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Epicardial fat, rather than pericardial fat, is independently associated with diastolic filling in subjects without apparent heart disease

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Abstract *Background and aim:* Epicardial and pericardial fat are separate fat depots surrounding the heart. Previous studies found epicardial fat to be associated with diastolic dysfunction, but they had some limitations. Pericardial fat association with diastolic dysfunction was not examined. Our aim was to assess the relation of epicardial and pericardial fat with diastolic filling.

Methods and results: In 73 volunteers without known heart disease or complaints, using echocardiography, we measured epicardial and pericardial fat thickness from long(LAX) and short(SAX) axis views and assessed diastolic filling: mitral inflow (E/A ratio, E wave deceleration time[DT]), pulmonary vein flow (systolic/diastolic ratio [S/D], systolic filling fraction[SFR], late retrograde velocity[Ar]), color M-mode flow propagation velocity [Vp], and tissue Doppler derived mitral early annular velocities at the septum [e′ sep] and lateral wall [e′-lat]. By Spearman's correlation, epicardial fat from LAX had a weak, but statistically significant correlations with several diastolic filling indices (SFR{rs = 0.29, $P = 0.02$}, Ar{rs = 0.3, $P = 0.01$}, Vp{rs = −0.3, $P = 0.01$}, e′ sep {rs = −0.23, $P = 0.04$}, e′ lat{rs = −0.26, $P = 0.03$}). In multivariate logistic regression model adjusting for age, gender, diabetes, systolic blood pressure and left ventricle mass index, epicardial fat thickness from LAX (and not from SAX) was the only independent predictor of e′ [e′ sep < 8: OR = 1.8, 95%CI = 1.1–2.9; e′ lat<10: OR = 1.6, 95%CI = 1.01–2.6]. After adjustment, Pericardial fat measured from LAX was independent predictor of e′ lat only[e′ lat < 10:OR = 1.3, 95% CI 1.03–1.6).

Conclusions: Epicardial fat measured from LAX is an independent predictor of myocardial relaxation. Pericardial fat independent association with diastolic filling is uncertain.

Introduction

Adipose tissue around the heart consists of two depots, epicardial and pericardial (mediastinal) fat [1]. Epicardial fat (EF) is located between the myocardium and visceral pericardium, mainly in the interventricular and atrioventricular grooves [1,2]. Pericardial fat (PF) is located on the external surface of the parietal pericardium [1,2].

Epicardial fat shares the same embryonic origin with mesenteric and omental fat [1], correlates with visceral obesity markers such as waist circumference [3] and measurements of visceral adipose tissue by Ultrasound [3] and computed tomography [4] (CT), shares the same microcirculation with the myocardium [1], is metabolically active and produces both harmful (proinflammatory) and

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protective cytokines [5]. Because of these properties, epicardial fat may play a role in the pathogenesis of cardiovascular disease. Indeed, epicardial fat is associated with increased left ventricle mass and left atrial dimensions [6,7], atrial fibrillation [8], endothelial dysfunction [9], carotid intima media thickness [10], coronary artery disease [11–15] and diastolic dysfunction [16–19].

Pericardial fat has a different embryonic origin; it originates from the embryonic primitive thoracic mesenchyme [1], it was studied much less than epicardial fat. Some studies found thoracic fat (which includes pericardial as well as other fat depots) to correlate with cardiac dimensions [3], visceral abdominal fat, metabolic syndrome and coronary calcium [4]. Only one study [2] examined epicardial and pericardial fat separately, and found pericardial fat rather than epicardial fat to be associated with visceral fat and metabolic syndrome features. So, the role of pericardial fat in the pathogenesis of heart diseases is unclear. Particularly, no studies examined its association with diastolic filling.

The amount of epicardial and pericardial fat can be assessed by cardiac CT, MRI and echocardiography. Most CT studies measured epicardial fat volume, but measurements of fat thickness and area is also possible and correlates with the volume [20,21]. Echocardiographic epicardial and pericardial fat thickness can be measured from parasternal long (LAX) and short axis (SAX) views [1]. Since these fat depots are three dimensional in structure, measurements from two orthogonal planes may yield a different thickness value. We sought to measure EF and PF from LAX and SAX views and to examine if these measurements are associated with diastolic filling.

Methods

Study population

Seventy-nine volunteers without known cardiac disease or complaints were initially included. Exclusion criteria were poor image quality (1 subject), atrial fibrillation (1), left ventricular wall thickness>1.1 cm (1), moderate or severe valvular stenosis or regurgitation (1) and mitral annulus calcification (2). Clinical and demographic data were collected. Body mass index (BMI) was defined as weight (kilograms) divided by height squared (meters). Blood pressure was measured at rest by a sphygmomanometer. Diabetes (type 2) was defined as fasting plasma glucose >126 mg/dl. Hypertension was defined as a history of blood pressure >140/90 at rest. Hyperlipidemia was defined as total cholesterol level >240 or triglycerides >150 mg/dl. Smoking was defined as current smoking. The study protocol was approved by our institutional review board, and all subjects gave their written informed consent.

Echocardiography

Transthoracic echocardiography was performed by a single experienced operator, in the left lateral decubitus position according to the ASE guidelines [22], by a commercially available ultrasound machine (Philips IE 33, Bothhell WA, USA). Left atrial dimension was measured from parasternal long axis view, by M-mode. Left ventricle dimensions were measured by M-mode from parasternal short axis view at papillary muscles level. Left ventricle mass was calculated by the cubed method and ejection fraction was calculated by Teicholz formula.

Measurement of epicardial and pericardial fat

Epicardial fat thickness was measured perpendicularly to the myocardium, as the echo lucent space between the right ventricular epicardium and the linear echo dense parietal pericardium [2,13]. Pericardial fat was measured as the echo lucent space anterior to parietal pericardium [2]. Measurements were performed in parasternal LAX and SAX views, on the still images of the two-dimensional echocardiogram at end diastole [2,12,13]. The maximal value at each site and view was measured in three cardiac cycles and the average value considered [2] for analysis.

Diastolic filling

According to the ASE [22] guideline, from the apical four chamber view, diastolic filling indices were measured at end expiration after optimizing gain, sweep speed, filters and scale. Values from three cardiac cycles were averaged. The following parameters were measured:

1 Mitral inflow: by pulsed wave Doppler, with the sample volume located between the tips of mitral leaflets, guided by color Doppler for parallel alignment with mitral inflow, the peak early filling velocity (E), peak late filling velocity (A), E deceleration time (DT) were measured and the E/A ratio calculated. In cases of partial fusion of E and A (E value at onset of A >20 cm/s) absolute A velocity (peak A minus the height of E at the onset of A) was used to calculate E/A ratio. With the sample volume at the level of the mitral annulus, A duration (Adur) was measured.
2 Pulmonary venous flow: color Doppler was used to identify flow within the right upper pulmonary vein, and a sample volume was placed >1 cm deep in the vein. Measurements of pulmonary venous waveforms included peak systolic velocity (S), peak diastolic velocity (D), S/D ratio, systolic flow time velocity integral(STVI), diastolic flow time velocity integral(DTVI), systolic filling fraction (SFR) defined as STVI/(STVI + DTVI), peak retrograde velocity in late diastole (Ar), the time difference between Ar and mitral A-wave durations ([Ar − A]dur).
3 Color M-Mode flow propagation velocity (Vp): color flow baseline was shifted to lower the Nyquist limit, and Vp was measured from the mitral annulus distally into the left ventricle, as the slope of the first aliasing velocity.
4 Tissue Doppler imaging (TDI): as described elsewhere [22], measurement of the septal and lateral early