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Original article

Accumulation of pericardial fat correlates with left ventricular diastolic dysfunction in patients with normal ejection fraction☆

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KEYWORDS
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Summary
Background: Left ventricular diastolic dysfunction (LVDD) plays an important role in heart failure with normal left ventricular ejection fraction (LVEF). Obesity is one of the major comorbid conditions of LVDD. Pericardial fat (PF) is an ectopic fat depot with possible paracrine or mechanical effects on the coronary circulation and myocardial function.
Methods: We measured PF volume on 64 slice computed tomography and analyzed echocardiographic parameters to confirm LVDD in 229 consecutive patients suspected of coronary artery disease with LVEF of more than 50% and no symptomatic heart failure (59% men, 67 ± 12 years). LVDD was defined as the ratio of transmitral Doppler early filling velocity to tissue Doppler early diastolic mitral annular velocity (E/e') >10.
Results: PF volume correlated significantly with E/e' ($r = 0.21$, $p < 0.01$), left ventricular mass index ($r = 0.23$, $p < 0.001$), and left atrial diameter ($r = 0.32$, $p < 0.001$). The mean PF volume was significantly greater in patients with LVDD (184 ± 61 cm^3, $n = 141$) than in those without LVDD

☆ Clinical trial registration: https://center.umin.ac.jp; ID: UMIN000001581.

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(154 ± 58, $n = 88$, $p < 0.001$). Multivariate logistic regression analysis indicated that PF volume correlated significantly with the presence of LVDD (odds ratio: 2.00 per 100 cm^3 increase in PF volume, $p = 0.02$) independent of age, gender, abdominal obesity, hypertension, and diabetes.
Conclusions: PF volumes are significantly associated with LVDD, independent of other factors such as hypertension or diabetes. PF may be implicated in the pathogenesis of LVDD in patients with normal LVEF.

Introduction

Increasing evidence suggests that approximately half of all patients with heart failure have a normal left ventricular ejection fraction (LVEF) [1], and the mortality rate for this group is similar to those with heart failure and reduced LVEF [2]. Left ventricular diastolic dysfunction (LVDD) plays an important role in heart failure with normal ejection fraction (EF) [3]. However, there is no specific therapeutic strategy for LVDD partly because of the lack of understanding of its pathophysiological mechanism(s).

LVDD is most prevalent among elderly obese women with hypertension, diabetes, coronary artery disease, and/or atrial fibrillation [4,5]. Obesity is one of the important features of LVDD and fat tissue is known to secrete many adipokines that have local and systemic effects on the cardiovascular system [6]. Ectopic fat depots in muscle, liver, and pancreas are described as lipotoxic and pericardial fat (PF) is recognized as an ectopic visceral fat depot in close proximity to the myocardium and coronary arteries. PF volume is increased in obese patients and correlates with the presence [7,8] and incidence [9] of coronary atherosclerosis independent of other risk factors, indicating that PF may have paracrine or mechanical effects on the coronary circulation and myocardium. PF volume has also been reported to correlate with left atrial diameter, which is an indirect structural parameter of LVDD [10—12]. However, there is currently no report of a functional parameter of LVDD by tissue Doppler echocardiography that correlates with PF volume. The purpose of this study was to assess the association between PF volume and LVDD, as determined by tissue Doppler echocardiography.

Methods

Study sample

We analyzed consecutive inpatients in a stable condition who underwent 64-slice computed tomography (CT) coronary angiography and echocardiography between 2006 and 2009 on suspicion of coronary artery disease. None of the patients had history of previous thoracic surgery, percutaneous coronary intervention, or symptomatic heart failure. We screened 304 patients, each with LVEF more than 50%, and excluded those with previous pacemaker implantation ($n = 19$), chronic atrial fibrillation ($n = 12$), end-stage renal disease ($n = 14$), significant valvular disease ($n = 9$), poor image quality ($n = 17$), and incomplete data ($n = 6$). Thus, we measured PF volumes from CT images and examined echocardiographic parameters in 229 consecutive patients. The study was approved by the ethics review committee of our institution and a signed informed consent was obtained from each patient before participation. This study was registered at UMIN protocol registration system with the identification number UMIN000003361.

Cardiac CT scan protocol

The 64-detector CT (Brilliance-64, Phillips Medical Systems, Cleveland, OH, USA) was used with the following parameters: detector collimation 64 mm × 0.625 mm, table feed 19.7 mm/s, 0.2 beam pitch, rotation time 420 ms, tube current 429 mA, and voltage 120 kVp, as reported previously [7]. 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-350; 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 arterial enhancement across patients, we used a body-weight-tailored contrast material dose (0.7 mL/kg) and a fixed injection duration (9 s) [13]. An oral β-blocker (metoprolol, 20 mg) was administered 1 h prior to CT imaging, and nitroglycerin (0.3 mg) was administrated immediately prior to CT imaging. The reconstructed CT image data were transferred to a workstation for post-processing (ZIO M900, Amin/ZIO, Tokyo, Japan).

Cardiac CT image analysis

PF volume was measured three-dimensionally in all patients using contrast-enhanced images, as reported previously [7]. A predefined image display setting was used [window width = 150 Hounsfield units (HU), window center = −120 HU] to identify pixels that correspond to fat tissue [14]. The readers, who were blinded to the clinical results, trimmed along the pericardial sac using axial, coronal, and sagittal slices and volume-rendered images. PF was defined to be any adipose tissue located within the pericardial sac (Fig. 1). A slice 1 cm above the most cranial slice including the left anterior descending coronary artery was defined to be the superior border of the PF.

Three major coronary arteries were analyzed visually and quantitatively by contrast-enhanced coronary CT angiography. Coronary artery disease was defined to be ≥75% stenosis (according to the American Heart Association classification) on conventional coronary angiography ($n = 136$) analyzed quantitatively by coronary angiography software (CAAS, Pie Medical Imaging, Maastricht, Netherlands) or ≥50% luminal