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ARTICLE

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Age- and sex-specific visceral fat reference cutoffs and their association with cardio-metabolic risk

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Abstract

Background Although excess visceral fat (VAT) is associated with numerous cardio-metabolic risk factors, measurement of this fat depot has historically been difficult. Recent dual X-ray absorptiometry approaches have provided an accessible estimate of VAT that has shown acceptable validity against gold standard methods. The aims of this study were to (i) evaluate DXA measured VAT as a predictor of elevated blood lipids and blood pressure and (ii) calculate thresholds associated with these cardio-metabolic risk factors.

Subjects/methods The sample comprised 1482 adults (56.4% women) aged 18–66 years. Total body scans were performed using a GE Lunar Prodigy, and VAT analyses were enabled through Corescan software (v 16.0). Blood pressure and blood lipids were measured by standard procedures. Regression models assessed how VAT mass was associated with each cardio-metabolic risk factor compared to other body composition measures. Measures of sensitivity and specificity were used to determine age- and sex-specific cut points for VAT mass associated with high cardio-metabolic risk.

Results Similar to waist circumference, VAT mass was a strong predictor of cardio-metabolic risk especially in men over age 40. Four cut-offs for VAT mass were proposed, above which the cardio-metabolic risk increased: 700 g in women <40 yrs; 800 g in women 40+ yrs; 1000*g* in men <40 yrs; and 1200 g in men 40+ yrs. In general, these cut-offs discriminated well between those with high and low cardio-metabolic risk.

Conclusions In both sexes, DXA measured VAT was associated with traditional cardio-metabolic risk factors, particularly high blood pressure in those 40+ yrs and low HDL < 40 yrs. These reference values provide a simple, accessible method to assess cardio-metabolic risk in adults.

Introduction

Although a high level of body fat is a known risk factor for metabolic disease, an excess of fat in the abdominal region is a better predictor of coronary heart disease and type 2 diabetes, as well as their risk factors (dyslipidaemia, glucose intolerance, and hypertension), than the total amount of adipose tissue [1]. Advances in technology have identified that two distinct types of fat exist in the abdominal region, namely the visceral component (VAT) and the subcutaneous component. VAT, due to its proximity to the liver, and more pathogenic cytokine profile, has been implicated in insulin resistance as well as a number of other related cardiovascular and metabolic conditions including type 2 diabetes [2]. In many studies, the association between VAT and disease remains significant even after statistical adjustments for other measures of obesity and

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regional adiposities such as body mass index (BMI) and waist circumference [3, 4].

The two most commonly used imaging techniques for measuring VAT are abdominal X-ray computed tomography (CT) and magnetic resonance imaging (MRI). However, neither option is a viable screening tool for VAT because of radiation dose (CT), and/or the need for access to heavily utilised clinical equipment. Over the past several years, the two leading DXA manufacturers (GE Healthcare and Hologic) have developed dedicated software to calculate VAT by subtracting abdominal subcutaneous fat from total abdominal fat. Estimates of VAT using these applications have been shown to be highly correlated ($r = 0.98$) with actual CT measures of VAT [5].

However, the ability to interpret the clinical significance of the results from DXA-derived VAT estimates has been challenging as the specific amount of DXA-derived VAT that confers a health risk has not been firmly established. Several previous studies have established normative DXA derived VAT values [6–8] on the basis of percentiles, and a small number of studies have attempted to identify clinical thresholds associated with the presence of cardio-metabolic disease risk [7, 9]. However, all of these studies have been conducted in small samples or predominantly young, healthy populations.

The aims of this study were to determine whether DXA-derived VAT mass is a predictor of cardio-metabolic risk and to estimate a critical level of VAT mass associated with elevated cardio-metabolic risk factors in a large sample of men and women of varying age, sex, and BMI using the GE Healthcare Lunar Prodigy instrument along with the dedicated CoreScan application.

Methods

Study participants

The sample includes participants from the Department of Medicine's Bone and Body Composition Unit who were enroled in various research studies conducted at the University of Otago, Departments of Medicine and Human Nutrition between 2009 and 2019, and who provided informed consent prior to their DXA scans. All studies were approved by the University of Otago Ethics Committee. Participants were generally healthy (no specific patient groups were recruited) and had to be aged at least 18 years (with no upper age limit). Women who were pregnant and individuals who weighed more than 160 kg (DXA table weight limit) were excluded. Of the six studies included, five were randomised controlled trials that involved a diet or exercise intervention, and therefore only baseline measures were included in the current analyses. The other sample comprised members of the Dunedin Multidisciplinary Health and Development Study who were assessed using DXA for the first time at the most recent (age 45) assessment (2017–2019). This birth cohort study is representative of the general population of the South Island of New Zealand. It has been running for 48 years with very low sample attrition [10]. Details of each study are described in Supplementary Table 1. In total, 1482 adults; 836 women and 646 men aged 18–66 years were included in these analyses. Because the sample size was small in some age groups and visceral fat accumulation is known to increase with age [11] the groups were subdivided by sex (female, male) and age (<40 years, 40+ years). These age groups were chosen as others have suggested that values of waist circumference that corresponded to 'critical' levels of VAT were lower in subjects aged more than 40 than among those who were less than 40 years of age. [12] A histogram showing the age distribution is presented in Supplementary Fig. 1.

Procedures

Total body DXA scans were conducted with participants wearing light clothing and with all-metal artefacts removed from their body. No participants were fasted or asked about their current hydration status or liquid/food ingestion prior to their DXA scan. Alongside measures of VAT, the scanner determines total fat and lean mass (kg), per cent body fat, total body bone mineral content (BMC), and total body bone mineral density (BMD). Each participant attended the research unit for one visit where their weight (Seca electronic scale; Seca Corp., Birmingham, UK) and height (Harpenden stadiometer; Holtain, Ltd., Crymych, Pembs., UK) were measured in duplicate using standard techniques and BMI calculated (kg/m^2). Scans were conducted on a fan-beam GE Lunar Prodigy (GE Healthcare, Madison WI, USA) by one skilled technologist according to the manufacturer's guidelines for patient positioning. Participants were placed in a supine position on the scanning table with the body aligned with the central horizontal axis. Arms were positioned parallel to, but not touching, the body. Participant's hands were placed at the side with thumbs up, palms facing legs. Arms were placed alongside the participant's body with a small air gap (~1 cm) between the arms and torso. Legs were fully extended and feet were secured with a canvas and Velcro support to avoid foot movement during the scan acquisition. For participants that did not fit within the scanning field of view, 'offset scanning' was performed as per the Official Position of the International Society for Clinical Densitometry [13]. Offset scanning involves positioning the participant so that the midsagittal line of the participant is offset from the midline of the table to allow complete scanning of the right limbs and trunk when the left

upper or lower limbs are incompletely visualised. The software then 'mirrored' the results of the completely imaged side and replaced the incompletely visualised limb values as needed. In all instances of offset scanning, the entire abdomen was kept within the scan boundaries. This procedure was considered valid by technicians at GE (personal communication) and is similar to a precision study conducted by Carver et al. [14]. The same skilled technician analysed all scans using the Lunar Encore software (Version 16, GE Healthcare). The machine's calibration was checked and passed on a daily basis using the GE Lunar calibration phantom and the Lunar Spine Phantom was scanned three times per week. There was no significant drift in calibration for the study period. CV for repeat in vivo measurements in adults in our laboratory of total body lean (g), fat (g), BMC (g), BMD (g/cm^2), and VAT, respectively, are as follows: 0.8%, 1.8%, 1.0%, 1.1% and 29% [15].

Other assessments included measurement of resting blood pressure, waist circumference and blood lipids. High levels of each cardio-metabolic risk factor were defined according to Ministry of Health Guidelines as follows: total cholesterol (TC) > 4.0 mmol/L, low-density lipoprotein (LDL) > 2.0 mmol/L, high-density lipoprotein (HDL) < 1.0 mmol/L, triglycerides (TAG) > 1.7 mmol/L, TC:HDL > 4.0, systolic blood pressure ≥ 130 mmHg, diastolic blood pressure ≥ 85 mmHg [16].

Statistical analysis

Data from the six studies were combined and participants with missing VAT data excluded. Participants had to have either lipid or blood pressure results to be included in this analysis. Three participants were enroled in two studies, but as their measures were taken at different times and these three only constituted 0.2% of the total sample, it was decided to keep these participants in the dataset and not account for repeat measures in the analysis.

To assess how VAT mass was associated with cardio-metabolic risk compared to other body composition measures, separate mixed-effects regression models, with a random effect for Study, were used for each risk factor (as the outcome variable) and each body composition variable (VAT mass, BMI or per cent body fat) as the predictor variable. Each model was run for each age and sex group separately and only with participants who had data for all body composition measures. Models for the age groups combined were also run with adjustment for age. All body composition measures were log-transformed to normalise the distribution and then standardised. Standardisation (subtracting the mean and dividing by the standard deviation (SD)) puts all of the body composition variables into the same units (units of SD) so that the size of the estimated associations can be directly compared. The same was done with waist circumference included as a body composition variable, but because there were substantial missing data for waist circumference, this was undertaken separately on the reduced sample size. The analyses that include waist circumference are reported in the Supplementary Material. A separate analysis was also undertaken using VAT mass adjusted for body size (VAT mass index kg/m^2 and % VAT mass), but as the relationships with cardio-metabolic risk did not differ from those with VAT mass (kg) these data are not shown. Regression coefficients and 95% CI were reported. The proportion of variance explained by the body composition variable was also calculated for each model and reported in the Supplementary Material. Residuals for all models were plotted and visually assessed for homogeneity of variance and normality.

To determine the level of VAT mass that discriminated best between those of high and low levels of each cardio-metabolic risk factor, the Liu method [17] was used, which finds the value of VAT mass (the cut-point) that maximises the product of sensitivity and specificity. Sensitivity, specificity and the area under the curve of the receiver operating characteristic (ROC) curve were calculated along with 95% CIs. This was undertaken for each risk factor separately by each age and sex category. Medians, 25th and 75th percentiles of VAT mass were also determined for the high- and low-risk categories of the cardio-metabolic factor.

To estimate an overall cut-point for all cardio-metabolic risk factors, the median VAT mass cut-point for each age and sex group was rounded to the nearest 100 g. This resulted in four hypothesised cut-points of VAT mass to identify those at high health risk for each age and sex group. The sensitivity and specificity of these overall cut-points for each of the cardio-metabolic risk factors was calculated and reported in the Supplementary Material. To further assess these cut-points, all participants were classified as either 'high VAT mass' (if they had VAT mass greater than or equal to the cut-point) or 'not high VAT mass'. Median, 25th and 75th percentiles for each cardio-metabolic risk factor was calculated by these two VAT mass categories for the whole sample, and mean differences (95% CI) between the categories were estimated using a linear regression model. Relative risks (95% CI) were also calculated to assess the increased risk of being in the high-risk category for each cardio-metabolic risk factor if classified as having high VAT mass (according to the overall cut-point for each age and sex group). The relative risks were calculated as the proportion 'at risk' in the 'high VAT mass' group divided by the proportion 'at risk' in the 'not high VAT mass' group. Although a recent report suggests differences between nonfasting and fasting lipid profiles are small [18] a sensitivity analysis for the LDL analyses were undertaken excluding the high-intensity interval training (HIIT) study and the Dunedin Study because these studies did not

Table 1 Age, body composition, and health variables by sex and age group.

	Women			Men		
	<40 yrs	40+ yrs	Combined	<40 yrs	40+ yrs	Combined
n	191	645	836	130	516	646
Age, mean (SD) years	30.2 (5.8)	45.3 (3.2)	41.9 (7.5)	29.5 (5.5)	45.0 (1.7)	41.9 (6.9)
Age range, years	19–39.5	40–66	19–66	18–29	40–64	18–64
Study, *n* (%)						
HIIT	0	117 (18.1)	117 (14.0)	0	25 (4.8)	25 (3.9)
Ice Tea	51 (26.7)	8 (1.2)	59 (7.1)	42 (32.3)	16 (3.1)	58 (9.0)
POWER	15 (7.9)	27 (4.2)	42 (5.0)	1 (0.8)	3 (0.6)	4 (0.6)
Snack	13 (6.8)	6 (0.9)	19 (2.3)	10 (7.7)	2 (0.4)	12 (1.9)
SWIFT	112 (58.6)	41 (6.4)	153 (18.3)	77 (59.2)	18 (3.5)	95 (14.7)
Dunedin study	0	446 (69.2)	446 (53.4)	0	452 (87.6)	452 (70.0)
BMI, mean (SD), kg/m^2	29.8 (6.7)	29.2 (6.6)	29.3 (6.6)	28.9 (5.2)	28.8 (5.0)	28.8 (5.1)
BMI category, *n* (%)						
Healthy (BMI < 25 kg/m^2)	52 (27.2)	209 (32.4)	261 (31.2)	32 (24.6)	108 (20.9)	140 (21.7)
Overweight (BMI 25 to <30 kg/m^2)	39 (20.4)	172 (26.7)	211 (25.4)	39 (30.0)	224 (43.4)	263 (40.7)
Obese (BMI 30+ kg/m^2)	100 (52.4)	264 (40.9)	364 (43.5)	59 (45.4)	184 (35.7)	243 (37.6)
VAT mass, median (25th, 75th percentile) kg	0.55 (0.13, 1.03)	0.68 (0.22, 1.16)	0.63 (0.21, 1.11)	1.16 (0.36, 1.98)	1.25 (0.77, 1.93)	1.25 (0.67, 1.94)
Percent body fat, median (25th, 75th percentile)	40.1 (31.8, 45.2)	38.4 (31.3, 44.3)	38.8 (31.3, 44.5)	29.2 (21.4, 33.7)	28.3 (23.8, 32.8)	28.5 (23.6, 32.9)
Waist circumference[b], median (25th, 75th percentile) cm	95 (87, 104)	90 (79, 103)	91 (80, 103)	106 (98, 113)	97 (89, 106)	98 (90, 107)
Total cholesterol[b], mean (SD) mmol/L	5.0 (0.9)	5.1 (1.0)	5.0 (1.0)	5.1 (1.1)	5.3 (1.0)	5.3 (1.0)
HDL[b], mean (SD) mmol/L	1.4 (0.3)	1.6 (0.5)	1.6 (0.4)	1.1 (0.3)	1.3 (0.4)	1.3 (0.3)
Total cholesterol: HDL[b], mean (SD)	3.7 (1.1)	3.3 (1.1)	3.4 (1.1)	4.7 (1.5)	4.3 (1.4)	4.4 (1.5)
LDL[b], mean (SD) mmol/L	3.1 (0.9)	2.8 (0.9)	2.9 (0.9)	3.3 (1.0)	3.0 (0.9)	3.1 (0.9)
Triglycerides[b], median (25th, 75th percentile) mmol/L	1.1 (0.4)	1.5 (0.9)	1.4 (0.8)	1.4 (0.6)	2.6 (1.6)	2.3 (1.5)
Systolic blood pressure[b], mean (SD) mmHg	118 (13)	119 (15)	119 (15)	132 (13)	126 (14)	127 (14)
Diastolic blood pressure[b], mean (SD) mmHg	76 (9)	78 (10)	77 (10)	81 (8)	85 (10)	84 (9)

HIIT high-intensity interval training, *POWER* prevention of weight regain, *SWIFT* support strategies for whole-food diets, intermittent fasting, and training, *BMI* body mass index, *VAT* visceral adipose tissue, *VMI* VAT mass index.

[a]The combined sample included 1479 unique participants (2 participants in the Ice Tea study were also participants in the Snack study, and one participant in the HIIT study was also in the Dunedin Study).

[b]Waist circumference was missing in 65 women and 59 men; total cholesterol was missing in 39 women and 13 men; HDL and total:HDL was missing in 41 women and 13 men; LDL was missing in 144 women and 91 men; triglyceride concentration was missing in 135 women and 38 men, and blood pressure was missing in 81 women and 70 men.

measure fasting lipid profiles. Stata 16.0 (StataCorp, College Station, TX, USA) was used for all analyses.

Results

The average age of the sample was 41.9 years (SD 7.2), ranging from 18 to 66 years. The majority of the sample (56%) were female and 40+ yrs (77–79%). The average BMI was 29.1 kg/m^2 (SD 5.9), ranging from 18 to 52 kg/m^2 (Table 1). Median VAT mass increased with age in both sexes and was higher overall among males compared to females. The mean values of measurements were higher than the recommended levels for waist circumference, TC, and LDL in both sexes, but within normal levels for blood pressure, HDL, and TAG.

Table 2 Associations between standardised body composition measures and metabolic measures by age category and sex.

	Standardised regression coefficient (95% CI)[a]					
	Women			Men		
	< 40 yrs	40+ yrs	Combined[b]	< 40 yrs	40+ yrs	Combined[b]
TC (mmol/L), *n*	189	608	797	130	503	633
BMI	0.05 (−0.13, 0.23)	**0.11 (0.03, 0.18)**	0.08 (0.01, 0.15)	0.53 (0.36, 0.71)	0.09 (0.00, 0.17)	0.11 (0.02, 0.20)
Fat percent	0.12 (−0.04, 0.28)	**0.11 (0.04, 0.19)**	**0.10 (0.03, 0.17)**	**0.59 (0.43, 0.76)**	0.11 (0.02, 0.20)	**0.17 (0.08, 0.25)**
VAT mass	**0.20 (0.05, 0.35)**	0.08 (0.00, 0.16)	0.09 (0.01, 0.16)	0.52 (0.35, 0.69)	**0.12 (0.03, 0.21)**	0.15 (0.07, 0.24)
HDL (mmol/L), *n*	189	606	795	130	503	633
BMI	**−0.11 (−0.17, −0.04)**	**−0.22 (−0.25, −0.18)**	**−0.21 (−0.24, −0.18)**	**−0.08 (−0.13, −0.03)**	−0.11 (−0.14, −0.08)	−0.12 (−0.14, −0.09)
Fat percent	−0.06 (−0.12, −0.01)	−0.18 (−0.22, −0.15)	−0.17 (−0.20, −0.14)	−0.07 (−0.12, −0.02)	−0.12 (−0.15, −0.09)	−0.12 (−0.14, −0.09)
VAT mass	−0.09 (−0.14, −0.03)	−0.17 (−0.20, −0.13)	−0.16 (−0.19, −0.12)	−0.06 (−0.11, −0.01)	**−0.14 (−0.17, −0.11)**	**−0.14 (−0.16, −0.11)**
TC: HDL, *n*	189	606	795	130	503	633
BMI	0.33 (0.18, 0.48)	**0.49 (0.41, 0.57)**	**0.46 (0.38, 0.54)**	0.76 (0.54, 0.98)	0.41 (0.29, 0.53)	0.45 (0.33, 0.57)
Fat percent	0.32 (0.17, 0.47)	0.39 (0.31, 0.48)	0.37 (0.29, 0.45)	**0.79 (0.57, 1.01)**	0.42 (0.31, 0.54)	0.48 (0.37, 0.60)
VAT mass	**0.38 (0.23, 0.53)**	0.38 (0.30, 0.46)	0.37 (0.29, 0.45)	0.71 (0.48, 0.94)	**0.49 (0.37, 0.60)**	**0.52 (0.41 (0.64)**
LDL (mmol/L), *n*	189	503	692	130	425	555
BMI	0.16 (0.00, 0.31)	0.15 (0.07, 0.23)	0.13 (0.06, 0.20)	0.47 (0.32, 0.62)	0.04 (−0.05, 0.12)	0.07 (−0.01, 0.16)
Fat percent	0.19 (0.05, 0.33)	**0.17 (0.09, 0.25)**	**0.15 (0.09, 0.22)**	**0.52 (0.37, 0.67)**	**0.06 (−0.03, 0.14)**	**0.12 (0.04, 0.21)**
VAT mass	**0.26 (0.13, 0.39)**	0.10 (0.03, 0.18)	0.12 (0.05, 0.19)	0.44 (0.28, 0.59)	0.05 (−0.04, 0.13)	0.08 (0.00, 0.16)
TAG (mmol/L), *n*	189	512	701	130	478	608
BMI	0.09 (0.03, 0.15)	**0.36 (0.28, 0.44)**	**0.31 (0.25, 0.38)**	**0.32 (0.23, 0.40)**	0.51 (0.37, 0.65)	0.50 (0.38, 0.63)
Fat percent	0.09 (0.03, 0.15)	0.27 (0.19, 0.34)	0.23 (0.16, 0.29)	0.31 (0.22, 0.39)	0.51 (0.37, 0.65)	0.49 (0.36, 0.61)
VAT mass	**0.12 (0.06, 0.18)**	0.28 (0.21, 0.36)	0.24 (0.18, 0.31)	**0.32 (0.23, 0.40)**	**0.55 (0.42, 0.69)**	**0.54 (0.42, 0.66)**
Systolic BP (mmHg), *n*	126	629	755	78	498	576
BMI	**1.8 (−0.4, 4.0)**	**6.0 (4.9, 7.1)**	**5.5 (4.5, 6.5)**	3.4 (0.7, 6.2)	**4.7 (3.5, 5.8)**	**4.7 (3.6, 5.8)**
Fat percent	0.6 (−1.6, 2.8)	4.8 (3.7, 5.9)	4.4 (3.3, 5.3)	−0.3 (−3.1, 2.6)	3.6 (2.4, 4.8)	3.3 (2.2, 4.5)
VAT mass	0.7 (−1.6, 2.9)	3.6 (2.5, 4.7)	3.1 (2.1, 4.1)	**4.8 (2.1, 7.4)**	3.8 (2.6, 5.0)	3.8 (2.7, 4.9)
Diastolic BP (mmHg), *n*	126	629	755	78	498	576
BMI	2.3 (0.8, 3.9)	**3.3 (2.5, 4.1)**	**3.2 (2.5, 3.9)**	2.2 (0.4, 3.9)	**2.9 (2.1, 3.7)**	**2.7 (2.0, 3.4)**
Fat percent	**2.8 (1.3, 4.3)**	2.6 (1.8, 3.3)	2.6 (1.9, 3.3)	1.2 (−0.6, 3.0)	**2.9 (2.1, 3.7)**	**2.7 (2.0, 3.4)**
VAT mass	1.9 (0.3, 3.5)	2.3 (1.6, 3.1)	2.2 (1.5, 2.9)	**3.4 (1.7, 5.0)**	2.7 (1.9, 3.5)	2.6 (1.9, 3.3)

[a]The regression coefficient represents the difference in the metabolic health variable for a standard deviation (SD) higher body composition measure. Because all body composition measures are all standardised, these coefficients can be compared, with the biggest number (in bold) representing the strongest association with the health measure. All body composition measures were log-transformed before standardisation. Mixed-effects regression models were used to estimate these associations with study as a random effect.

[b]The combined estimates were further adjusted for age.

TC total cholesterol, *HDL* high-density lipoprotein, *TC:HDL* the ratio of total cholesterol to high-density lipoprotein, *LDL* low-density lipoprotein, *BP* blood pressure.

VAT mass was highly correlated with anthropometric indices (BMI, waist circumference, per cent fat) (all $r > 0.8$, data not shown). Table 2 describes the association between each index and cardio-metabolic risk factor, where the largest regression coefficient (in bold) represents the strongest association with a given risk factor. In those <40 yrs, VAT mass was the body composition measurements that were most strongly positively associated with TC, TC/HDL ratio, LDL, and TAG among women, and TAG and blood pressure among men. In those 40+ yrs, VAT mass was most strongly positively associated with TC, TC/HDL ratio and TAG (Table 2) and negatively associated with HDL among men.

The calculated age- and sex-specific VAT cutoffs for the cardio-metabolic risk factors varied with each factor (Table 3). Examination of the area under the ROC curve showed that VAT mass best discriminated between those of high risk and low risk for the TC/HDL ratio among all women, HDL among women 40+ years, and TC and BP for men <40 yrs. The overall VAT mass cutoffs for each age- and sex-group were determined by the median cutoff for all cardio-metabolic risk factors (rounded to the nearest 100 g). In women <40 years this was 700 g; in women 40+ years it was 800 g; in men <40 years it was 1000 g; and in men 40+ years it was 1200 g.

Figure 1 shows the distribution of VAT mass for each low- and high-risk cardio-metabolic factor among women, illustrating the discriminatory validity of the overall VAT mass cutoffs for distinguishing between those with high- and low-cardio-metabolic risk. Although the cutoffs appear to discriminate well between women with high and low risk for HDL, TAG and blood pressure this was less apparent for TC and LDL. The discriminatory ability of the cutoffs among males <40 yrs was high for all factors except HDL

Table 3 Visceral fat mass and health risk.

Health risk	Low-risk group for each factor		High-risk group for each factor		Cut-point, g	Sensitivity	Specificity	The area under ROC curve (95% CI)
	n	Median (25th, 75th percentiles), g	*n*	Median (25th, 75th percentiles), g				
Women, <40 yrs								
TC	25	222 (9, 730)	164	581 (161, 1072)	476	0.57	0.68	0.67 (0.56, 0.78)
HDL	172	537 (120, 1010)	17	758 (215, 1746)	685	0.59	0.62	0.59 (0.41, 0.77)
TC:HDL	134	317 (80, 758)	55	884 (549, 1619)	685	0.69	0.72	0.75 (0.67, 0.83)
LDL	15	215 (34, 731)	174	568 (136, 1062)	476	0.56	0.73	0.65 (0.52, 0.79)
TAG	170	514 (97, 999)	19	884 (439, 2030)	643	0.74	0.61	0.69 (0.55, 0.82)
BP	98	672 (466, 1087)	28	1052 (745, 1662)	803	0.71	0.61	0.68 (0.57, 0.80)
Median cut-point (to nearest 100)					700			
Women, 40+ yrs								
TC	69	523 (188, 951)	539	685 (224, 1172)	558	0.57	0.52	0.54 (0.47, 0.61)
HDL	570	626 (214, 1072)	36	1467 (874, 1959)	1045	0.67	0.74	0.77 (0.68, 0.85)
TC:HDL	463	475 (185, 942)	143	1079 (796, 1662)	839	0.73	0.70	0.75 (0.71, 0.80)
LDL	102	409 (185, 942)	496	688 (223, 1168)	443	0.62	0.52	0.56 (0.50, 0.62)
TAG	345	403 (183, 942)	167	1003 (705, 1585)	687	0.77	0.63	0.72 (0.68, 0.77)
BP	435	483 (178, 922)	194	1028 (591, 1542)	897	0.60	0.73	0.71 (0.66, 0.75)
Median cut-point (to nearest 100)					800			
Men < 40 yrs								
TC	20	210 (148, 368)	110	1407 (554, 2052)	536	0.76	0.95	0.83 (0.73, 0.93)
HDL	92	906 (253, 1853)	38	1670 (554, 2052)	1551	0.58	0.67	0.62 (0.52, 0.72)
TC:HDL	49	355 (161, 1245)	81	1608 (884, 2061)	513	0.86	0.67	0.75 (0.65, 0.84)
LDL	10	210 (186, 365)	120	1288 (417, 2014)	368	0.78	0.80	0.77 (0.59, 0.95)
TAG	95	745 (227, 1649)	35	1945 (1393, 2360)	1602	0.71	0.75	0.78 (0.70, 0.86)
BP	32	1288 (929, 1792)	46	2043 (1679, 2779)	1571	0.87	0.69	0.82 (0.72, 0.92)
Median cut-point (to nearest 100)					1000			
Men, 40+ yrs								
TC	49	1062 (562, 1864)	454	1273 (784, 1942)	1129	0.58	0.59	0.56 (0.47, 0.65)
HDL	418	1157 (673, 1773)	85	1890 (1255, 2681)	1461	0.68	0.63	0.71 (0.65, 0.77)
TC:HDL	244	960 (499, 1602)	259	1529 (1047, 2239)	1137	0.70	0.59	0.69 (0.64, 0.73)
LDL	50	1068 (579, 1765)	375	1196 (709, 1863)	1137	0.53	0.58	0.54 (0.46, 0.63)
TAG	156	937 (380, 1615)	322	1423 (937, 2109)	1167	0.62	0.62	0.67 (0.62, 0.72)
BP	249	1022 (538, 1549)	249	1576 (1006, 2312)	1252	0.65	0.65	0.68 (0.63, 0.73)
Median cut-point (to nearest 100)					1200			

High total cholesterol: ≥4.0 mmol/L; low HDL: <1 mmol/L; high total cholesterol to HDL ratio: ≥4.0; high LDL: ≥2.0 mmol/L; high TAG: ≥1.7 mmol/L; high blood pressure: SBP ≥ 130 or DBP ≥ 85 mmHg.

TC total cholesterol, *HDL* high-density lipoprotein, *TC:HDL* the ratio of total cholesterol to high-density lipoprotein, *LDL* low-density lipoprotein, *BP* blood pressure.

and blood pressure and did not perform as well in older males (Fig. 2).

Table 4 shows the relative risks for being in the high-risk category for each cardio-metabolic risk factor for those scoring above the VAT mass cutoff (high) compared to those below the cutoff. Adults with high VAT mass are 3.3 more likely to have a low HDL cholesterol (mean difference −0.31 95% CI: −0.35, −0.27 mmol/L) and 2.5 times more likely to have a low TC/HDL ratio (1.1 95% CI: 1.0, 1.2). Adults with high VAT mass were also twice as likely to have high TAG (0.8, 95% CI: 0.7, 0.9 mmol/L), and higher blood pressure (mean difference for systolic: 10, 95% CI: 8,

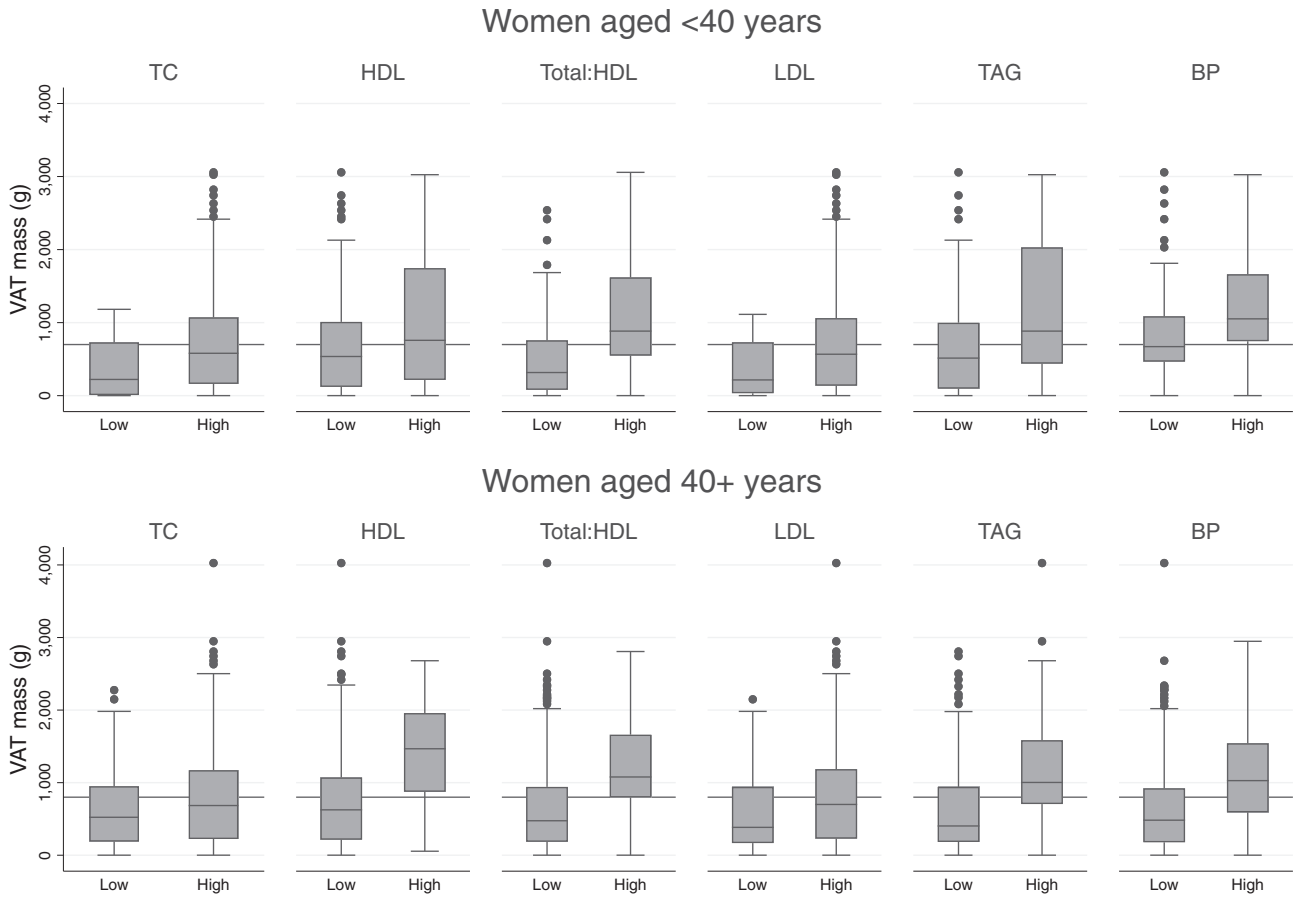

Fig. 1 Box plots of VAT mass (g) by high- and low-risk metabolic measures for women. The red line is the proposed cut-off (700 for women <40 yrs; 800 for women 40+ yrs). TC total cholesterol, TAG triglycerides, BP blood pressure.

11 mmHg; mean difference for diastolic: 6, 95% CI 5, 8 mmHg) compared with adults with low levels of VAT mass. In addition, adults with a high VAT mass are at a higher risk of having high TC and LDL, although the differences were not large (1.07, 95% CI: 1.03, 1.11 mmol/L for both TC and LDL).

A sensitivity analysis was carried out on the LDL analyses after exclusion of the HIIT and Dunedin Study which did not change the conclusions. The VAT mass cut-offs for each age-group remained the same and the risk of having high LDL when classified as having high VAT mass was the same (RR (95% CI): 1.07 (1.01, 1.13)).

Discussion

Using a GE Healthcare Lunar Prodigy densitometer in a large sample of adults, we have shown that DXA measured VAT is associated with several traditional cardio-metabolic risk factors across a wide age range and for both sexes. Furthermore, our proposed DXA-measured VAT cutoffs were able to discriminate between those at low and high risk for these risk factors.

In our study, VAT was highly correlated with all anthropometric indices of abdominal obesity and more strongly associated with dyslipidaemia in both sexes compared to other anthropometric indices. It was also associated with hypertension in males <40 yrs. Previous studies have consistently shown positive correlations between VAT and metabolic abnormalities including fasting glucose, HOMA and TAG and negative correlations with HDL [6, 7, 19], whereas mixed findings have been reported for blood pressure [6, 19]. In our study, those classified as having high VAT mass were 3.3 times more likely to have low levels of HDL and twice as likely to have high levels of triglycerides. This is in keeping with previous research that has shown the dyslipidaemic state among those with visceral obesity can be characterised by high levels of TAG, low levels of HDL, and relatively normal total and LDL cholesterol levels [20]. This metabolic dysregulation associated with VAT can be explained by an increased free fatty acid flux to the liver, inducing a state of chronic low-grade

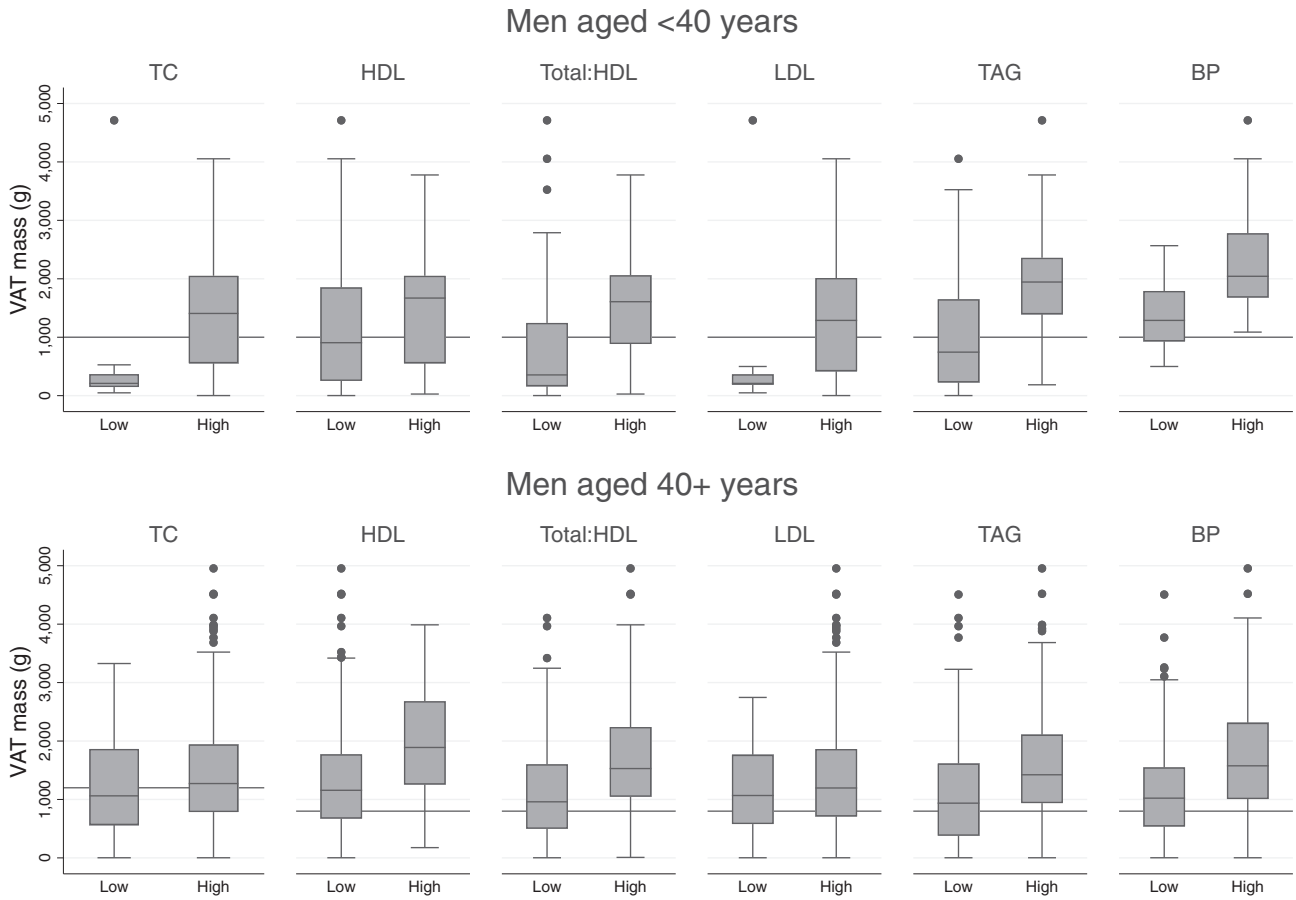

Fig. 2 Box plots of VAT mass (g) by high- and low-risk metabolic measures for men. The red line is the proposed cut-off (1000 for men <40 yrs; 1200 for men 40+ yrs). TC total cholesterol, TAG triglycerides, BP blood pressure.

inflammation and disrupting lipolytic and glycolytic regulation [20].

To date, few studies have reported associations between DXA measured VAT and cardio-metabolic risk. In a smaller homogenous sample ($n = 421$) of mostly normal weight Europeans aged 20–30 years, using the same DXA system as the current study, stronger relationships were observed between VAT and high levels of BP, TAG, and LDL and low levels of HDL than was observed with total body fat [7]. However, VAT cutoffs associated with these risk factors were considerably lower (161–759 g) than those developed in the current study (368–1602 g). Our proposed cutoffs are lower than those proposed in a study of 229 obese women where reported DXA measured VAT cutoffs for increased risk of metabolic syndrome and impaired glucose tolerance were 1700 and 2400 g, respectively [9]. In the only large study ($n = 2317$) to date using a different DXA scanner to the current study (Hologic vs. Lunar), the optimal VAT threshold to predict two or more cardio-metabolic risk factors was approximately 118 g for the overall sample [6], which is within the range of thresholds (94 to 150 g) from other studies using CT or MRI [21–23]. Differences in cutoffs across studies are likely due to the differences in the algorithms developed for VAT measurement between DXA manufacturers (sites for regions of interest, anatomic landmarks, etc.), differences in the outcomes used to assess cardio-metabolic risk (insulin resistance, dyslipidaemia, etc.), as well as differences in analytic methods used to determine the cutoffs (regression versus ROC analysis). It is also widely known that inter-device differences in body composition between two dominant manufacturers (GE Healthcare and Hologic) exist [24]. However, and most importantly, the majority of these previous studies were conducted on small, homogenous, mostly healthy samples, which limit their generalisability.

We have also shown that males had more VAT mass than females and VAT mass was higher in the older age groups for both sexes. This is in keeping with several studies which have derived DXA measured VAT reference values in populations from the UK [8], USA [25], and Europe [7, 26] showing that VAT mass increases with advancing age [8, 25, 26] and is generally higher among males compared to females [7, 26]. The lower cut points for those <40 yrs of age reflect this age trend but may also be

Table 4 Health measures in those classified as having high and not high VAT mass ($n = 1482$).

	Not high VAT mass median (25th, 75th percentile)	High VAT mass median (25th, 75th percentile)	Mean difference (95% CI) between groups	Relative risk (95% CI) for 'at risk'[b] level of health measure if classified as high VAT mass
n	784	698		
BMI, kg/m^2	25.0 (22.6, 28.0)	32.3 (29.6, 36.3)	7.9 (7.5, 8.4)	
Percent fat	28.4 (23.0, 35.1)	39.0 (32.3, 45.2)	9.9 (9.1, 10.7)	
Waist[a], cm				
Women	82 (75, 89)	103 (96, 112)	21 (20, 23)	
Men	89 (84, 95)	105 (99, 112)	17 (16, 19)	
TC[a], mmol/L	4.9 (4.3, 5.5)	5.4 (4.6, 6.0)	0.4 (0.3, 0.5)	1.07 (1.03, 1.11)
HDL cholesterol[a], mmol/L	1.5 (1.3, 1.9)	1.3 (1.0, 1.5)	−0.31 (−0.35, −0.27)	3.27 (2.37, 4.51)
TC:HDL cholesterol[a]	3.1 (2.6, 3.9)	4.2 (3.4, 5.2)	1.1 (1.0, 1.2)	2.51 (2.16, 2.92)
LDL cholesterol[a], mmol/L	2.6 (2.2, 3.2)	3.1 (2.5, 3.8)	0.4 (0.3, 0.5)	1.07 (1.03, 1.11)
TAG[a], mmol/L	1.2 (0.9, 1.7)	1.8 (1.3, 2.7)	0.8 (0.7, 0.9)	2.00 (1.75, 2.29)
Systolic BP[a], mmHg	117 (108, 124)	126 (116, 137)	10 (8, 11)	2.18 (1.87, 2.54)
Diastolic BP[a], mmHg	76 (71, 83)	83 (77, 90)	6 (5, 8)	

TC total cholesterol, *HDL* high-density lipoprotein, *TC:HDL* the ratio of total cholesterol to high-density lipoprotein, *LDL* low-density lipoprotein, *BP* blood pressure.

[a]124 participants did not have waist circumference; 52 did not have cholesterol or triglycerides; 54 did not have HDL; 115 did not have LDL; 151 did not have blood pressure.

[b]High TC: ≥4.0 mmol/L; low HDL: < 1 mmol/L; high TC to HDL ratio: ≥4.0; high LDL: ≥2.0 mmol/L; high TAG: ≥1.7 mmol/L; high blood pressure: SBP ≥ 130 or DBP ≥ 85 mmHg.

due to differences between the studies from which the data was generated; the younger age groups mostly came from the SWIFT study, a treatment-seeking group, whereas the older group mostly consisted of members from the Dunedin Study, a birth cohort. As VAT mass increases later in life, it appears that a greater volume of VAT is required to discriminate between those of high and low risk.

One notable strength of our study is the large sample of men and women of varying BMI with measurements of DXA ascertained VAT and several important cardio-metabolic risk factors. However, the sample was predominantly >40 yrs and although just over 60% of the adults in this study came from a representative birth cohort, the rest of the sample represented volunteers who attended baseline visits for diet and exercise intervention studies. As these samples did not include adults with serious health conditions, such as diabetes, or adults older than 66 years of age, the results may not be generalisable to these groups.

Measurements of lipid profiles in two studies (HIIT and Dunedin Study) were performed in the non-fasted state, which may make the results less reliable. However, non-fasting levels are more representative of the usual triglyceride levels of an individual and recent evidence suggests that lipids and lipoproteins change minimally in response to normal food intake [18]. However, because the Friedwalde equation is only valid when triglycerides are <4.5 mmol/L, a small sample ($n = 63$) with high triglycerides were removed from the analyses, which may affect the relationships between VAT mass and LDL. Finally, although VAT mass may be affected by total body fat mass, we chose to present our analyses for total VAT mass since we were more interested in determining an absolute level of VAT associated with cardio-metabolic risk. However, we also analysed several indices of VAT adjusted for body size (VAT mass index, percentage VAT mass) and the relationships between these variables and cardio-metabolic risk were similar to total VAT mass (data are not shown). Others have shown large interindividual differences in the amount of visceral fat at any level of body fat content [27, 28]. These cut-points serve as a general guide to levels associated with risk or incidence of disease, however, they are not definitive. They could be useful for defining 'visceral obesity' or identifying adults likely to benefit from preventive interventions, but further research is needed to confirm this.

The results of this study indicate that DXA VAT is correlated with a range of cardio-metabolic risk factors, with strongest associations observed for non-anthropometric indices, especially among men over 40 years of age. Our study also presents thresholds that could be used to identify those at increased health risk. DXA is reliable and precise across a range of body sizes and provides a more efficient, accessible and less-invasive tool than MRI and CT to determine VAT. These new data suggest a useful method for classifying individuals into more or less favourable VAT mass groups, quantifying disease risk and providing a readily accessible and comparatively

cost-effective method for monitoring and interpreting change during and after lifestyle interventions.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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