values between −2 and +2. Continuous variables were expressed as sex-specific means and ± standard deviation.

Pearson correlation analysis and stepwise multiple regression were used to evaluate correlations among DXA and laboratory parameters (as dependent variables). First, the relationships between DXA and laboratory parameters were investigated using simple regression. Then we analyzed the correlation between every laboratory parameter (fasting glucose, TC, TGs, HDL-C aspartate aminotransferase [AST], and alanine aminotransferase [ALT]) and DXA parameters through multiple stepwise regression to find the best predicting DXA parameters and highlight their relationships with the different laboratory parameters. In particular, we performed two stepwise regressions: DXA "wide" parameters + DXA indexes and DXA "standardized to height" parameters + DXA indexes.

Finally, a receiver operating characteristic (ROC) curve was used to assess the accuracy to identify individuals with at least one laboratory risk factor. As the matter of fact, the area under the curve (AUC) is considered a measure of utility and represents the tradeoff between the correct identification of high-risk individuals (sensitivity) and of low-risk individuals (specificity). To obtain the optimal cutoff point to discriminate the laboratory risk from non-laboratory risk participants, we calculated the distance for each observed cutoff point and located the point where the distance between the ROC curve and the point (0, 1) was minimum (d^2 = [{1 − sensitivity}^{2} + [1 - specificity]^2) [25].

Two-tailed $P < 0.05$ were considered significant for all regression analysis, and AUCs were considered significant when statistically different from 0.5 [25].

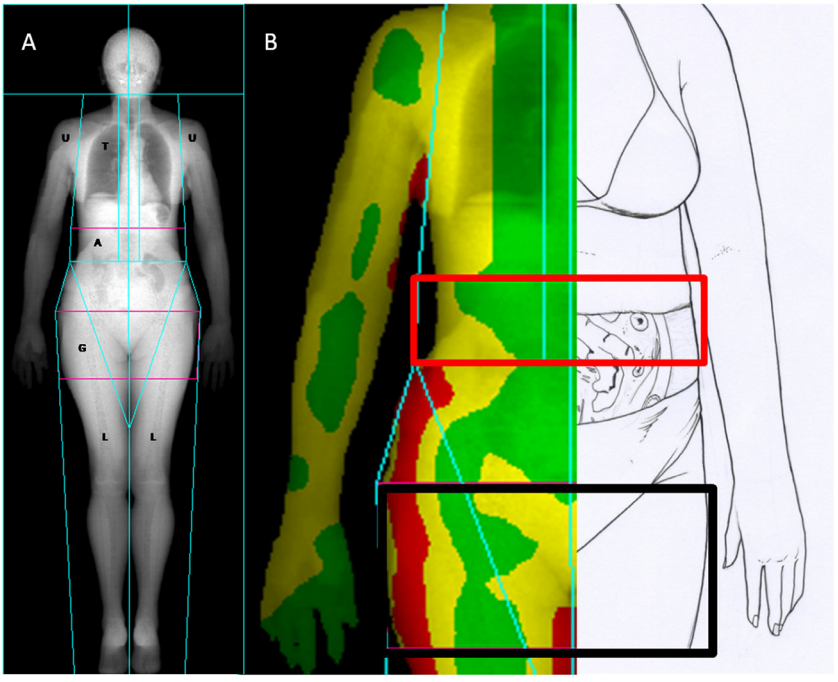

Fig. 1. (A) ROIs defined by the software. T, trunk; U, upper limbs; L, lower limbs; A, android region; G, gynoid region. In (B), the android (red box) and gynoid (black box) ROIs are highlighted. Left side, color fat mapping showing the fat percentage in the different body areas (red, high fat percentage, conventionally >60%; yellow, medium fat percentage, conventionally between 25 and 60%; green, low fat percentage, conventionally <25%).

Table 2
Group M: Pearson's correlation *r* among body composition parameters by DXA and laboratory markers

Group M	WeightBMI	FM totFMI	LM totLMI	ALMALMI	VAT gVATI	SAT gSATI	FM%	FM/LM	AFM/ALM	T/L FM	A/G FM	VAT/SAT
AST	NS	NS	NS	NS	0.275†	NS	0.236*	0.222*	0.243*	NS	NS	0.299†
103/134	0.204*	0.206*	NS	NS	0.287†	NS						
ALT	0.423‡	0.426‡	0.295§	0.303§	0.453‡	0.337‡	0.433‡	0.434‡	0.460‡	NS	0.287§	0.192*
129/134	0.445‡	0.438‡	0.336‡	0.354‡	0.454‡	0.353‡						
Total-cholesterol 130/134	NS	NS	NS	NS	NS	NS	NS	NS	NS	0.291§	0.262†	NS
	NS	NS	NS	NS	NS	NS						
Glycemia 130/134	0.526§ 0.602‡	0.524‡	0.333‡	0.345‡	0.606‡	0.345‡	0.527‡	0.539‡	0.546‡	0.329‡	0.408‡	0.335‡
		0.559‡	0.477†	0.373‡	0.626‡	0.375‡						
HDL-cholesterol 70/134	−0.508‡	−0.490‡	−0.445‡	−0.441‡	−0.484‡	−0.416§	−0.501‡	−0.492‡	−0.499‡	−0.284*	−0.399§	NS
	−0.496‡	−0.487‡	−0.418§	−0.436§	−0.472‡	−0.421§						
Tricylglycerides 127/134	0.269†	0.283†	NS	NS	0.400‡	NS	0.351‡	0.312§	0.351‡	0.457‡	0.448‡	0.360‡
	0.296§	0.297§	0.203*	NS	0.401‡	NS						

AFM/ALM, android FM/LM; A/G FM, android/gynoid FM; ALM, appendicular lean mass; ALMI, appendicular lean mass index; ALT, alanine aminotransferase; AST, aspartate transaminase; BMI, body mass index; DXA, dual-energy x-ray absorptiometry; FM, fat mass; FMI, fat mass index; HDL, high-density lipoprotein; LM, non-bone lean mass; LMI, non-bone lean mass index; NS, not statistically significant; SAT, subcutaneous adipose tissue; SATI subcutaneous adipose tissue index; T/L FM, trunk to leg fat mass ratio; VAT, visceral adipose tissue; VATI, visceral adipose tissue index
*$P \leq 0.05$.
†$P \leq 0.01$.
‡$P \leq 0.0001$.
§$P \leq 0.001$.

StatView statistical package (version 5.0.1 for Windows SAS Inc., Chicago, IL, USA) and Stata statistical package (StataCorp, College Station, TX, USA) were used for the analysis.

Results

The normal distribution of the population was proved for all densitometric parameters and BMI, as well as for metabolic dependent variables.

In both groups, BMI and densitometric parameters showed linear correlations with fasting glucose, TGs, ALT, and AST levels and an inverse correlation with HDL-C values ($P < 0.05$) Linear correlation with TC levels was only found in the men.

According to Pearson analysis, statistically significant relationships were demonstrated between all DXA parameters and fasting glucose (Tables 2 and 3); in particular the DXA parameter more closely related to fasting blood glucose was VAT (and VATI) in both groups (M: $r = 0.606$; F: $r = 0.629$; all $P < 0.0001$). With regard to TGs and HDL-C, a statistical significance was achieved with most of the DXA parameters. For TGs, the highest correlations were observed with VAT/VATI in women ($r = 0.493$) and with T/L FM in men ($r = 0.457$), whereas for HDL-C the highest correlations were observed with VAT/VATI in women ($r = -0.371$) and with weight and AFM/ALM in men (respectively $r = -0.508$ and $r = -0.499$; all $P < 0.0001$). TC showed good correlation with T/L FM ($r = 0.291$) and A/G FM ($r = 0.622$) only in the men, with no statistically significant relationship with any DXA parameter in the women.

As reported in Table 4, the densitometric parameters in both groups always retained in the final model of stepwise multiple regression were VAT and VATI for fasting blood glucose (group F: $\beta = 0.4627$, $P < 0.0001$ and $\beta = 0.4544$, $P < 0.0001$; group M: $\beta = 0.6221$, $P < 0.0001$ and $\beta = 0.6256$, $P < 0.0001$; respectively) and TG levels (group F: $\beta = 0.4931$, $P < 0.0001$ and $\beta = 0.5022$, $P < 0.0001$; group M: $\beta = 0.1990$, $P = 0.0261$ and $\beta = 0.1970$, $P = 0.0271$), independently of BMI . In women, the only DXA parameters retained in the final model of stepwise multiple regression considering HDL-C as dependent variables were VAT and VATI, whereas in men it was %FM.

Table 3
Group F: Pearson's correlation *r* among body composition parameters by DXA and laboratory markers

Group F	WeightBMI	FM totFMI	LM totLMI	ALMALMI	VAT gVATI	SAT gSATI	FM%	FM/LM	AFM/ALM	T/L FM	A/G FM	VAT/SAT
AST	0.166*	NS	NS	NS	0.181*	NS	0.176*	0.170*	0.189*	0.195*	NS	0.193*
147/182	0.180*	0.166*	NS	NS	0.182*	NS						
ALT	0.334†	0.329†	0.259‡	0.251‡	0.304†	0.300† 0.304†	0.341†	0.336†	0.356†	0.326†	0.211§	0.237§
169/182	0.326†	0.332†	0.288†	0.280‡	0.297†							
Total cholesterol 172/182	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	NS	NS	NS	NS	NS	NS						
Glycemia 176/182	0.546†	0.577†	0.495†	0.434†	0.629†	0.501† 0.517†	0.532†	0.549†	0.531†	0.492†	0.294†	0.390†
	0.572†	0.595†	0.566†	0.496†	0.633†							
HDL-cholesterol 132/182	−0.328†	−0.317†	−0.300‡	−0.288‡ −0.327†	−0.371†	−0.207*	−0.306‡	−0.295‡	−0.264§	−0.213*	−0.200*	−0.288‡
	−0.333†	−0.327†	−0.343†		−0.371†	−0.215*						
Tricylglycerides	0.401†	0.394†	0.319†	0.306†	0.493†	0.290† 0.309†	0.423†	0.404†	0.407†	0.421†	0.330†	0.437†
170/182	0.441†	0.419†	0.400†	0.367†	0.502†							

AFM/ALM, android FM/LM; A/G FM, android/gynoid FM; ALM, appendicular lean mass; ALMI, appendicular lean mass index; ALT, alanine aminotransferase; AST, aspartate transaminase; BMI, body mass index; DXA, dual-energy x-ray absorptiometry; FM, fat mass; FMI, fat mass index; HDL, high-density lipoprotein; LM, non-bone lean mass; LMI, non-bone lean mass index; NS, not statistically significant; SAT, subcutaneous adipose tissue; SATI subcutaneous adipose tissue index; T/L FM, trunk to leg fat mass ratio; VAT, visceral adipose tissue; VATI, visceral adipose tissue index
*$P \leq 0.05$.
†$P \leq 0.0001$.
‡$P \leq 0.001$.
§$P \leq 0.01$.

Table 4
Multiple stepwise regression

		Model 1					Model 2					
		BC	Regression coefficient	SE	β	R^2	*P*-value	BC	Regression coefficient	SE	β	R^2	*P*-value
Fasting glucose	M	VAT	0.006635	0.0007410	0.6221	0.3870	<0.0001	VATI	0.2067	0.02278	0.6256	0.3913	<0.0001
	F	VAT	0.007451	0.001085	0.4627	0.4115	<0.0001	VATI	0.2379	0.03556	0.4544	0.4356	<0.0001
		SAT	0.001844	0.0008550	0.1618		0.0324	SATI	0.1322	0.04221	0.2323		0.0020
								AFM/ALM	−0.1206	0.05475	−0.1656		0.0290
Tricylglycerides	M	VAT	0.009441	0.004192	0.1990	0.2376	0.0261	VATI	0.2907	0.1299	0.1970	0.2391	0.0271
		T/L FM	0.4153	0.1166	0.3058		0.0005	T/L FM	0.4164	0.1164	0.3059		0.0005
	F	VAT	0.02230	0.003026	0.4931	0.2432	<0.0001	VATI	0.5894	0.07807	0.5022	0.2522	<0.0001
HDL cholesterol	M	%FM	−0.005876	0.001303	−0.4826	0.2329	<0.0001	%FM	−0.006074	0.001273	−0.5008	0.2508	<0.0001
	F	VAT	−0.005481	0.001205	−0.3705	0.1373	<0.0001	VATI	−0.1426	0.03131	−0.3710	0.1376	0.0001
Total cholesterol	M	ALM	−0.001420	0.0006001	−0.2063	0.1271	0.0195	ALMI	−0.02930	0.01302	−0.1963	0.1234	0.0199
		T/L FM	0.2001	0.05123	0.3286		0.0002	T/L FM	0.2102	0.05137	0.3251		0.0001
	F	–	–	–	–	–	–	–	–	–	–	–	–
AST	M	VAT/SAT	0.03130	0.3286	0.3023	0.09138	0.0020	VAT/SAT	0.03100	0.009859	0.986	0.08917	0.0022
	F	T/L FM	0.02590	0.01083	0.1948	0.038	0.180	T/L FM	0.02590	0.01083	0.1948	0.038	0.0180
ALT	M	AFM/ALM	0.1577	0.02955	0.4293	0.1843	<0.0001	AFM/ALM	0.1661	0.02836	0.4612	0.2127	<0.0001
	F	AFM/ALM	0.06542	0.01332	0.3552	0.1261	0.0001	AFM/ALM	0.06542	0.01332	0.3552	0.1261	0.0001

AFM/ALM, android FM/LM; A/G FM, android/gynoid FM; ALM, appendicular lean mass; ALMI, appendicular lean mass index; ALT, alanine aminotransferase; AST, aspartate transaminase; β, standardized partial regression coefficient; BC, body composition parameter; FM, fat mass; FMI, fat mass index; LM, non-bone lean mass; LMI, non-bone lean mass index; SAT, subcutaneous adipose tissue; SATI subcutaneous adipose tissue index; T/L FM, trunk to leg fat mass ratio; VAT, visceral adipose tissue; VATI, visceral adipose tissue index
P-values for entry and removal, 0.05 and 0.10, respectively

Neither VAT nor VATI were retained in the final model of stepwise multiple regression considering AST, ALT, and TC as dependent variables.

Among BMI and BC parameters, VAT had the highest AUC both in men and in women (0.823, 95% confidence interval [CI], 0.748—0.884 and 0.811, 95% CI, 0.746—0.865, respectively) to identify the presence of at least one laboratory risk factor (Fig. 2). The optimal cutoff points (maximum sum of sensibility and specificity) of VAT were >1395 g and > 1479 cm^3 for men (sensibility of 73.8 and specificity of 81.5) and >1281 g and >1357 cm^3 for women (sensibility of 72.5 and specificity of 85.8). For VATI, the optimal cutoff points were similar: >0.40 for men (sensibility of 76.2 and specificity of 79.3) and >0.30 for women (sensibility of 82.6 and specificity of 74.5).

Discussion

The regional distribution of adipose tissue is more important than the total amount of body fat in predicting metabolic abnormalities and complications related to obesity [26]. In the present study, among the wide spectrum of densitometric parameters, VAT turned out to be the best predictor of cardiometabolic risk factors such as high fasting blood glucose, TGs, and low HDL-C levels. These results are in agreement with other recently published clinical studies [27–29].

In the literature, anthropometric measurements and DXA-assessed body composition parameters (total body fat, %body fat, FMI) are widely correlated with laboratory values (positive correlation for TG, fasting plasma glucose, and systolic and diastolic blood pressure and negative correlation for HDL-C). The correspondence is much more significant when the trunk regional evaluation is considered, and VAT shows the strongest associations [30–33].

Visceral obesity is part of the complex phenotype that involves adipose tissue storage dysfunction and ectopic TG accumulation in several sites. VAT ectopic accumulation, particularly in the liver, is strongly associated with an increased risk for metabolic diseases [26].

BMI has long been considered the best index to evaluate body fat. Whereas a very low BMI value is associated with increased mortality, a BMI above the normal-weight threshold of 25 kg/m^2 is correlated to a progressive increase in the risk for comorbidities such as hypertension, dyslipidemia, type 2 diabetes, CVDs, gallstones, and cancers [26,34,35]. An example of the limits of BMI is seen in metabolically obese, normal-weight individuals. These individuals have normal BMI but an excess of VAT, similar to what measured in obese individuals [26,36], and have metabolic complications commonly found in obese people [26,37]. Obese individuals with high levels of VAT also have altered glucose and insulin response to glucose (impaired glucose tolerance and insulin resistance) and a proinflammatory, prothrombotic milieu [26,38,39]. VAT is a hormonally active tissue, releasing different bioactive molecules and hormones (e.g., adiponectin, leptin, tumor necrosis factor, resistin, and interleukins). Among these hormones, adiponectin, inversely correlated with VAT, is of particular interest because of its antiangiogenic activity. Decreased concentrations of adiponectin are instead associated with type 2 diabetes, elevated glucose levels, hypertension, and CVD [38].

The study was based on DXA assessment of visceral fat. Most commonly, VAT is measured by anthropometric parameters (BMI, WHR, and WC), bioelectrical impedance analysis (BIA), US, DXA, CT, and MRI [38,40–42]. However routine use of these measurements is limited because of lack of accuracy (for anthropometric parameters), misinterpretation of the results (for BIA), operator dependence (for US), high radiation dose (for CT), and high costs (for MRI) [38].

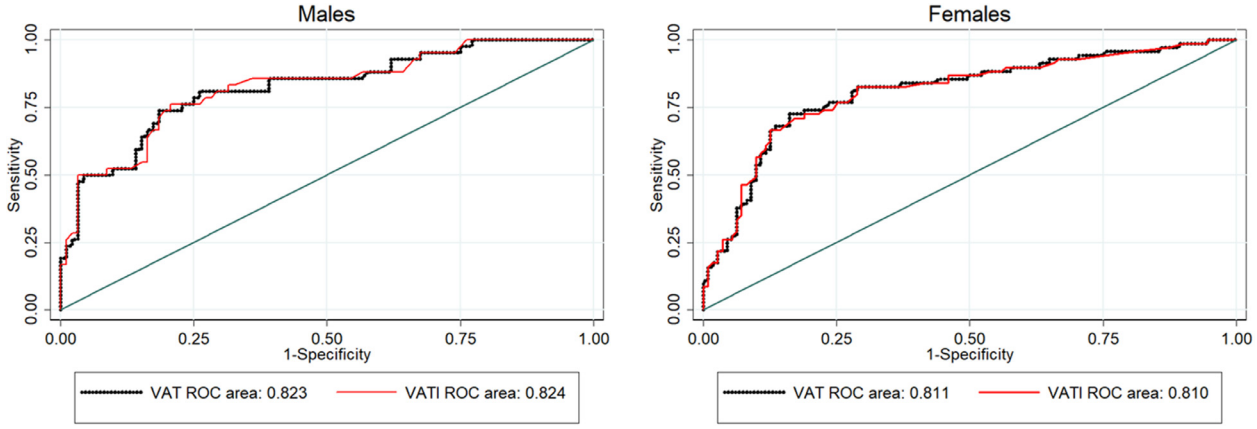

Fig. 2. Receiver operating characteristic (ROC) curves for VAT and VATI for the identification of individuals with at least one laboratory risk factor.

Technological advances have improved the estimation of VAT by DXA by using new software options [8,21,22,38,43] [8,21,22,38,43] released by the main companies (Hologic, GE Lunar). In particular, GE Lunar CoreScan software measures the width of the anteroposterior and lateral SAT layer in the abdominal android region (an area located between the top of the iliac crests and a line set at 20% of the distance from the top of the iliac crests to the chin) [8,21–23]. In a different way, Hologic APEX 3.1 software measures VAT in a 5-cm wide region placed just above the iliac crests at the level of the fourth lumbar vertebrae on the whole body and can directly measure SAT on each side of the abdominal cavity. Using complex mathematical algorithms, the lateral abdominal subcutaneous fat seen in the DXA image is used to estimate the anterior and posterior subcutaneous abdominal fat [43]. Both techniques elaborate changes in gray scale from darker to lighter given that tissues such as the muscles of the abdominal wall present a lower percentage of fat. VAT is finally calculated by subtracting the android SAT from the total android with a high degree of precision and accuracy. The main difference between GE Lunar and Hologic software is the final result, as the former provides VAT estimation as an expression of the weight and volume, whereas the latter provides a measurement of the area, like MRI and CT [8,43].

Several studies are available on comparative assessment of VAT using DXA and CT [8,23,41,43,44]. DXA assessment offers several advantages: It is fast; it presents a high level of compliance, wider availability, lower costs, and lower exposure to radiation with comparable results (~4.7 μSv for a standard-mode total body DXA examination versus 3100 μSv of radiation for an abdominal CT scan), making it suitable for repeated measurements [8,23,41,43,44].

Several clinical studies documented significant associations between VAT and metabolic diseases [25,33,38]. In the present analysis, VAT was positively correlated with CVD risk factors also in healthy and lean individuals, where an excess of VAT may be the key factors in the pathogenesis of MetS and CVDs. According to the literature, a dyslipidemic disorder is commonly observed in patients with visceral obesity [26,45–47]. Namely, hypertriglyceridemia and low levels of HDL-C remain the two main blood lipid abnormalities associated with visceral obesity [26,45,47].

Regardless of the method used for the assessment, only a few reference values have been reported in the literature for BC parameters and VAT [27–31]. In agreement with data from Bi et al,. among anthropometric and BC variables DXA-assessed VAT had the highest AUC both for cardiometabolic risk (0.749) and impaired glucose tolerance (0.766). In determining thresholds where the likelihood of developing risk was ≥50%, they found the cutoff points identified DXA-VAT ≥1713 cm^3 in white women and DXA-VAT ≥1320 cm^3 in black women for cardiometabolic risk and DXA-VAT ≥2550 cm^3 in white women and DXA-VAT ≥2120 cm^3 in black women for impaired glucose tolerance [27] .

This study had several limitations. A relevant limitation was that the sample size was relatively limited based almost entirely on white individuals, already involved in different research studies in the institute. A second limitation was the small number of laboratory parameters available for all individuals, only covering the different features of the MetS. As from any cross-sectional study, no causal relationship may be inferred from correlation analysis.

Another important limitation is that there is no information of the level of physical activity of the subjects [48]. Cardiorespiratory fitness (CRF) as a result of physical exercise has been overwhelmingly backed by evidence as an independent predictor of all-cause and disease-specific mortality [49,50], associated with reduced CVD [51] above weight loss [52–55].

Future plans could extend the study to other laboratory parameters or clinical data (namely, blood pressure) to cover the full aspects of the MetS, but drug use might bias the association with VAT measurement in treated patients. An additional step could be the design of a longitudinal study for the correlation between densitometric and laboratory parameters in other populations (e.g., athletes), where an enlarged fat-free mass might completely change the correlations.

Conclusion

The present study confirms that VAT is the parameter more closely correlated with cardiometabolic risk factors, and the thresholds we identified might be used to define patients at increased health risk. The lower and upper values around these cutoff points remain to be determined in future research. Longitudinal studies are required to determine the association between DXA-VAT and health outcomes such as the incidence of chronic disease (e.g., diabetes and MetS) and long-term mortality rates. The greatest utility would be to characterize DXA-VAT values, a screening tool in individuals at risk and a tool for the assessment of therapeutic efficacy (longitudinal assessment of body composition during dieting).

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