Journal of Cardiovascular Computed Tomography 7 (2013) 125–132

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.JournalofCardiovascularCT.com

Original Research Article

Relationship of epicardial fat volume to coronary plaque, severe coronary stenosis, and high-risk coronary plaque features assessed by coronary CT angiography

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ARTICLE INFO

Article history:
Received 8 November 2012
Received in revised form
15 January 2013
Accepted 21 February 2013

Keywords:
Epicardial fat volume
Coronary computed tomography angiography
Coronary artery stenosis
High-risk plaque features

ABSTRACT

Background: Associations of epicardial fat volume (EFV) measured on noncontrast cardiac CT (NCT) include coronary plaque, myocardial ischemia, and adverse cardiac events.

Objectives: This study aimed to define the relationship of EFV to coronary plaque type, severe coronary stenosis, and the presence of high-risk plaque features (HRPFs).

Methods: We retrospectively evaluated 402 consecutive patients, with no prior history of coronary artery disease, who underwent same day NCT and coronary CT angiography (CTA). EFV was measured on NCT with the use of validated, semiautomated software. The coronary arteries were evaluated for coronary plaque type (calcified [CP], noncalcified [NCP], or partially calcified [PCP]) and coronary stenosis severity ≥70% with the use of coronary CTA. For patients with NCP and PCP, 2 high-risk plaque features were evaluated: low-attenuation plaque and positive remodeling.

Results: There were 402 patients with a median age of 66 years (range, 23–92 years) of whom 226 (56%) were men. The EFV was greater in patients with CP (112 ± 55 cm^3 vs 89 ± 39 cm^3), PCP (110 ± 57 cm^3 vs 98 ± 45 cm^3), and NCP (115 ± 44 cm^3 vs EFV 100 ± 52 cm^3). In the 192 patients with PCP or NCP, on multivariable analysis, after adjusting for conventional cardiovascular risk factors, EFV was an independent predictor of ≥70% coronary artery stenosis (odds ratio [OR], 3.0; 95% CI, 1.3–6.6; $P = 0.008$), any high-risk plaque features (OR, 1.7; 95% CI, 0.9–3.4; $P = 0.04$), and low attention plaque (OR, 2.4; 95% CI, 1.1–5.1; $P = 0.02$) but not of positive remodeling.

Conclusions: EFV is greater in patients with CP, PCP, and NCP. In patients with NCP and PCP, EFV is significantly associated with severe coronary stenosis, high-risk plaque features, and low attenuation plaque.

Conflict of interests: The authors report no conflict of interest.

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1934-5925/$ – see front matter
http://dx.doi.org/10.1016/j.jcct.2013.02.003

1. Introduction

Epicardial fat volume (EFV), measured on noncontrast enhanced CT (NCT), has emerged as an important parameter in understanding the pathophysiology of coronary atherosclerosis. Recent studies have shown a relationship between EFV and the presence and severity of coronary plaque as assessed by coronary artery calcification.[1,2] Furthermore, emerging data now suggest that this parameter may be related to myocardial ischemia,[3] acute coronary syndrome,[4] and also prognosis.[4,5] However, despite these observations, uncertainty remains as to how epicardial fat may exert these detrimental effects. One potential hypothesis that has emerged is that EFV may exert a local paracrine effect on adjacent coronary artery segments and lead to local inflammation and changes in plaque architecture.[6] Supporting this hypothesis are data showing that specific structural plaque characteristics identified on coronary CT angiography (CTA) are associated with culprit coronary lesions and an increased risk of future cardiac events.[7–10]

Although EFV has been shown to be related to coronary plaque[11,12] and coronary stenosis,[13–15] whether EFV is related to high-risk plaque features (HRPFs) is a subject of ongoing investigation. Oka et al[16] showed an independent association between EFV and HRPFs in patients with noncalcified coronary plaques, and Schlett et al[17] have shown EFV to be associated to HRPFs in 13 patients with a high-risk coronary lesion presenting with chest pain. The relationship between EFV and thin-capped fibroatheroma has also been recently confirmed on invasive coronary angiography and optical coherence tomography.[18] One area of current uncertainty is the association of EFV to severe coronary stenosis, plaque type, and HRPFs in patients with stable symptoms being referred for coronary CTA. The principal aims of the present study were to investigate the relationship of EFV to coronary plaque type, severe coronary stenosis, and HRPFs in stable patients with either noncalcified or partially calcified coronary plaques.

2. Methods

2.1. Patients

We retrospectively studied 402 consecutive patients who underwent same-day coronary CTA and NCT at Cedars-Sinai Medical Center from January 2009 through December 2009. Patients were excluded if they had a prior history of coronary artery disease (myocardial infarction, coronary stenting, and prior bypass surgery), if their body mass index (BMI; calculated as weight divided by height; kg/m^2) was beyond limits set by mean BMI $\pm$ 2 SDs, and if their image quality was not considered good or excellent by an expert reader. Cardiovascular risk factors were determined by preset criteria. Hypertension was defined as a systolic blood pressure of >140 mm Hg, a diastolic blood pressure of >90 mm Hg, or antihypertensive drug use. Smoking was defined as a current smoker or past heavy smoker (>20 package-years). Diabetes mellitus was defined as a previously established diagnosis, insulin or oral hypoglycemic therapy, fasting glucose of >126 mg/dL, or nonfasting glucose of >200 mg/dL. Family history of coronary artery disease was defined as myocardial infarction, coronary revascularization, or sudden cardiac death in a first-degree male relative <55 years or female relative aged <65 years. EFV of all patients was measured on NCT with the use of semiautomated quantitative software. Detailed assessment of coronary plaque severity, type, and structural characteristics was performed on coronary CTA images.

2.2. Non–contrast-enhanced CT scan

All subjects underwent NCT on a on a dual-source CT scanner (SOMATOM Definition; Siemens Medical Solutions, Forchheim, Germany). The scan extended from the aortic arch to the diaphragm and was obtained in a single breathhold. Heart rate–dependent electrocardiogram (ECG)–triggering was performed, typically at 45%–60% of the R-R interval. The field of view was 35 cm. Matrix size was 512 $\times$ 512. Tube voltage was 120 kVp with multislice scanning. The slice thickness was 3 mm for electron-beam CT and 2.5 mm for multislice CT. Each set of NCT images was evaluated for Agatston score by an experienced reader blinded to results of epicardial fat measurements, using semi-automatic, commercially available software (ScImage, Los Altos, CA, USA). The total Agatston score was the sum of calcified plaque (CP) scores of all coronary arteries.[19]

2.3. Epicardial fat quantification

Epicardial fat quantification was performed on the NCT scan with the use of validated software (QFAT) developed at the Cedars-Sinai Medical Center.[20] Scans were presented to blinded experienced readers in random order. Readers identified the superior epicardial fat boundary at the takeoff of the right pulmonary artery, and the inferior boundary at the first slice where the posterior descending artery was first visualized. Five to 10 contour points were then traced on the pericardium at each slice from the upper slice limit to the lower slice in the axial view (total number of slices ranged from 20 to 40 for typical subjects). From these control points, piecewise cubic Catmull-Rom spline functions were automatically generated to form a smooth, closed pericardial contour (Fig. 1). The EFV was then automatically calculated (reported in cm^3), using contiguous 3-dimensional voxels with Hounsfield units between -190 and -30 as the range of attenuation values defining fat.[21–23] The reproducibility of QFAT software measurement of EFV has previously been shown to be high for both intrascanner (multidetector CT [MDCT]–MDCT) and interscanner (electron beam CT–MDCT) data (correlation coefficient $\geq$ 0.98). The reproducibility coefficient values are lowest (4.3% for EFV) for intrascanner same-observer measurement. For intrascanner cross-observer measurement, reproducibility values are 10.7% for EFV.[24]

2.4. Coronary CTA image acquisition and reconstruction

Coronary CTA was performed on a dual-source CT scanner (SOMATOM Definition; Siemens Medical Solutions). The imaging protocol has been previously described in detail.[25,26]