Clinical Utility of Measuring Epicardial Adipose Tissue Thickness with Echocardiography Using a High-Frequency Linear Probe in Patients with Coronary Artery Disease

Yukina Hirata, RMS, Hirotsugu Yamada, MD, PhD, Kenya Kusunose, MD, PhD, Takashi Iwase, MD, PhD, Susumu Nishio, RMS, Shuji Hayashi, MD, PhD, Mika Bando, MD, Rie Amano, RT, Koji Yamaguchi, MD, PhD, Takeshi Soeki, MD, PhD, Tetsuzo Wakatsuki, MD, PhD, and Masataka Sata, MD, PhD, *Tokushima, Japan*

Background: The relationship between epicardial adipose tissue (EAT) and coronary artery disease (CAD) has recently attracted a great deal of attention in the medical community. The objective of this study was to determine whether measuring EAT thickness in the anterior interventricular groove (AIG) using echocardiography is feasible and whether this index can be a marker of CAD.

Methods: A total of 311 patients (mean age, 67 ± 11 years; 208 men) who underwent coronary angiography between December 2011 and December 2013 were prospectively enrolled. EAT-AIG thickness and EAT thickness on the free wall of the right ventricle (RV) were measured in systole using a high-frequency linear probe. Seventy-one patients who underwent multidetector-row computed tomography were enrolled to validate the method for measuring EAT thickness using echocardiography. Subjects were divided into two groups, those with and without significant coronary stenosis, on the basis of findings on coronary angiography (≥75% luminal narrowing).

Results: EAT-AIG thickness measured using echocardiography was validated by computed tomography. EAT-AIG thickness was strongly correlated with EAT volume ($r = 0.714$, $P < .001$). The CAD group had thicker EAT-AIG than the non-CAD group (8.3 ± 3.0 vs 6.3 ± 2.5 mm, $P < .001$). EAT-RV thickness was greater in the CAD group than in the non-CAD group (5.0 ± 2.1 vs 4.4 ± 2.3 mm, $P = .009$) as well. The area under the curve on receiver operating characteristic curve analysis of EAT-AIG thickness for predicting CAD was 0.704, which was higher than the EAT-RV thickness.

Conclusions: Measuring EAT thickness using echocardiography with a high-frequency linear probe was validated with computed tomography. EAT-AIG was thicker in the CAD group than in the non-CAD group, as was EAT-RV thickness. This noninvasive index may have potential as a diagnostic marker for predicting coronary atherosclerosis. (J Am Soc Echocardiogr 2015;28:1240-6.)

Keywords: Epicardial adipose tissue, Echocardiography, Computed tomography, Coronary artery disease, Anterior interventricular groove

From the Ultrasound Examination Center (Y.H., H.Y., K.K., T.I., S.N., S.H., M.B., R.A., K.Y., T.S., T.W., M.S.); and the Department of Cardiovascular Medicine (Y.H., H.Y., K.K., T.I., S.N., S.H., M.B., R.A., K.Y., T.S., T.W., M.S.), Tokushima University Hospital, Tokushima, Japan.

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Reprint requests: Hirotsugu Yamada, MD, PhD, FESC, Tokushima University Hospital, Department of Cardiovascular Medicine, 2-50-1 Kuramoto, Tokushima, 770-8503, Japan (E-mail: yamadah@tokushima-u.ac.jp).

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Epicardial adipose tissue (EAT) consists of ectopic visceral fat surrounding the heart that is in close proximity to the coronary arteries. Increased EAT thickness or volume has been associated with known cardiovascular risk factors.[1,2] Moreover, several investigators have shown that excessive EAT can be a marker of the presence and severity of coronary artery disease (CAD).[3-6] In previous studies, magnetic resonance imaging,[7-11] computed tomography (CT),[12-18] and echocardiography[4,19,20] have been used to quantify EAT thickness and volume. Magnetic resonance imaging and CT are superior to echocardiography for measuring overall EAT volume. Although echocardiography can provide only measurements of the regional thickness of EAT, it has some advantages. For example, it is noninvasive, relatively cheap, and easy to perform as a screening test. EAT thickness has been defined as the thickness of the echolucent area on the free wall of the right ventricle (RV) in the parasternal long-axis and short-axis views.[21-23] However, EAT is not uniformly distributed, and adipose tissue concentrates primarily in

Abbreviations

AIG = Anterior interventricular groove

CAD = Coronary artery disease

CT = Computed tomography

EAT = Epicardial adipose tissue

PAT = Paracardial adipose tissue

ROC = Receiver operating characteristic

RV = Right ventricle

the interventricular and atrioventricular grooves rather than in nongroove segments such as the free wall of the RV.[13,15]

We hypothesized that EAT in the groove may be more strongly related to the development of atherosclerosis in patients with CAD, because there is growing evidence that the presence of inflammatory mediators in tissues surrounding the epicardial coronary arteries plays an important role in the vascular wall.[24,25] We found that EAT in the anterior interventricular groove (AIG) can be visualized by echocardiography. Furthermore, we were able to obtain better resolution for measuring EAT thickness using a higher frequency linear probe. The aim of this study was to investigate the feasibility of making echocardiographic measurements of EAT thickness in the AIG compared with obtaining EAT parameters using CT. We also evaluated the clinical utility of measuring EAT thickness with echocardiography by comparing measurements in patients with and without CAD.

METHODS

Study Population

We prospectively enrolled 318 patients suspected of having CAD who underwent their first coronary angiographic examinations between December 1, 2011, and December 1, 2013, at Tokushima University Hospital. Patients with histories of coronary stenting or open heart surgery (including bypass and valve surgery) were excluded from this study. Seven subjects (2.2%) were excluded because EAT thickness could not be measured using echocardiography because of poor image quality as a result of emphysema or obesity. Ultimately, 311 subjects were included in this study. Seventy-one patients who underwent multidetector-row CT for various clinical indications within 2 weeks of echocardiography were enrolled to validate our method for measuring EAT thickness with echocardiography. Subsequently, to assess the association between regional EAT thickness and CAD, all subjects were classified into two groups: the CAD group and the non-CAD group. The CAD group was defined as having ≥75% luminal narrowing in at least one major coronary artery. Hypertension was defined as systolic blood pressure > 140 mm Hg and/or diastolic pressure > 90 mm Hg or current treatment with antihypertensive medication. Diabetes was defined as fasting blood glucose > 200 mg/dL, glycated hemoglobin ≥ 6.5%, and/or the need for oral hypoglycemic agents or insulin. Dyslipidemia was defined as plasma total cholesterol > 220 mg/dL or the use of lipid-lowering therapy. Smoking was defined as current or previous use of cigarettes. This study was approved by the institutional research ethics committee, and all participants gave written informed consent.

Echocardiographic Examination

All subjects underwent echocardiography to measure EAT thickness either 1 day before or after coronary angiography. Routine echocardiography was performed using commercially available ultrasound machines (Vivid E9, GE Healthcare, Milwaukee, WI; iE33, Philips Healthcare, Best, The Netherlands; Aplio 500, Toshiba Medical Systems, Tochigi, Japan; or α10, Preirus, Hitachi-Aloka Medical, Ltd, Tokyo, Japan) with a sector transducer. Next, a high-frequency linear probe (7.5–11 MHz) was used to measure the thickness of the EAT and paracardial adipose tissue (PAT). EAT thickness at two locations was measured at the end of systole, as shown in Figure 1: (1) in the AIG (EAT-AIG), where the left anterior descending artery runs, and (2) on the free wall of the RV (EAT-RV). While assessing EAT-AIG thickness, we searched for the distal portion of the left anterior descending coronary artery and carefully rotated the probe until a longitudinal section was identified. EAT-AIG thickness was measured as the distance from the outer wall of the myocardium to the visceral layer of the epicardium, perpendicular to the pericardium. EAT-RV was measured using the method previously reported by Iacobellis and Willens.[23] The thickness of PAT over the free wall of the RV outside of the parietal pericardium was also measured at end-systole from the same image used to measure EAT-RV thickness.[21] Measurements were performed during three cardiac cycles for each parameter, and the mean for each parameter was used for analysis.

Multidetector-Row CT

Cardiac CT was performed with a 320-slice scanner (Aquilion One; Toshiba Medical Systems). During a single breath-hold, images were acquired from above the level of the tracheal bifurcation to below the base of the heart using prospective electrocardiographic triggering, with the center of acquisition at 30% and 70% of the R-R interval to assess the systolic and diastolic phases, respectively. EAT volume was assessed using a dedicated offline workstation (AZE Virtual Place, Tokyo, Japan). EAT was defined as the adipose tissue between the surface of myocardium and the visceral layer of the pericardium.[17,18] We manually traced the pericardium from the lower surface of the EAT at the origin of the pulmonary artery to the EAT on the ventricular apex on axial, sagittal, and coronal volume images. A density of −190 to −30 Hounsfield units was used to isolate adipose tissue. The area outside of the traced pericardium was excluded.

Statistical Analysis

All continuous variables are expressed as means ± SD. Categorical data are expressed as frequencies and proportions. Data were tested for normality using the Kolmogorov-Smirnov test. Linear regression was used to examine the relationship between EAT thickness by echocardiography and EAT volume by CT. Intraobserver and interobserver variability were determined by comparing EAT-AIG measurements by each observer for 30 randomly selected patients. There were two experienced readers who were blinded to patients' clinical data. We assessed reproducibility using a single-measure intraclass correlation coefficient model. Student's t test was used to test for differences in continuous variables between the two groups. The performance of clinical risk factors (including age, male gender, body mass index, diabetes mellitus, hypertension, dyslipidemia, and smoking) plus various combinations of EAT thickness in predicting CAD was assessed using the area under the curve on receiver operating characteristic (ROC) curve analysis. To evaluate the impact of EAT parameters obtained by echocardiography for predicting CAD along with clinical variables, three models were constructed and compared using ROC curve