Original Article

Relation of Visceral Adipose Tissue to Coronary Artery Calcium in Thai Patients

Jongjirasiri S, MD[1], Nimitkul K, MD[1], Laothamatas J, MD[1], Vallibhakara SA MD, PhD[2]

[1] Department of Diagnostic and Therapeutic Radiology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

[2] Department of Clinical Epidemiology and Biostatistics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Objective: To determine the relationship among body mass index (BMI), waist circumference (WC), abdominal fat area of visceral (VFA), and subcutaneous fat (SFA) on coronary artery calcium (CAC) using a multidetector computed tomography (MDCT) in asymptomatic Thai patients, and describe the prevalence of CAC in Thai patients.

Materials and Methods: Participants (n=1,900, mean age 61 years, 64% women) who were moderate to high risk for coronary artery disease (CAD) according to the RAMA-EGAT score, underwent a MDCT for CAD screening between January and December 2012. BMI, WC, CAC score, abdominal fat area, and cardiovascular risk factors were determined for all patients.

Results: The prevalence of CAC in all patients was 56.7% (67.9% men, 50.3% women). Using multivariate logistic regression analysis adjusting for traditional cardiovascular risk factors and abdominal fat measurement, VFA as visceral to total fat ratio represented an independent risk factor of the presence of CAC (OR 1.55, 95% CI 1.12 to 2.00, p=0.001). Similar relationships were observed across gender, age, WC, history hypertension, and serum fasting blood sugar (FBS).

Conclusion: The authors found that visceral adiposity measured by MDCT is significantly associated with the presence of CAC as a marker of subclinical atherosclerosis in Thai patients.

Keywords: Visceral adipose tissue, Coronary artery calcification, Computed tomography

Received 5 Apr 2019 | Revised 24 Jun 2019 | Accepted 2 Jul 2019

J Med Assoc Thai 2020;103(5):434-41
Website: http://www.jmatonline.com

In recent years, there has been a dramatic increase in global prevalence of obesity, which is major risk factor for multiple cardiovascular disease (CVD) risk factors, including hypertension (HT), dyslipidemia (DLP), diabetes, metabolic syndrome, and some types of cancers[1,2]. In Thailand, some studies showed a high prevalence of overweight and obesity, which increased in the past two decades[3,4].

Many studies have demonstrated that different adipose tissue compartment may be associated with differential metabolic risk. In particular, the visceral adipose tissue (VAT) poses a greater risk for developing obesity-related disorders than subcutaneous adipose tissue (SAT) accumulation[5-8].

The VAT may be a unique pathogenic fat depot because it secretes vasoactive substances and other various bioactive adipocytokines[8-11]. Adipocytokines levels are increased in obesity-related diseases such as type 2 diabetes, metabolic syndrome, and CVDs[12-14]. Other studies suggested that VAT is strongly associated with an adverse metabolic risk profile[15].

Currently, the gold standard for the quantitative assessment of intra-abdominal adipose tissue is computed tomography (CT) and magnetic resonance imaging (MRI)[16]. Cross-sectional view can be measured in single or multiple slices at pre-determined landmarks, which generates strong correlations with the fat volume. Thus, determining quantity of VAT can be measured at the visceral fat area (VFA) from CT[17,18].

Previous studies showed an association between

Correspondence to:

Jongjirasiri S.

Department of Diagnostic and Therapeutic Radiology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

Phone: +66-2-2012465, +66-2-2011212, **Fax**: +66-2-2011297

Email: sjongjirasiri@hotmail.com

How to cite this article: Jongjirasiri S, Nimitkul K, Laothamatas J, Vallibhakara SA. Relation of Visceral Adipose Tissue to Coronary Artery Calcium in Thai Patients. J Med Assoc Thai 2020;103:434-41.

obesity and coronary artery calcium (CAC)[19-21]. CAC is a marker for atherosclerotic burden, which positively associate with cardiovascular event[22-24]. It is usually found using a low radiation dose CT scanning technique as a screening method[25].

The goal of the present study was to determine the relationship of abdominal adiposity, including body mass index (BMI), waist circumference (WC) and CT measurements of adiposity including VFA and subcutaneous fat area (SFA) on the presence of CAC as detected by multidetector computed tomography (MDCT) in asymptomatic Thai patients. Moreover, the prevalence of the presence of CAC in Thai patients was also evaluated.

Materials and Methods

Subjects

Between January and December 2012, asymptomatic participants underwent MDCT for assessment of coronary artery disease (CAD) at the advanced diagnostic imaging center (AIMC), Ramathibodi Hospital, Mahidol University. The 2,105 participants determined as moderate to high risk according to RAMA-EGAT score[26] were recruited. Of these patients, 205 were excluded due to incomplete data. Finally, the study consisted of 1,900 patients.

The present study was a retrospective cross-sectional analytic study, had been approved by the Local Research Ethics Committee, and written informed consents were obtained from all patients.

Risk factor assessment

All patients provided details of their demographics, medical history, and medication usage in clinical risk factor questionnaires. The BMI was calculated by the formula weight in kg divided by height-square in m². WC was measured in inches by using a tape measure at the umbilicus level. The cardiovascular risk factor was calculating using the Framingham risk score[27].

HT was defined by documented data or current treatment with anti- hypertensive drugs. Diabetes was characterized by self-report or current treatment with hypoglycemic agent or insulin. Hyperlipidemia was defined by documented data or current treatment with lipid lowering agent.

Smoking was classified as current smoking, quitting more than 1-month, and never smoking. Family history of CAD was determined as CAD in male relative before the age of 55 and female relative before the age of 65.

Prior to the CT scan, fasting blood samples were obtained. Serum fasting blood sugar (FBS) and lipid profile were also measured.

CAC scoring using MDCT

All patients were imaged using a 320-slice CT scanner (Aquilion ONE, Toshiba, Tokyo, Japan). Prospective electrocardiogram-gated scans were performed in supine position, single breath hold from the carina to the apex of the heart. A tube current of 200 to 250 mA, voltage of 120 kVp and 3-mm slice thickness, 75% of R-R images were obtained. The mean effective doses were calculated to be about 1.1 to 1.7 mSv.

The calcium score was determined using a commercially available external workstation (Vitrea fx 3.0.1, Vital Images, Minnesota, USA). CAC score was calculated according to the Agatston method as previously described[22,23]. The regions of interest were defined based on the vessels and slices, and using the threshold option for pixels greater than 130 Hounsfield units (HU) to measure the area and peak density of the plaques. Depending on the peak density of the plaque, an area of at least 0.52 mm² (2 pixels) was multiplied by one of the following cofactors, a factor of one for 130 to 199 HU, a factor of two for 200 to 299 HU, a factor of three for 300 to 399 HU, and a factor of four for densities greater than 400 HU. The total CAC score was calculated as the sum of the individual lesion scores in all coronary arteries.

MDCT abdominal fat measurements

In addition to cardiac CT scans, single-slice abdominal scan was performed in supine position with both arms stretched above the head and single breath hold, using 320-slice CT scanner (Aquilion ONE, Toshiba, Tokyo, Japan). Conventional CT scan was obtained at the umbilicus level (L4 to L5 level) with a tube current of 400 mA, voltage of 120 kVp and single slice. The mean effective doses were calculated to be about 0.04 to 0.07 mSv.

The abdominal fat area was obtained using a commercially supplied software (ViTrak 1.5, AccuImage Diagnostics, CA, USA) (Figure 1). Subcutaneous fat was defined as the extraperitoneal fat between the skin and muscles, with attenuation ranging from –150 to 0 HU. The intraperitoneal part with the same density as the subcutaneous fat layer was defined as visceral fat. The VFA and SFA were determined.

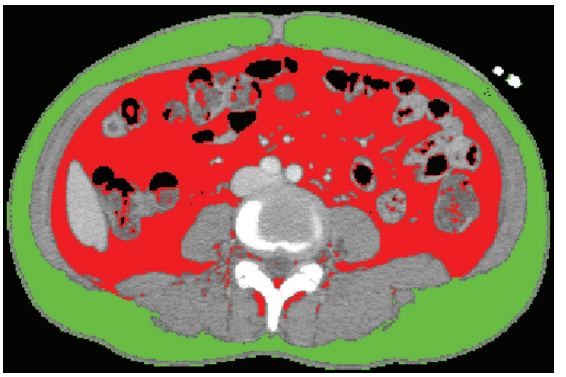

Figure 1. Demonstrates CT measurement of abdominal fat area at umbilical level; green color represents SFA and red color represents VFA.

Statistical analysis

Categorical variables were presented as numbers of patients [n (%)]. Continuous variables were expressed as mean ± standard deviation (SD) in normal distribution or median, range in non-normal distribution. Analyses of each risk factor were performed using Mann-Whitney U test and chi-square test for continuous and categorical variables, respectively. The correlation coefficient was estimated by Pearson's correlation.

Univariate analysis was used to assess the associations among the presence of CAC, risk factors and abdominal fat area. However, utilization of CAC as a continuous variable in standard parametric analyses is challenging due to high frequency of zero scores resulting in high skewed distribution, CAC was dichotomized in presence or absence of CAC. For analyses of some of the risk factors such as age, WC, BMI, FBS, TG, and high-density lipoprotein (HDL), the authors also categorized based on RAMA-EGAT score[26], Framingham risk score[27], and Adult Treatment Panel (ATP) III criteria for metabolic syndrome[28]. The results of univariate analyses, which had a p-value of less than or equal to 0.10, were further used in multivariate logistic regression analysis for parsimonious model.

Multivariate logistic regression analysis was performed to assess the independent relationship of each risk factor to the presence of CAC. A 95% confidence interval (CI) and p-value of less than or equal to 0.05 were considered to indicate significant results. All of statistical tests were performed using Stata version 13.0. The present study was approved by the Ethics Committee of the Faculty of Medicine, Mahidol University (study code: ID 09-56-41).

Table 1. Baseline characteristic

Characteristics	All subject (n=1,900) n (%)
Demographic	
Age (year); median (range)	61 (31 to 90)
Sex	
• Male	685 (36)
• Female	1,215 (64)
Weight (kg); median (range)	63 (35 to 172)
Height (cm); median (range)	159 (133 to 186)
BMI (kg/m^2); median (range)	24.9 (15.7 to 64.7)
WC (inch); median (range)	33 (19 to 55)
Risk factor	
Diabetes mellitus	374 (19.7)
Hypertension	768 (40.6)
Dyslipidemia	1,222 (65.4)
Smoking	
• Current smoker	96 (5.1)
• Quit more than 1 month	515 (27.1)
• Never smoke	1,284 (67.8)
Family history of CAD	370 (19.5)
Physical exam and lab; median (range)	
SBP (mmHg)	132 (87 to 217)
DBP (mmHg)	81 (38 to 129)
FBS (mg/dl)	94 (40 to 289)
Total cholesterol (mg/dl)	207 (42 to 374)
Triglyceride (mg/dl)	109 (75 to 809)
HDL (mg/dl)	53 (4 to 124)
LDL (mg/dl)	124 (20 to 285)
Fat screening data; median (range)	
TFA (cm^2)	366.1 (64.7 to 842.8)
VFA (cm^2)	136.6 (9.3 to 372.6)
SFA (cm^2)	219.6 (25.3 to 643.5)
Visceral to total fat ratio	37.2 (7.9 to 71.5)
Visceral to subcutaneous fat ratio	59.2 (8.6 to 666.2)

SD=standard deviation; BMI=body mass index; WC=waist circumference; CAD=coronary artery disease; FBS=fasting blood sugar; SBP=systolic blood pressure; DBP=diastolic blood pressure; HDL=high density lipoprotein; LDL=low density lipoprotein; TFA=total fat area; VFA=visceral fat area; SFA=subcutaneous fat area

Results

Patient characteristics

Two thousand one hundred five participants were enrolled in the present study. Two hundred five participants were excluded due to incomplete data, resulting in 1,900 patients being included in this study (Table 1).

Table 2. Fat screening data according to gender

Fat screening data	Female n (%)	Male n (%)
TFA tertile (cm^2)		
<320	374 (30.8)	260 (37.0)
320 to 409	404 (33.2)	208 (30.3)
≥410	437 (36.0)	217 (31.7)
VFA tertile (cm^2)		
<115	506 (41.7)	138 (20.1)
115 to 159	436 (35.9)	187 (27.3)
≥160	273 (22.4)	360 (52.6)
SFA tertile (cm^2)		
<190	289 (23.8)	352 (51.4)
190 to 259	423 (34.8)	225 (32.8)
≥260	503 (41.4)	108 (15.8)
Visceral to total fat ratio tertile		
<33	593 (48.8)	53 (7.7)
33 to 42	474 (39.0)	199 (29.1)
≥43	148 (12.2)	433 (63.2)
Visceral to subcutaneous fat ratio tertile		
<48	559 (46.0)	51 (7.5)
48 to 69	455 (37.5)	165 (24.1)
≥70	201 (16.5)	469 (68.5)

TFA=total fat area; VFA=visceral fat area; SFA=subcutaneous fat area

Table 3. CAC score according to gender

CAC score	Total n (%)	Female n (%)	Male n (%)
0	823 (43.3)	603 (49.6)	220 (32.1)
1 to 10	238 (12.5)	152 (12.5)	86 (12.6)
>10 to 100	424 (22.3)	270 (22.2)	154 (22.5)
>100 to 400	239 (12.6)	123 (10.1)	116 (16.9)
>400	176 (9.3)	67 (5.5)	109 (15.9)
Total	1,900	1,215	685

CAC=coronary artery calcium

The study patients consisted of 685 men (36%) and 1,215 women (64%), with a mean age of 61 years (range 31 to 90). The median BMI was 24.9 kg/m^2 (range 15.7 to 64.7). The median WC was 33 inches (range 19 to 55). The median of fat screening data was total fat area (TFA), VFA, and SFA as 366.1 cm^2 (range 64.7 to 842.8), 136.6 cm^2 (9.3 to 372.6), 219.6 cm^2 (25.3 to 643.5), respectively. The VFA was larger in men than women, however, the SFA was larger in women than men (Table 2).

Prevalence of CAC

The prevalence of presence of CAC in all patients was 56.7% (1,077 of 1,900) (Table 3). The prevalence of CAC in men was 67.9% (465 of 685) and in women was 50.3% (612 of 1215).

Risk factors and CAC

The patient characteristics according to CAC status are shown in Table 4. The patients with presence of CAC were significant in men, older, higher weight, higher BMI, large WC, higher prevalence of diabetes mellitus (DM), HT, DLP, smoking, and high FBS.

Abdominal fat measurement and CAC

According to tertiles of TFA, VFA, SFA, visceral to total fat ratio and visceral to subcutaneous fat ratio, all were significantly associated with presence of CAC, except for SFA.

After adjusting the multivariate logistic regression analysis, visceral to total fat ratio remained significantly associated with the presence of CAC with an adjusted odds ratio (OR) of 1.55 (95% CI 1.12 to 2.00, p=0.001). Additionally, gender, age, WC, history of DM, and HT were also significantly associated with the presence of CAC as shown in Table 5.

Discussion

The present research is a large study to investigate the relationship between abdominal adiposity measured by multi-slice CT and the presence of CAC in Thai patients. VFA as visceral to total fat ratio, an index of visceral adiposity, was found to be an independent risk factor predictor of the presence of CAC even after adjustment for sex, age, BMI, WC, and traditional cardiovascular risk factors. These results are consistent with the accumulating evidence that measurements of visceral adiposity are more strongly related to CVD compared with BMI[6,7].

The present study also assessed the prevalence of presence of CAC in Thai patients, which increase with advancing age and is higher in male than in female.

Previously, Hoff et al[29] studied 35,246 asymptomatic self-referred adults and found that the prevalence of CAC increased with the age for men and women and total CAC scores were higher in men than in women across all age groups. Additionally, men consistently demonstrated CAC scores equal to women who were 15 years older, suggesting that subclinical CAD is detected earlier in men compared with women. The Multi-Ethnic Study of Atherosclerosis (MESA)[30] showed that

Table 4. Univariate analysis of factors associated with CAC

Factors	Group; n (%)		OR	95% CI	p-value
	Presence of CAC	No CAC			
Demographics					
Age (years)					
• ≤55	126 (37.3)	211 (62.7)	1		
• >55	951 (60.8)	296 (39.2)	3.05	2.51 to 3.71	<0.001
Sex					
• Female	612 (50.4)	603 (49.6)	1		
• Male	465 (67.9)	220 (32.1)	2.08	1.71 to 2.54	<0.001
Weight (kg)					
• <60	416 (51.3)	395 (48.7)	1		
• >60	661 (60.7)	428 (39.3)	1.47	1.22 to 1.76	<0.001
Height (cm)					
• <160	575 (61.6)	359 (38.4)	0.67	0.56 to 0.81	<0.001
• >160	502 (51.9)	464 (48.1)	1		
BMI (kg/m^2)					
• ≤25	563 (53.7)	485 (46.3)	1		
• >25	514 (60.3)	338 (39.7)	1.31	1.09 to 1.57	0.004
WC					
• Abdominal obesity*	627 (58.8)	439 (41.2)	1.22	1.01 to 1.46	0.034
• No abdominal obesity	450 (54.0)	384 (46.0)	1		
Risk factors					
Diabetes mellitus					
• Yes	252 (67.4)	122 (32.6)	1.76	1.38 to 2.23	<0.001
• No	825 (54.1)	701(45.9)	1		
Hypertension					
• Yes	515 (67.1)	253 (32.9)	2.06	1.70 to 2.50	<0.001
• No	558 (49.7)	564 (50.3)	1		
Dyslipidemia					
• Yes	721 (59.0)	501 (41.0)	1.32	1.09 to 1.60	0.050
• No	333 (52.2)	309 (47.8)	1		
Smoking					
• Yes	65 (67.7)	31 (32.3)	1.79	1.15 to 2.78	0.001
• Quit	318 (61.8)	197 (38.2)	1.38	1.12 to 1.70	
• No	693 (54.0)	591 (46.0)	1		
Family history					
• Yes	201 (54.3)	169 (45.7)	0.88	0.70 to 1.11	0.294
• No	875 (57.3)	655 (42.8)	1		
Laboratory data					
FBS (mg/dl)					
• >100	623 (52.6)	526 (47.4)	1.57	1.29 to 1.90	<0.001
• <100	454 (63.5)	261 (36.5)	1		
Triglyceride (mg/dl)					
• >150	254 (57.7)	186 (42.3)	1.05	0.85 to 1.31	0.648
• <150	779 (56.5)	600 (43.5)	1		
HDL					
• Low	287 (58.6)	203 (41.4)	1.11	0.09 to 1.37	0.328
• Normal	790 (56.0)	120 (44.0)	1		
Fat screening data					
TFA tertile (cm^2)					<0.001
• <320	334 (52.7)	300 (47.3)	1		
• 320 to 409	345 (56.4)	267 (43.6)	1.16	1.12 to 1.74	
• ≥410	398 (60.9)	256 (39.1)	1.40	0.95 to 1.30	
VFA tertile (cm^2)					<0.001
• <115	314 (48.8)	330 (51.2)	1		
• 115 to 159	336 (53.9)	287 (46.1)	1.23	0.99 to 1.53	
• ≥160	427 (67.5)	206 (32.5)	2.18	1.74 to 2.73	
SFA tertile (cm^2)					0.259
• <190	380 (59.3)	261 (40.7)	1.16	0.93 to 1.45	
• 190 to 259	357 (55.1)	291 (44.9)	0.98	0.78 to 1.22	
• ≥260	340 (55.7)	271 (44.4)	1		
Visceral to total fat ratio tertile					<0.001
• <33	311 (48.1)	335 (51.9)	1		
• 33 to 42	359 (53.3)	314 (46.7)	1.23	0.99 to 1.53	
• ≥43	407 (70.1)	174 (29.9)	2.52	2.00 to 3.19	
Visceral to subcutaneous fat ratio tertile					<0.001
• <48	296 (48.5)	314 (51.5)	1		
• 48 to 69	323 (52.1)	297 (47.9)	1.15	0.92 to 1.44	
• ≥70	458 (68.4)	212 (31.5)	2.29	1.83 to 2.88	

OR=odds ratio; CI=confidence interval; BMI=body mass index; WC=waist circumference; FBS=fasting blood sugar; HDL=high density lipoprotein; TFA=total fat area; VFA=visceral fat area; SFA=subcutaneous fat area; CAC=coronary artery calcium

* Waist circumference in male more than 36 inch and female more than 32 inch

Table 5. Multivariate logistic regression of the association between factors and CAC

	Coefficient	OR	95% CI	p-value
Demographics				
Age	1.15	3.18	(2.61 to 3.88)	<0.001
Sex	0.62	1.85	(1.44 to 2.37)	<0.001
WC	0.22	1.24	(1.01 to 1.53)	0.034
Risk factors				
Hypertension	0.58	1.79	(1.46 to 2.20)	<0.001
Lab data				
FBS	0.25	1.28	(1.04 to 1.58)	0.021
Fat screening data				
Visceral to total fat ratio	0.44	1.55	(1.12 to 2.00)	0.001

OR=odds ratio; CI=confidence interval; WC=waist circumference; FBS=fasting blood sugar

men had greater calcium levels than women, and calcium amount and prevalence were steadily higher with increasing age. Besides, there were significant difference in calcium by race where Chinese had lowest calcium value among white, Hispanic, and black.

Among the studies in Asia, Shisen et al[31] examined 953 physician-referred Chinese patients and demonstrated that prevalence of CAC increased significantly with age and was much higher in male than female (77% in male). The finding is in contrast to the present study and might have resulted from the higher male patients than the present study and the selected nature of the sample (i.e., physician-referred subjects), which might have over-estimated the true prevalence of CAC. In Korea, Park et al[32] showed similar age and gender associations to the present study but the prevalence of CAC tended to be lower in Koreans, which could be due to larger sample size and the present study were self-referred subjects.

Many prior studies have identified association between visceral adiposity and CAC. In St. Francis Heart Study[33], visceral obesity measured by waist to hip ratio or intra-abdominal adiposity was positively correlated with CAC among 1,269 U.S. women and men in 50 to 70 years old. The CARDIA study[34] has demonstrated that abdominal obesity measured by waist girth or waist to hip ratio was associated with CAC in 2519 African-American and white young adults in models adjusted for cardiovascular risk factors. For diabetic individuals, the PREDICT study[35] showed waist to hip ratio was significant predictor after adjustment for multiple cardiovascular risk factors in 495 diabetic subjects. In another multiethnic study on type 2 diabetes, visceral fat measured by CT predicted CAC.

For the previous studies that have used as a direct measure of VAT, the findings were similar. A sub-study from MESA[36] found an association between non-subcutaneous fat adiposity and CAC in both gender. Fox et al examined 3,130 participants from the Framingham Heart Study[20] and Lui et al studied 2,884 African-Americans in the Jackson Heart Study[37] found similarly that BMI, WC, SAT, VAT were all associated with CAC.

Among 390 Japanese patients, Ohashi et al[21] observed that VFA was significant related to CAC in both men and women. However, the authors cannot compare these findings directly with the results of the study as they included both symptomatic and asymptomatic patients.

The significant association between visceral fat and CAC observed in the present study could explain, at least in part, the excess risk of atherosclerosis in abdominal obese patients. Therefore, measuring visceral fat is a useful clinical tool for identifying patients with potential future CVD risk.

The large sample size, the low dose non-contrast study assessment of CAC, and abdominal adiposity by MDCT are strengths of the present investigation.

Limitation

The present study had some limitations. First, the data were exclusively collected from Thai patients with moderate to high risk for CVD in a single institute using across sectional retrospective method. Considering the cross-sectional nature of the present study, causality cannot be established. As well as, it is uncertain whether the present study findings can be generalized to all Thai population or even low risk subjects. Prospective-cohort study should be warranted.

Second, the outcome was used as the presence of CAC not the extent of CAC. As the result, the authors cannot tell whether presence of higher VFA associated with higher or progression of CAC. It is possible that measures of adiposity may be associated with progression of CAC.

Conclusion

The authors found that visceral adiposity measured by MDCT is significantly associated with the presence of CAC as a marker of subclinical atherosclerosis in Thai patients. Additionally, the prevalence of the presence of CAC is higher in male

than female and increased with advancing age.

What is already known on this topic?

VAT is strongly associated with an adverse metabolic risk profile.

What this study adds?

Visceral adiposity measured by MDCT is significantly associated with the presence of CAC as a marker of subclinical atherosclerosis in Thai patients.

Conflicts of interest

The authors declare no conflict of interest

References

1. Manson JE, Colditz GA, Stampfer MJ, Willett WC, Rosner B, Monson RR, et al. A prospective study of obesity and risk of coronary heart disease in women. N Engl J Med 1990;322:882-9.
2. 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.
3. Aekplakorn W, Mo-Suwan L. Prevalence of obesity in Thailand. Obes Rev 2009;10:589-92.
4. Jitnarin N, Kosulwat V, Rojroongwasinkul N, Boonpraderm A, Haddock CK, Poston WS. Prevalence of overweight and obesity in Thai population: results of the National Thai Food Consumption Survey. Eat Weight Disord 2011;16:e242-9.
5. Goodpaster BH, Krishnaswami S, Harris TB, Katsiaras A, Kritchevsky SB, Simonsick EM, et al. Obesity, regional body fat distribution, and the metabolic syndrome in older men and women. Arch Intern Med 2005;165:777-83.
6. See R, Abdullah SM, McGuire DK, Khera A, Patel MJ, Lindsey JB, et al. The association of differing measures of overweight and obesity with prevalent atherosclerosis: the Dallas Heart Study. J Am Coll Cardiol 2007;50:752-9.
7. Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, 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.
8. 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.
9. 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.
10. Nielsen S, Guo Z, Johnson CM, Hensrud DD, Jensen MD. Splanchnic lipolysis in human obesity. J Clin Invest 2004;113:1582-8.
11. Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. Endocr Rev 2000;21:697-738.
12. 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.
13. Matsuzawa Y. Adiponectin: Identification, physiology and clinical relevance in metabolic and vascular disease. Atheroscler Suppl 2005;6:7-14.
14. Steppan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM, et al. The hormone resistin links obesity to diabetes. Nature 2001;409:307-12.
15. Fox CS, Massaro JM, Hoffmann U, Pou KM, Maurovich-Horvat P, Liu CY, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. Circulation 2007;116:39-48.
16. Seidell JC, Bakker CJ, van der Kooy K. Imaging techniques for measuring adipose-tissue distribution--a comparison between computed tomography and 1.5-T magnetic resonance. Am J Clin Nutr 1990;51:953-7.
17. Yoshizumi T, Nakamura T, Yamane M, Islam AH, Menju M, Yamasaki K, et al. Abdominal fat: standardized technique for measurement at CT. Radiology 1999;211:283-6.
18. Kobayashi J, Tadokoro N, Watanabe M, Shinomiya M. A novel method of measuring intra-abdominal fat volume using helical computed tomography. Int J Obes Relat Metab Disord 2002;26:398-402.
19. Cassidy AE, Bielak LF, Zhou Y, Sheedy PF 2nd, Turner ST, Breen JF, et al. Progression of subclinical coronary atherosclerosis: does obesity make a difference? Circulation 2005;%19;111:1877-82.
20. Fox CS, Hwang SJ, Massaro JM, Lieb K, Vasan RS, O'Donnell CJ, et al. Relation of subcutaneous and visceral adipose tissue to coronary and abdominal aortic calcium (from the Framingham Heart Study). Am J Cardiol 2009;104:543-7.
21. Ohashi N, Yamamoto H, Horiguchi J, Kitagawa T, Hirai N, Ito K, 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.
22. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15:827-32.
23. Rumberger JA, Sheedy PF, Breen JF, Schwartz RS. Electron beam computed tomographic coronary calcium score cutpoints and severity of associated angiographic lumen stenosis. J Am Coll Cardiol 1997;29:1542-8.
24. Wong ND, Hsu JC, Detrano RC, Diamond G, Eisenberg H, Gardin JM. Coronary artery calcium evaluation by electron beam computed tomography and its relation to new cardiovascular events. Am J Cardiol 2000;86:495-8.

25. Detrano R, Guerci AD, Carr JJ, Bild DE, Burke G, Folsom AR, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. N Engl J Med 2008;358:1336-45.
26. Pattanaprichakul S, Jongjirasiri S, Yamwong S, Laothammatas J, Sritara P. Rama EGAT risk score for predicting coronary artery disease evaluated by 64 slice CT angiography. ASEAN Heart J 2007;15:18-22.
27. D'Agostino RB Sr, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation 2008;117:743-53.
28. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/ American Heart Association conference on scientific issues related to definition. Circulation 2004;109: 433-8.
29. Hoff JA, Chomka EV, Krainik AJ, Daviglus M, Rich S, Kondos GT. Age and gender distributions of coronary artery calcium detected by electron beam tomography in 35,246 adults. Am J Cardiol 2001;87:1335-9.
30. McClelland RL, Chung H, Detrano R, Post W, Kronmal RA. Distribution of coronary artery calcium by race, gender, and age: results from the Multi-Ethnic Study of Atherosclerosis (MESA). Circulation 2006;113:30-7.
31. Shisen J, Leung DY, Juergens CP. Gender and age differences in the prevalence of coronary artery calcification in 953 Chinese subjects. Heart Lung Circ 2005;14:69-73.
32. Park HE, Kim MK, Choi SY, Lee W, Shin CS, Cho SH, et al. The prevalence and distribution of coronary artery calcium in asymptomatic Korean population. Int J Cardiovasc Imaging 2012;28:1227-35.
33. Arad Y, Newstein D, Cadet F, Roth M, Guerci AD. Association of multiple risk factors and insulin resistance with increased prevalence of asymptomatic coronary artery disease by an electron-beam computed tomographic study. Arterioscler Thromb Vasc Biol 2001;21:2051-8.
34. Lee CD, Jacobs DR Jr, Schreiner PJ, Iribarren C, Hankinson A. Abdominal obesity and coronary artery calcification in young adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Am J Clin Nutr 2007;86:48-54.
35. Elkeles RS, Feher MD, Flather MD, Godsland IF, Nugara F, Richmond W, et al. The association of coronary calcium score and conventional cardiovascular risk factors in Type 2 diabetic subjects asymptomatic for coronary heart disease (The PREDICT Study). Diabet Med 2004;21:1129-34.
36. Ding J, Kritchevsky SB, Hsu FC, Harris TB, Burke GL, Detrano RC, et al. Association between non-subcutaneous adiposity and calcified coronary plaque: a substudy of the Multi-Ethnic Study of Atherosclerosis. Am J Clin Nutr 2008;88:645-50.
37. Liu J, Musani SK, Bidulescu A, Carr JJ, Wilson JG, Taylor HA, et al. Fatty liver, abdominal adipose tissue and atherosclerotic calcification in African Americans: the Jackson Heart Study. Atherosclerosis 2012;224:521-5.