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ORIGINAL ARTICLE

Influence of the age on the correlation of obesity measures with coronary atherosclerotic markers

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Abstract *Objectives:* To assess the influence of age on the association of pericardial fat volume (PFV), weight and body mass index (BMI) with coronary stenosis, plaque and coronary artery calcification (CAC).
Materials and methods: A total of 127 consecutive patients with intermediate pretest probability of ischemic heart disease who underwent CT angiography examination were enrolled in this study. Of these, only 86 patients were found to be eligible to enroll in this study.
Results: Statistical analysis was performed in two steps. First we studied the relationship of anthropometric measures and coronary atherosclerotic markers in the whole sample. Second, we classified the patients into two groups according to age: age $\leqslant$50 group [30 patients, 18 (60%) male, 12 (40%) female with age <50 years] and age >50 group [56 patients, 38 male (68%), 18 female (32%) with age above 50 years]. PFV was significantly associated with coronary artery stenosis ($r = 0.381$, $P = 0.00$) and this association persisted even after dividing the patients into young and older age group while there was inconsistent relationship between PFV and coronary plaque. There was a significant association between PFV and CAC in older age group only ($P = 0.03$). Weight and body mass index failed to demonstrate a significant association with coronary atherosclerotic markers in both young and older age groups.
Conclusion: Weight and BMI showed no significant correlation with coronary atherosclerotic markers while PFV as a new imaging marker for obesity showed a significant correlation with coronary atherosclerotic markers particularly stenosis severity.

1. Introduction

There is a substantial increase in cardiovascular burden in the elderly and the predictive value of cardiac risk score and risk factors diminishes significantly with advancing age. Hence, the introduction of new non-invasive imaging biomarkers to

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increase the predictive accuracy of cardiac risk score is of paramount importance in primary and secondary prevention.[1]

On the other hand, coronary artery disease occurs less frequently in young with different cardiac risk profiles and long term prognosis compared to elderly patients.[2,3]

Body mass index (BMI) and weight are classical anthropometric measures used in large epidemiological and clinical studies to define obesity, metabolic syndrome and estimate the risk of cardiovascular disease.[4]

Pericardial fat, as a new marker of atherosclerosis is an adipose tissue surrounding the heart and epicardial coronary arteries with reported influence on coronary circulation via local secretion of numerous pro-inflammatory hormones and cytokines.[5–8]

The main aims of this study were to investigate the influence of age on the association of emerging biomarker of obesity (pericardial fat volume) and classical anthropometric measures of obesity with coronary atherosclerotic markers in patients with intermediate pretest probability of ischemic heart disease assessed by coronary CT angiography.

2. Patients and methods

This cross sectional study was carried out in the Cardiology center between January and July 2013. All patients gave their written informed consent for taking part in this study. The study was approved by Ethical Committee of our institute. Exclusion criteria for multi-detector CT examination included a history of cardiac surgery, iodine-based contrast allergy, renal failure (creatinine, >1.5 mg/dL), atrial fibrillation or other unstable heart rhythm, inability to perform breath-holding, hemodynamically unstable patients, presence of intracardiac devices (pacemaker or ICD), pregnant women and contraindications for beta blocker use. A total of 127 consecutive Iraqi patients with intermediate pretest probability of ischemic heart disease based on their age, sex and cardiac symptoms who underwent 64 multi-slice multi-detector CT angiography examinations for assessment of coronary artery disease were enrolled in this study. 41 patients were excluded due to missing or losing of data (31 patients), poor examination technique (6 patients) and difficulty in accurate pericardial fat volume calculation or segmentation of fat (4 patients). Only 86 patients (56 patients $>$ 50 years and 30 patients $\leqslant$ 50 years) were found to be eligible to enroll in this study.

A standardized questionnaire was employed by physicians at the time of coronary CT angiography examination to obtain a history of conventional cardiac risk factors for coronary disease from each patient including a positive family history of premature atherosclerosis (occurring in men before the age of 55 years and before the 65 years in women), current smoking history (more than 10 cigarettes per day in the last year), a history of hypertension, or use of anti-hypertension medications; hyperlipidemia was defined as total cholesterol $\geqslant$200 mg/dl or triglyceride levels $\geqslant$150 mg/dl or use of lipid lowering drugs; a history of diabetes mellitus or use of insulin or diabetic lowering drugs and body mass index was calculated as weight in kg/height squared in meters. Patient with 2 and more of cardiac risk factors was labeled as having multiple risk factors.

For coronary CT analysis, calcified plaques were defined as a structure of >1 mm consisting of only calcium within and/or adjacent to vessel lumen.

Severity of coronary artery stenosis was visually graded as non-significant stenosis with a mean lumen diameter reduction of $<50\%$ or significant stenosis with a mean lumen diameter reduction of $\geqslant 50\%$ in a single vessel by comparing the lumen diameter of the narrowest segment with that of a more proximal or distal normal segment in two orthogonal projections.

Calcium score was categorized as 0 (no calcification), 1–9 (minimal calcification), 10–99 (mild), 100–399 (moderate) and $\geqslant$400 (extensive calcification).

3. CT scan protocol and pericardial fat volume quantification

CT coronary angiography was performed with a 64-slice scanner (Aquillon 64, V4.51 ER 010, Toshiba Medical Systems, Tochigi, Japan) with retrospective electrocardiography (ECG) gating. Before Multi-Slice CT angiography, a non-contrast CT was acquired to measure calcium score according to the Agatston method using sequence scan with slice thickness of 3 mm. When the patient heart rate was less than 65 bpm, a b-blocker (metoprolol 20–60 mg orally) was administered before the scan. A bolus of 80 ml contrast medium (Omnipaque, 350 mg/mL iodine) was injected intravenously at a rate 5 ml/s, followed by 30 mL of normal saline. The scan was obtained from the aortic arch to the level of the diaphragm during a single breath hold. With ECG triggered scanning protocol was performed, and the following parameters were used: collimation width 32.5×32.5 cm, slice thickness 0.5 mm, rotation time 0.35 s, tube voltage 120 kV, maximum effective tube current 890 mA, table feed 0.3 mm/rotation. Examination time was about 10 s.

CT images were reconstructed using a smooth kernel (B25f) with a slice thickness of 0.5 mm (increment 0.3 mm). CT data sets were transferred to dedicated workstation (Vitrea 2 workstation vital image Plymouth, Minnesota, USA) for image analysis.

Pericardial fat volume was defined as any fat tissue located within pericardial sac and measured three-dimensionally with the contrast-enhanced phase. The layer of the pericardium was manually traced and a three-dimensional image of the heart was constructed. Then the pericardial fat volume was quantified by calculating the total volume of the tissue whose CT density ranged from -250 to -20 HU within the pericardium by using three D workstation statistical analysis. All MDCT images were assessed by two independent radiologists with more than 5 years' experience in coronary MDCT angiography interpretation

3.1. Statistical analysis

Data are presented as mean $\pm$ standard deviation or as number with percentages. Categorical data are expressed as frequencies and were compared with Pearson's Chi-square test. Continuous variables are presented as the mean $\pm$ standard deviation and were compared using Student's t test or ANOVA. Pearson's correlation coefficient was used to estimate the correlation of continuous variables. All data were collected and analyzed with SPSS for MAC version 17 (IBM,