Journal of Cardiology 65 (2015) 37–41

Contents lists available at ScienceDirect

Journal of Cardiology

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

Original article

Pericardial fat volume is an independent risk factor for the severity of coronary artery disease in patients with preserved ejection fraction

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ARTICLE INFO

Article history:
Received 22 January 2014
Received in revised form 25 March 2014
Accepted 30 March 2014
Available online 17 May 2014

Keywords:
Pericardial fat volume
Ischemic heart disease
Severity of coronary lesions
Body mass index
Waist circumference

ABSTRACT

Objectives: The aim of this study was to assess the relationship between the pericardial fat volume (PFV) and the characteristics of coronary plaques in patients with ischemic heart disease (IHD).
Background: It has been suggested that pericardial adipose tissue promotes plaque development in coronary artery disease (CAD).
Methods: We analyzed the cardiac computed tomography scans in consecutive patients suspected of CAD. PFV was quantified using validated software and indexed to body surface area, and the severity of coronary stenosis was evaluated in the patients who underwent coronary angiography. A total of 105 subjects (mean age, 68 ± 10 years) with IHD were categorized into tertiles of body surface area-indexed PFV values (PFVi, cm^3/m^2): low-tertile, PFVi < 81.2 cm^3/m^2; mid-tertile, 81.2 $cm^3/m^2 \leq$ PFVi $\leq$ 114 cm^3/m^2; high-tertile, PFVi > 114 cm^3/m^2. Their body mass index (BMI), waist circumference, Gensini score (GS), and coronary plaque component were evaluated.
Results: The GS was significantly different between the high-tertile and the low-tertile groups, indicating a stepwise decrease in GS from high-tertile to mid-tertile and to low-tertile. PFVi had a significant positive correlation with BMI ($p = 0.0001$) and GS ($p < 0.0001$). However, no significant association was found between GS and BMI. On the multivariate analysis, high PFVi remained an independent predictor for the coronary artery disease severity ($p < 0.001$), while BMI and waist circumference were not independent predictors.
Conclusions: Obese patients were found to have more PFVi, and the characteristics of their coronary lesions were more severe. Pericardial adipose tissue as unique ectopic fat might be more highly associated with IHD progression.

Introduction

Pericardial fat is a type of visceral adipose tissue (VAT) that is defined as the adipose tissue between the surface of the myocardium and the epicardium. Similar to other VAT, pericardial fat serves an important endocrine and inflammatory function, given its direct apposition to the myocardium and coronary arteries [1,2]. Pericardial fat may play a central role in the pathogenesis of cardiovascular disease, mediated by its inflammatory properties [3]. Kaya et al. [4] reported that an echocardiographic epicardial fat thickness is independently associated with the presence of coronary artery disease (CAD), and Dagvasumberel et al. [5] reported epicardial adipose tissue/body surface area was the single predictor for >50% coronary luminal narrowing in men. Recent studies demonstrated that 64-multi detector computed tomography (MDCT) is suitable for volumetric quantization. However, there have been no reports on the association between the pericardial fat volume (PFV) and the severity of coronary lesions. We, therefore, hypothesized that the pericardial fat increased steeply in patients with significant CAD. In this study, body surface area-indexed PFV (PFVi, cm^3/m^2) was measured by MDCT, and the relationship between the PFVi and the severity of CAD was evaluated in patients referred for coronary angiography.

DOI of commentary article: http://dx.doi.org/10.1016/j.jjcc.2014.07.004.
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http://dx.doi.org/10.1016/j.jjcc.2014.03.015
0914-5087/

Methods

Study population

A total of 105 consecutive ischemic heart disease (IHD) patients who underwent MDCT angiograms and coronary angiography between May 2012 and September 2013 were evaluated. Patients with a history of previous cardiac surgery, percutaneous coronary intervention, symptomatic heart failure, acute coronary syndrome, cardiomyopathy, and severe renal failure were excluded from the study. Written, informed consent was obtained from all patients.

Cardiac computed tomography scan protocol

Cardiac CT scans were performed with MDCT scanner (Aquilion 64, Toshiba Medical Systems, Tokyo, Japan) used with parameters as previously reported [6]. Reconstruction sets at 75% of the cardiac cycle or at a particular optimal phase were prepared from the raw data files. The contrast material (Omnipaque-300; Daiichi-Sankyo Pharmaceutical, Tokyo, Japan) was administered using a mechanical power injector through a 20-gauge cannula inserted into the antecubital vein. To minimize differences in the arterial enhancement across the patients, a body weight-tailored contrast material dose (0.7 mL/kg) and fixed injection duration (9 s) were used [7]. An oral β-blocker (metoprolol, 20 mg) was administered immediately prior to CT imaging to maintain heart rates at <65 bpm and thus improve image resolution. The reconstructed CT image data were transferred to a workstation for post-processing (ZIO M900, Admin/ZIO, Tokyo, Japan).

Quantification of epicardial fat volume with CT

PFV was measured three-dimensionally in all patients using contrast-enhanced images, as reported previously [7–9]. Segmentation of the overall volume was automatically interpolated using manually defined tracings. Next, PFV was quantified by calculating the total volume of the tissue whose CT density ranged from −190 to −30 Hounsfield units within the pericardial cavity using the workstation (Fig. 1). We trimmed along the pericardial sac using axial, coronal, and sagittal slices, volume-rendered images. PFV was defined as any adipose tissue located within the pericardial sac. A slice 1 cm above the most cranial slice including the left anterior descending coronary artery (LAD) was defined to be the superior border of the pericardial fat. Patients were categorized according to tertiles of PFVi: low-tertile (PFVi < 81.2 cm^3/m^2, n = 35); mid-tertile (81.2 cm^3/m^2 ≤ PFVi ≤ 114 cm^3/m^2, n = 35), and high-tertile (PFVi > 114 cm^3/m^2, n = 35).

Coronary angiography and analysis

Based on the modified AHA classification, the coronary arteries were divided into 17 segments, and the segments with a diameter >2.0 mm were analyzed.

CAD was defined as ≥75% stenosis (according to the American Heart Association classification) on conventional coronary angiography. Conventional coronary angiograms were recorded in multiple projections for the left and the right coronary arteries and reviewed for significant coronary artery obstructions by cardiologists unaware of the amounts of pericardial fat.

The Gensini score (GS), an index of the severity of coronary lesions, was calculated as the sum of all segment scores [10]. Severity scores assigned to the specific percentage luminal diameter reduction of the coronary artery segment were 32 for 100%, 16 for 99%, 8 for 75%, 2 for 50%, and 1 for 25%. Each principal vascular segment was assigned a multiplier in accordance with the functional significance of the myocardial area supplied by that segment: the left main coronary artery 5×; the proximal segment of the LAD 2.5×; the proximal segment of the circumflex artery 2.5×, and the mid-segment of the LAD 1.5×.

Assessment of risk factors and covariates

Blood was drawn after an overnight fast. Hypertension was defined as a systolic blood pressure ≥130 mmHg, a diastolic blood pressure ≥85 mmHg, or the use of an antihypertensive treatment. A fasting triglyceride level ≥ 150 mg/dL and a high-density lipoprotein (HDL) cholesterol level < 40 mg/dL were considered abnormal. Diabetes mellitus was diagnosed based on the criteria set by the World Health Organization or by the use of hypoglycemic agents or insulin. Abdominal obesity was defined as a waist circumference ≥85 cm for Japanese males and ≥90 cm for Japanese females [11]. Metabolic syndrome (MetS) was diagnosed according to the modified Adult Treatment Panel III criteria, which include the waist circumference with the presence of three or more metabolic abnormalities [9].

Statistical analysis

Categorical variables are reported as numbers (%), and continuous variables are reported as mean ± SD. The chi-square test was used for comparing categorical variables, and the unpaired t-test was used for continuous variables. A p-value < 0.05 was considered significant, and all tests were two-tailed. All analyses were performed using SPSS 17.0 (SPSS Inc., Chicago, IL, USA).

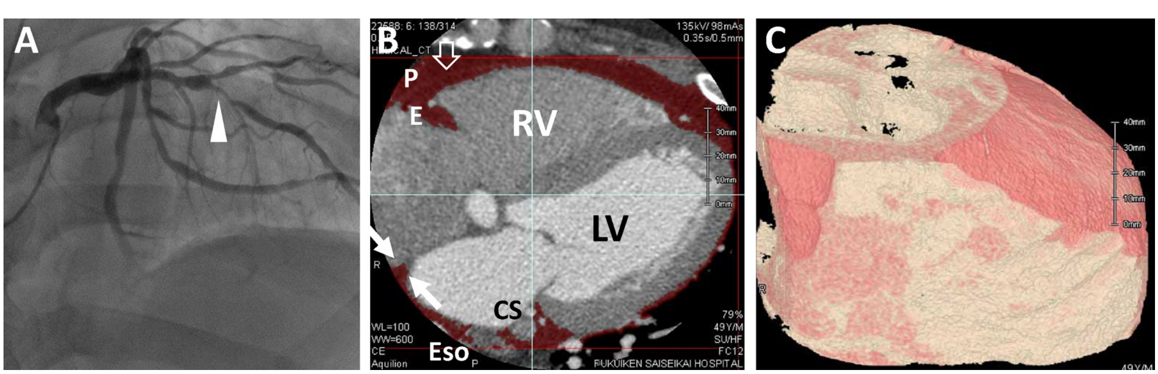

Fig. 1. Representative case with high pericardial fat volume of a 49-year-old male with metabolic syndrome with a waist circumference of 106 cm. Invasive coronary angiography shows a significant stenosis at the middle segment of the left anterior descending coronary artery (A, arrow). Angiography with 64-multi detector computed tomography shows a large amount of pericardial fat (B). The parietal pericardium (open arrow), paracardial fat (P), epicardial fat (E), coronary sinus (CS), and esophagus (Eso) are visible. Solid arrows (B), fatty deposits within the atrial septum. And pericardial adipose tissue has been reconstructed three-dimensionally (C). RV, right ventricle; LV, left ventricle.