Atherosclerosis 209 (2010) 481–486

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Relation between visceral fat and coronary artery disease evaluated by multidetector computed tomography

Mateus D. Marques, Raul D. Santos*, Jose R. Parga, Jose A. Rocha-Filho, Luiz A. Quaglia, Marcio H. Miname, Luiz F. Ávila

Heart Institute (InCor) University of Sao Paulo Medical School, Brazil

ARTICLE INFO

Article history:
Received 26 March 2009
Received in revised form 8 October 2009
Accepted 15 October 2009
Available online 29 October 2009

Keywords:
Visceral fat
Obesity
Computed tomography angiography
Coronary artery disease
Atherosclerosis

ABSTRACT

Visceral abdominal fat has been associated to cardiovascular risk factors and coronary artery disease (CAD). Computed tomography (CT) coronary angiography is an emerging technology allowing detection of both obstructive and nonobstructive CAD adding information to clinical risk stratification. The aim of this study was to evaluate the association between CAD and adiposity measurements assessed clinically and by CT. We prospectively evaluated 125 consecutive subjects (57% men, age 56.0 ± 12 years) referred to perform CT angiography. Clinical and laboratory variables were determined and CT angiography and abdominal CT were performed in a 64-slice scanner. CAD was defined as any plaque calcified or not detected by CT angiography. Visceral and subcutaneous adiposity areas were determined at different intervertebral levels. CT angiography detected CAD in 70 (56%) subjects, and no association was found with usual anthropometric adiposity measurements (waist and hip circumferences and body mass index). Otherwise, CT visceral fat areas (VFA) were significantly related to CAD. VFA T12-L1 values ≥145 cm^2 had an odds ratio of 2.85 (95% CI 1.30–6.26) and VFA L4-L5 ≥150 cm^2 had a 2.87-fold (95% CI 1.31–6.30) CAD risk. The multivariate analysis determined age and VFA T12-L1 as the only independent variables associated to CAD. Visceral fat assessed by CT is an independent marker of CAD determined by CT angiography.

1. Introduction

Obesity, defined by a body mass index of at least 30 kg/m^2, is associated with an increased risk for cardiovascular disease and cardiac mortality [1–5]. Most studies designed to assess the health risk of body fat distribution have used anthropometric adiposity measurements such as waist circumference or waist-to-hip ratio to estimate the amount of abdominal adipose tissue. Both of these measurements are independently related to coronary heart disease (CHD), and it is likely that this association is due to an enlargement of visceral fat stores [5–7]. In fact, the association between risk factors for CHD and visceral fat, measured directly with computed tomography (CT), is stronger than the associations observed with waist circumference or waist-to-hip ratio [8,9].

The visceral adipose tissue may be a unique pathogenic fat depot, in part because it secretes vasoactive substances and other various bioactive adipocytokines [10–13]. Adipocytokines levels are increased in obesity-related diseases such as type 2 Diabetes, metabolic syndrome and cardiovascular diseases [14–16]. A number of prospective and cross-sectional studies have shown a higher risk of diabetes, impaired glucose tolerance, insulin resistance, hypertension, dyslipidemia, metabolic syndrome in association with a greater visceral adiposity [11,17–20]. In addition to visceral fat depots, hepatic steatosis has also been associated with metabolic risk [21]. Although its pathogenesis remains unclear, it is suggested that sustained liver exposure to an increased flux of free fatty acids from visceral adipose tissue would lead to an increase in lipid deposition [22]. The fatty liver is resistant to insulin action to suppress hepatic glucose production, which results in hyperglycemia and hyperinsulinemia. Non-invasive methods like CT have been widely used in both research and clinical practice to assess hepatic fat [21,23].

Besides the association between visceral adipose depots and CHD risk factors, studies reported relations of greater abdominal adiposity and subclinical atherosclerosis, defined as coronary artery calcification (CAC) [24]. Recently multidetector CT angiography has taken a leading role in early detection of coronary artery disease (CAD) since it allows both vessel luminal evaluation and plaque detection [25]. Studies show that plaque identification by cardiac CT might have prognostic information in addition to clinical risk stratification [26–29].

* Corresponding author at: Unidade Clinica de Lipides, InCor HCFMUSP Av. Dr Enéas C. Aguiar 44, Segundo Andar Bloco 2, Sala 4, CEP 05403-000 São Paulo, Brazil. Tel.: +55 11 30695320; fax: +55 11 30695320.
E-mail address: raul.santos@incor.usp.br (R.D. Santos).

0021-9150/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.atherosclerosis.2009.10.023

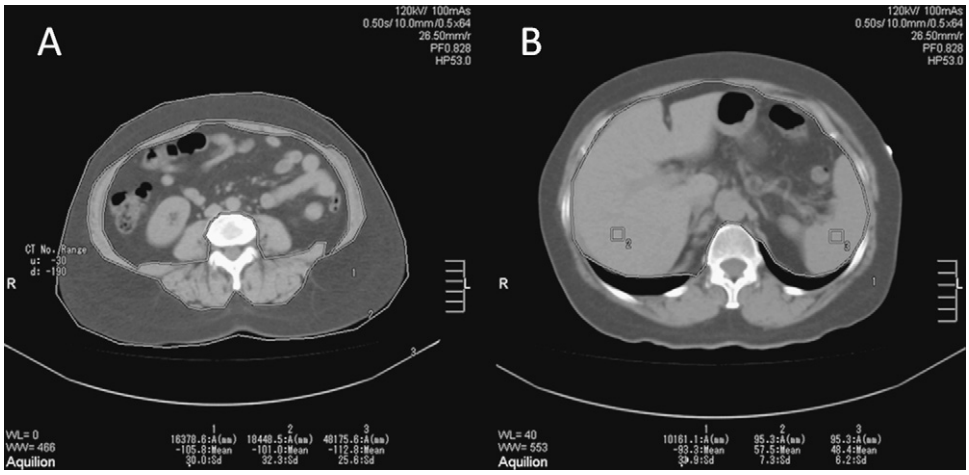

Fig. 1. Computed tomography in L4-L5 (A) and T12-L1 (B) intervertebral levels to assess visceral adiposity. (A) The visceral fat area (VFA) (1), the muscular and VFA summed (2) and the total fat areas in mm^2 (3) are manually determined at L4-L5 level. The subcutaneous fat area is determined subtracting the total fat area from the muscular summed VFA. These measurements represent the umbilicus topography. (B) The VFA (1) is manually determined at T12-L1 level and two regions of interest are located at the liver (2) and at the spleen (3) to determine the attenuation ratio between them. These measurements represent the VFA in the liver topography.

The aim of this study was to investigate whether CT adiposity measurements (e.g. visceral adipose tissue, subcutaneous adipose tissue and hepatic fat) are associated with CAD assessed by cardiac CT. Furthermore, to assess whether these adiposity measurement by CT are better related to CAD than traditional adiposity anthropometric measurements.

2. Methods

2.1. Study population

The participants of this study were referred to perform a CT coronary angiography at the *Heart Institute* (*InCor*) – University of São Paulo Medical School Hospital, in Sao Paulo, Brazil by their assistant physicians to investigate the presence of CAD. Subjects with a previous history of myocardial infarction, percutaneous or surgical myocardial revascularization or that presented a diagnosis of coronary stenosis by a previously performed invasive or non-invasive coronary angiography were excluded. One hundred and twenty-five consecutive subjects were studied cross-sectionally from July 2007 and February 2008. Sixty individuals were asymptomatic (48%), thirty-two were evaluating thoracic pain and thirty-three individuals were performing the CT angiography after a positive or inconclusive non-invasive stress testing. This study was approved by the local ethics review board and all participants signed an informed consent.

2.2. CHD risk factors assessment and anthropometric measurements

All participants were asked to fast for 12 h before the clinical interview and examination. Risk factors for CHD were assessed during a medical interview and blood pressure was measured. The body mass index in kg/m^2 was calculated by the formula: weight/(height)^2. Waist girth was measured laterally at the midway between the iliac crest and the lowest lateral portion of the rib cage. The hip girth was measured in the maximum circumference of the buttocks and the waist-to-hip ratio was then calculated. The measurements described above were performed according to international guidelines [30,31].

Blood samples were drawn from an antecubital vein. Plasma concentrations of total, high-density lipoprotein and low-density lipoprotein cholesterol, triglycerides and glucose were measured by standard enzymatic methods in an automated system.

The presence of the metabolic syndrome was defined by the International Diabetes Federation (IDF) criteria that considered obligatory the presence of increased abdominal adiposity for the diagnosis [32], e.g. >80 cm and 94 cm for women and men, respectively. The 10-year hard CHD risk was calculated by Framingham risk score [33].

2.3. CT adiposity measurements

Axial images of the abdominal region were obtained using a 64 multidetector-row CT scanner (Aquilion, Toshiba Medical Systems, Otawara, Japan). The subjects were examined in a supine position with their arms stretched above their heads. CT scans were taken with 10 mm thickness, 120 kV and 200 mA at the level of L4-L5 to determine the visceral (VFA L4-L5) and subcutaneous abdominal fat areas (SFA L4-L5). These areas were manually determined using an attenuation range of −30 to −190 Hounsfield units that correspond to fat structures (Fig. 1) [13,34]. To evaluate upper abdomen and liver fat infiltration, the same imaging protocol was used at the level of T12-L1 (VFA T12-L1). At this level, besides the area measurement, a region of interest with 1.0 cm × 1.0 cm was placed in the liver and the spleen to determine the attenuation ratio between these organs (Fig. 1) [23]. Due to anatomical variations precluding clear spleen identification the liver–spleen attenuation ratio (LSAR) was determined in 111 of the 125 patients.

2.4. CT coronary evaluation

Coronary calcifications in the epicardial coronary arteries were determined with a prospective electrocardiographic gating with 400-ms gantry rotation, 120-kV tube voltage, and 300-mA tube current. CAC was measured by using the Agatston method and a total CAC score was determined from the sum of individual scores of the major epicardial coronary arteries [28,35].

Computed tomographic coronary angiography was acquired using 64 × 0.5 mm collimation, 400 ms gantry rotation, 300–500 mA with ECG trigger and 120 kV tube voltage. Contrast agent (80–110 ml; 300 mg iodine/ml) was injected intravenously (5 ml/s). Metoprolol (5–15 mg) was used in patients whenever

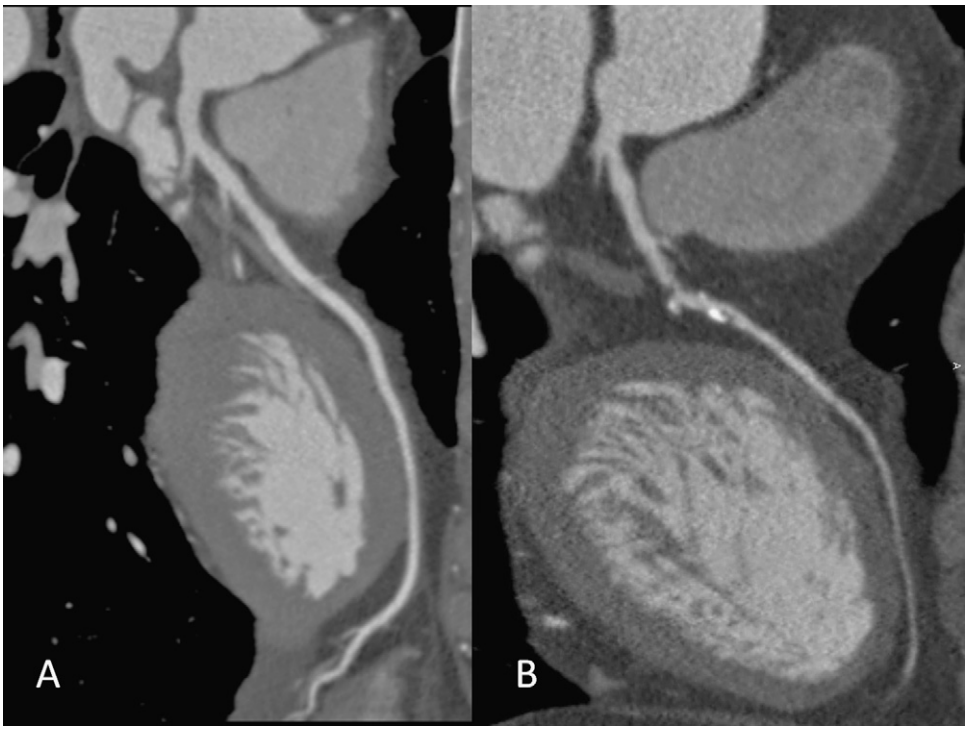

Fig. 2. Left main and left anterior descendent coronary arteries of two participants representing: (A) normal coronary computed tomography angiography (CTA) and (B) non-calcified and calcified coronary plaques identified by CTA.

heart rate was above 70 bpm prior to contrast infusion. These parameters are similar to a previously described protocol [36]. The mean effective doses reported for this protocol were 14 mSv for men and 15 mSv for women.

Images were reconstructed at several phases of the cardiac cycle and sent to 2 blinded and independent observers, to evaluate both coronary calcium scans and the CT coronary angiography data sets using axial and multiplanar reformatted images. Data sets were evaluated, using a coronary modified model [37], for the presence of atherosclerotic plaque (Fig. 2). CAD was defined by the visual assessment of coronary plaques. Plaques were defined as any vessel wall bulging above 1 mm, with low CT attenuation (non-calcified plaque), high and low attenuation (mixed plaque) and high CT attenuation (calcified plaque), as previously shown [38,39]. Clearly identified coronary plaques were classified according their stenosis grade in two groups: 1 to 49% stenosis and ≥50% stenosis. In case of non-agreement between the observers data was analyzed by a third investigator. The Agatston score and the CT angiographies were evaluated with commercially available software (Vitrea2, Vital Images, Plymouth, USA).

In this study, the presence of CAD was defined by visual assessment of any plaque calcified or not, obstructive or not detected by the CT angiography. When a plaque was identified, we considered significant stenosis as the presence of luminal narrowing ≥50%.

2.5. Statistical analysis

Continuous variables are expressed as mean, median, standard deviation and range, when applicable. Categorical variables were analyzed as relative and absolute frequencies. Data normality was calculated by the Kolmogorov–Smirnov test. Student *t* and Mann–Whitney tests were used to compare parametric and non-parametric data, respectively. Homogeneity between proportions was tested with Chi-square or Fisher's exact test when necessary. The univariate correlation between studied variables was calculated by the test of Spearman. The association of CAC and CAD with clinical and CT adiposity parameters was performed by logistic regression model and stepwise selection of variables. In order to further evaluate the specific contribution of each individual CT measurements of adiposity with CAD, multivariate models were built considering traditional risk factors, clinical measurements of adiposity and each one of these CT variables independently. A cut-off threshold was obtained by univariate analysis with receiver operating characteristic curves and efficiency indexes (sensitivity, specificity and accuracy). Statistical tests were performed using the SAS software (Cary, NC, USA).

3. Results

3.1. Clinical and CT angiography characteristics of the studied population

A total of 125 participants (57% men), from 24 to 83 year-old, mean age 56.0 ± 12 years were included in these analyses. Normal coronaries on CT angiography were found in 55 patients (44%) and CAD was found in 70 patients (56%). There was a good interobserver agreement for plaque identification (*kappa index* = 0.86, $p < 0.001$). A total of 1862 vessel segments were evaluated and 50 (2.7%) were classified as ineligible due to imaging artifacts. Among those with CAD, 22 patients (17.6%) presented ≥50% luminal narrowing and 48 patients (38.4%) presented non-significant obstructions. CAC was present in 65 subjects (52%) and the median calcium score (ranges) was 3.0 (0–12,033). Among patients with CAD, 7.1% ($n = 5$) showed a calcium score of zero.

Table 1 shows the clinical characteristics of subjects presenting or not CAD. When compared to normal CT angiography subjects, those with CAD were older ($p < 0.001$), presented higher fasting blood glucose levels ($p = 0.033$), greater prevalence of dyslipidemia ($p = 0.014$), metabolic syndrome ($p = 0.002$), lipid-lowering therapy use ($p = 0.035$), and a greater 10-year calculated hard CHD risk ($p = 0.002$).

Table 1
Baseline characteristics of the 125 participants according to CAD status.

	Normal angiography[a] ($n=55$)	CAD[a] ($n=70$)	p value
Age (years)	53 ± 10.7	60 ± 12	<0.001
Male gender, n (%)	29 (53)	42 (60)	0.415
Hypertension, n (%)	29 (53)	47 (67)	0.101
Diabetes mellitus, n (%)	5 (9)	12 (17)	0.172
Dyslipidemia, n (%)	32 (58)	55 (76)	0.014
Family history of early CHD, n (%)	10 (18)	22 (31)	0.092
Current smoking n (%)	4 (7)	9 (13)	0.310
Sedentarism n (%)	49 (89)	53 (76)	0.055
Systolic blood pressure (mmHg)	133 ± 22	137 ± 21	0.290
Diastolic blood pressure (mmHg)	78 ± 14	79 ± 15	0.849
Total cholesterol (mg/dl)	216 ± 82	213 ± 62	0.370
HDL cholesterol (mg/dl)	45 ± 10	47 ± 11	0.535
LDL cholesterol (mg/dl)	141 ± 77	135 ± 56	0.605
Triglycerides (mg/dl)	146 ± 133	163 ± 112	0.138
Fasting blood glucose (mg/dl)	95 ± 10	107 ± 37	0.033
Creatinine (mg/dl)	0.90 ± 0.17	0.95 ± 0.20	0.304
Metabolic syndrome n (%)	28 (50)	54 (81)	0.002
10-year CHD risk (%)	5 ± 6	9 ± 7	0.002
Antihypertensive agents n (%)	30 (56)	43 (61)	0.438
Hypoglicemic agents n (%)	5 (9)	11 (16)	0.271
Lipid-lowering agents n (%)	21 (38)	40 (57)	0.035

All data are presented as number of subjects (%) or mean ± SD.
CHD = coronary heart disease; HDL = high-density lipoprotein; LDL = low-density lipoprotein.
[a] Normal angiography and CAD (coronary artery disease) defined by computed tomography angiography.

Table 2
Univariate association of anthropometric and CT adiposity measurements according to CAD and CAC by CT angiography.

	CAD by CT angiography		CAC by the Agatston score	
	Normal angiography ($n=55$)	CAD ($n=70$)	No CAC ($n=60$)	CAC present ($n=65$)
Weight (kg)	79.5 ± 15	78 ± 16	78.8 ± 14.8	78.8 ± 15.8
Body mass index (kg/m^2)	28.8 ± 4	29.08 ± 4.7	28.6 ± 4.8	29.24 ± 4.8
Waist (cm)	97 ± 11.1	99 ± 12	96.8 ± 10.8	99.7 ± 12.5
Hip (cm)	98.5 ± 11.1	100.5 ± 11.3	98.3 ± 10.9	100.6 ± 11.4
Waist-to-hip ratio	0.99 ± 0.07	0.99 ± 0.08	0.99 ± 0.07	0.99 ± 0.08
CT measurements				
VFA L4-L5 (cm^2)	147 ± 54.34	183 ± 83.65**	147.9 ± 52.9	185.1 ± 86.2**
SFA L4-L5 (cm^2)	279 ± 111.0	274 ± 101.6	275.3 ± 109.4	277.1 ± 02.5
VFA T12-L1 (cm^2)	128 ± 76.07	169 ± 98.17*	130 ± 76.2	170.9 ± 99.5*
LSAR[a]	1.17 ± 0.42	1.01 ± 0.34*	1.15 ± 0.4	1.01 ± 0.34*

VFA L4-L5 = visceral fat area at the L4-L5 intervertebral level; SFA L4-L5 = subcutaneous fat area at the L4-L5 intervertebral level; VFA T12-L1 = visceral fat area at the T12-L1 intervertebral level; LSAR = liver/spleen attenuation ratio.
[a] LSAR was measured in 111 subjects, 49 with normal angiography and 62 with CAD.
* $p<0.05$.
** $p<0.01$.

3.2. Clinical and CT adiposity measurements in subjects presenting CAD or CAC

Clinical and CT measurements of adiposity in subjects presenting or not CAD and CAC are shown in Table 2. No differences were found in clinical adiposity measurements between the groups. In general there was a high prevalence of excess adiposity in both groups. Increased BMI defined as ≥25 kg/m^2 was found respectively in 81% and 73% of those presenting or not CAD ($p=0.17$). An increased abdominal adiposity defined as waist measurements >80 cm for women and >94 cm for men were found in 86% and 78% of those with and without CAD, respectively ($p=0.57$). On the other hand, CAD subjects had higher values of VFA L4-L5 ($p=0.01$), VFA T12-L1 ($p<0.05$) and LSAR ($p<0.05$). Similarly those presenting CAC had significantly higher VFA L4-L5 ($p<0.01$), VFA T12-L1 and lower LSAR than those without CAC ($p<0.05$).

Table 3 shows the univariate correlation coefficients between clinical and CT adiposity measurements. Waist circumference was better correlated with CT measurements than body mass index, hip and hip/waist ratio. The hip circumference showed the best correlation with SFA L4-L5.

Visceral fat measurements assessed by CT were related to each other. VFA L4-L5 was correlated to both VFA T12-L1 ($r=0.66$, $p=0.001$) and to LSAR ($r=-0.45$, $p=0.001$). The VFA T12-L1 and LSAR were also inversely correlated ($r=-0.39$, $p=0.001$).

Table 3
Pearson correlation coefficients between anthropometric and CT adiposity measurements.

	VFA L4-L5	SFA L4-L5	VFA T12-L1	LSAR[a]
Body mass index	0.60**	0.73**	0.47**	−0.21*
Waist	0.74**	0.63**	0.66**	−0.28*
Hip	0.48**	0.79**	0.32**	−0.07
Waist-to-hip ratio	0.43**	−0.13	0.57**	−0.32**

[a] LSAR measured in 111 subjects.
* $p<0.05$.
** $p<0.001$.

3.3. Relation of individual adiposity measurements with CAD

No correlations were found in both univariate and multivariate analysis between anthropometric adiposity measurements and

Table 4
Multivariate association between CT adiposity measurements and CAD.

	OR (95% CI) per 1 unit increase
Model 1	
VFA T12-L1	1.007 (1.002–1.012)
LSAR	6.28 (1.54–25.64)
VFA L4-L5	1.008 (1.002–1.015)
Model 2	
VFA T12-L1	1.007 (1.002–1.013)
LSAR	–
VFA L4-L5	–

Model 1: adjusted for age, risk factors an laboratory measurements.
Model 2: model 1+ adjusted for CT adiposity measurements.

CAD. The mean VFA T12-L1 and VFA L4-L5 were respectively $151.2 \pm 91\,cm^2$ and $167.2 \pm 74.2\,cm^2$. Table 4 show the multivariate adjusted relation between CT adiposity measurements and the presence of CAD. After adjustment for clinical and laboratory risk factors there was a significant association between VFA T12-L1, LSAR and VFA L4-L5 with CAD. Defining a threshold of $145\,cm^2$ to the VFA T12-L1, a 2.85-fold (95% CI 1.30–6.26) CAD risk was found. This threshold awards a sensitivity, specificity and accuracy of 72.9%, 56.4% and 65.6%, respectively. A threshold of 1.1 to LSAR confers and odds ratio of 3.0 (95% CI 1.31–6.90) for the presence of CAD. This cutoff confers a sensitivity, specificity and accuracy of 74.2%, 55.1% and 65.8%, respectively. Patients with VFA L4-L5 $\geq 150\,cm^2$ had a 2.87-fold (95% CI 1.31–6.30) increased CAD risk compared to those with lower values after adjustment for the other risk factors and the anthropometric measures. The threshold of $150\,cm^2$ was determined with sensitivity, specificity and accuracy of 68.6%, 60% and 64.8%, respectively. After adjustment for clinical, laboratory and CT measurements of adiposity, age OR 1.06 (95% CI 1.02–1.11) and VFA T12-L1 were independent predictors of the presence of CAD detected by CT angiography (Table 4).

3.4. Multivariate determinants of CAC

After adjustment for other parameters a calcium score > zero was related to family history of early CHD, to the 10-year CHD risk calculated by Framingham risk score and to the presence of the metabolic syndrome, odds ratios of 3.67 (1.42–9.45), 1.09 (1.02–1.16) and 3.06 (1.35–6.95), respectively, no association persisted between CAC and CT adiposity measurements.

4. Discussion

To the best of our knowledge, this is the first study evaluating the relation between visceral adiposity measurements and CAD detected by CT angiography. The upper abdominal fat (VFA T12-L1) was independently related to coronary atherosclerosis after adjustment for cardiovascular risk variables. The VFA T12-L1 and age had a better performance than anthropometric adiposity measurements and classical risk factors for CAD evaluation.

The early detection of subjects at an increased cardiovascular event risk is important to implement preventive measures. In clinical practice, adiposity estimated by usual anthropometric measurements like body mass index, waist circumference and the waist-to-hip ratio have been used to stratify CAD risk [5]. However, in our study differently from CT adiposity measurements no relation between these anthropometric measurements with CAD and CAC was found. Our results do not invalidate previously consecrated and easily obtainable and inexpensive measurements of adiposity like the BMI or waist circumference [1–9]. The lack of association of these markers with CAD probably occurred due the high prevalence of increased adiposity expressed by high BMI and waist circumference measurements in both study groups. In relation to CAC, we have found that the presence of the metabolic syndrome defined by IDF, in which increased abdominal adiposity is an obligatory condition was indeed associated with the presence of CAC [32].

In addition to CAC quantification CT angiography allows de detection of purely non-calcified plaques, mixed plaques as well as luminal obstruction, with this method presenting a greater sensitivity to detect early atherosclerotic disease than CAC quantification alone [36,42,43]. This study shows that when CT angiography is used for CAD detection CT visceral adiposity measurements were all related to CAD even when there was a high prevalence of clinical markers of obesity. These results confirm previous studies that demonstrated the CT superiority to evaluate CAD risk [8,9]. In addition, even considering the relative high prevalence of dyslipidemia, hypertension, and the metabolic syndrome the multivariate analysis showed that after age, VFA measured at T12-L1 level was the only other independent variable related to CAD. However, evaluating each visceral fat compartment separately, VFA L4-L5 (representing the umbilicus region) and LSAR (representing hepatic fat) were also related to CAD. One possible explanation for the superiority of upper visceral fat compartment as CAD determinant over the other fat depots is that VFA T12-L1 represents both visceral and hepatic fats. There is evidence that hepatic steatosis independently predicts the metabolic syndrome, type 2 Diabetes, cardiovascular and liver diseases [21,40].

Previously Kobayashi et al. [20] and Zamboni et al. [41], showed that visceral fat, evaluated by CT, was related to coronary stenosis determined by invasive coronary angiography. Recently, considerable advances have been made in the field of cardiac imaging with newer 64-slice multidetector-row CT, with high diagnostic accuracy for detection of coronary plaques, allowing early and reliable non-invasive detection of CAD [25,36,42,43]. The presence of atherosclerotic plaques even those considered non-significant (<50% luminal narrowing) are associated with an elevated event risk as compared with patients without CAD [26–29]. Early diagnosis might be important once these individuals usually are asymptomatic and present normal functional tests being unexpected candidates to invasive coronary angiographies. We were able to show a relation between CAD by CT angiography and visceral fat, highlighting the ability and high sensitivity of CT angiography to detect initial stages of atherosclerosis.

Identified limitations of our study are its cross-sectional design, a referred population from a single center with high prevalence of risk factors including obesity that limits the applicability of our results to the general population and other ethnicities. In addition, there was a high prevalence of lipid and blood pressure lowering medication use, a fact that might have weakened the association of parameters like Framingham risk score and CAD. However, even considering these facts visceral adiposity quantified by CT was still related to the presence of CAD detected CT angiography.

In conclusion, CT visceral fat evaluation in different sites was related to CAD and was an independent marker of CAD determined by CT angiography. Prospective studies are necessary to demonstrate its role in clinical practice.

Acknowledgements

This study was supported by a grant from FAPESP (Fundação de Amparo a Pesquisa do Estado de Sao Paulo, Sao Paulo Brazil).

References

[1] Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath Jr CW. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999;341:1097–105.
[2] Kannel WB, Wilson PW, Nam BH, D'Agostino RB. Risk stratification of obesity as a coronary risk factor. Am J Cardiol 2002;90:697–701.

[3] Peeters A, Barendregt JJ, Willekens F, et al. Obesity in adulthood and its consequences for life expectancy: a life-table analysis. Ann Intern Med 2003;138:24–32.
[4] Wilson PW, D'Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. Arch Intern Med 2002;162:1867–72.
[5] Yusuf S, Hawken S, Ounpuu S, et al. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. Lancet 2005;366:1640–9.
[6] Balkau B, Deanfield JE, Despres JP, et al. International Day for the Evaluation of Abdominal Obesity (IDEA): a study of waist circumference, cardiovascular disease, and diabetes mellitus in 168,000 primary care patients in 63 countries. Circulation 2007;116:1942–51.
[7] Canoy D, Boekholdt SM, Wareham N, et al. Body fat distribution and risk of coronary heart disease in men and women in the European Prospective Investigation Into Cancer and Nutrition in Norfolk cohort: a population-based prospective study. Circulation 2007;116:2933–43.
[8] Fox CS, Massaro JM, Hoffmann U, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. Circulation 2007;116:39–48.
[9] Nicklas BJ, Penninx BW, Ryan AS, et al. Visceral adipose tissue cutoffs associated with metabolic risk factors for coronary heart disease in women. Diabetes Care 2003;26:1413–20.
[10] Bacha F, Saad R, Gungor N, Arslanian SA. Adiponectin in youth: relationship to visceral adiposity, insulin sensitivity, and beta-cell function. Diabetes Care 2004;27:547–52.
[11] Kanaya AM, Harris T, Goodpaster BH, Tylavsky F, Cummings SR. Adipocytokines attenuate the association between visceral adiposity and diabetes in older adults. Diabetes Care 2004;27:1375–80.
[12] Nielsen S, Guo Z, Johnson CM, Hensrud DD, Jensen MD. Splanchnic lipolysis in human obesity. J Clin Invest 2004;113:1582–8.
[13] Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. Endocr Rev 2000;21:697–738.
[14] Hotamisligil GS, Shargill NS, Spiegelman BM. Adipose expression of tumor necrosis factor-alpha: direct role in obesity-linked insulin resistance. Science 1993;259:87–91.
[15] Matsuzawa Y. Adiponectin: identification, physiology and clinical relevance in metabolic and vascular disease. Atheroscler Suppl 2005;6:7–14.
[16] Steppan CM, Bailey ST, Bhat S, et al. The hormone resistin links obesity to diabetes. Nature 2001;409:307–12.
[17] Goodpaster BH, Krishnaswami S, Resnick H, et al. Association between regional adipose tissue distribution and both type 2 diabetes and impaired glucose tolerance in elderly men and women. Diabetes Care 2003;26:372–9.
[18] Goodpaster BH, Krishnaswami S, Harris TB, et al. Obesity, regional body fat distribution, and the metabolic syndrome in older men and women. Arch Intern Med 2005;165:777–83.
[19] Hayashi T, Boyko EJ, Leonetti DL, et al. Visceral adiposity is an independent predictor of incident hypertension in Japanese Americans. Ann Intern Med 2004;140:992–1000.
[20] Kobayashi H, Nakamura T, Miyaoka K, et al. Visceral fat accumulation contributes to insulin resistance, small-sized low-density lipoprotein, and progression of coronary artery disease in middle-aged non-obese Japanese men. Jpn Circ J 2001;65:193–9.
[21] Kotronen A, Yki-Jarvinen H. Fatty liver: a novel component of the metabolic syndrome. Arterioscler Thromb Vasc Biol 2008;28:27–38.
[22] Fong DG, Nehra V, Lindor KD, Buchman AL. Metabolic and nutritional considerations in nonalcoholic fatty liver. Hepatology 2000;32:3–10.
[23] Nguyen-Duy TB, Nichaman MZ, Church TS, Blair SN, Ross R. Visceral fat and liver fat are independent predictors of metabolic risk factors in men. Am J Physiol Endocrinol Metab 2003;284:E1065–71.
[24] Ohashi N, Yamamoto H, Horiguchi J, et al. Visceral fat accumulation as a predictor of coronary artery calcium as assessed by multislice computed tomography in Japanese patients. Atherosclerosis 2009;202:192–9.
[25] Leber AW, Knez A, von ZF, et al. Quantification of obstructive and nonobstructive coronary lesions by 64-slice computed tomography: a comparative study with quantitative coronary angiography and intravascular ultrasound. J Am Coll Cardiol 2005;46:147–54.
[26] Min JK, Shaw LJ, Devereux RB, et al. Prognostic value of multidetector coronary computed tomographic angiography for prediction of all-cause mortality. J Am Coll Cardiol 2007;50:1161–70.
[27] Nasir K, Shaw LJ, Liu ST, et al. Ethnic differences in the prognostic value of coronary artery calcification for all-cause mortality. J Am Coll Cardiol 2007;50:953–60.
[28] Ostrom MP, Gopal A, Ahmadi N, et al. Mortality incidence and the severity of coronary atherosclerosis assessed by computed tomography angiography. J Am Coll Cardiol 2008;52:1335–43.
[29] Pundziute G, Schuijf JD, Jukema JW, et al. Prognostic value of multislice computed tomography coronary angiography in patients with known or suspected coronary artery disease. J Am Coll Cardiol 2007;49:62–70.
[30] National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults—the evidence report. Obes Res 1998;6(Suppl. 2):51S–209S.
[31] Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003;289:2560–72.
[32] Zimmet P, Magliano D, Matsuzawa Y, Alberti G, Shaw J. The metabolic syndrome: a global public health problem and a new definition. J Atheroscler Thromb 2005;12:295–300.
[33] D'Agostino Sr RB, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation 2008;117:743–53.
[34] Yoshizumi T, Nakamura T, Yamane M, et al. Abdominal fat: standardized technique for measurement at CT. Radiology 1999;211:283–6.
[35] Agatston AS, Janowitz WR, Hildner FJ, et al. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15:827–32.
[36] Miller JM, Rochitte CE, Dewey M, et al. Diagnostic performance of coronary angiography by 64-row CT. N Engl J Med 2008;359:2324–36.
[37] Austen WG, Edwards JE, Frye RL, et al. A reporting system on patients evaluated for coronary artery disease. Report of the Ad Hoc Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association. Circulation 1975;51(4 Suppl.):5–40.
[38] Sun J, Zhang Z, Lu B, et al. Identification and quantification of coronary atherosclerotic plaques: a comparison of 64-MDCT and intravascular ultrasound. Am J Roentgenol 2008;190:748–54.
[39] Petranovic M, Soni A, Bezzera H, et al. Assessment of nonstenotic coronary lesions by 64 slice multidetector computed tomography in comparison to intravascular ultrasound: evaluation of nonculprit coronary lesions. J Cardiovasc Comput Tomogr 2009;3:24–31.
[40] Santos RD, Nasir K, Conceição RD, et al. Hepatic steatosis is associated with a greater prevalence of coronary artery calcification in asymptomatic men. Atherosclerosis 2007;194:517–9.
[41] Zamboni M, Armellini F, Sheiban I, et al. Relation of body fat distribution in men and degree of coronary narrowings in coronary artery disease. Am J Cardiol 1992;70:1135–8.
[42] Budoff MJ, Dowe D, Jollis JG, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. J Am Coll Cardiol 2008;52:1724–32.
[43] Meijboom WB, Meijs MF, Schuijf JD, et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. J Am Coll Cardiol 2008;52:2135–44.