Epicardial Adipose Tissue: An Emerging Role for the Development of Coronary Atherosclerosis

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There is a growing body of evidence that epicardial adipose tissue (EAT) plays an enhancing role in the development of coronary atherosclerosis.^{1,2} Pericardial fat is deposited around the heart at two locations, as epicardial and paracardial adipose tissue separated from each other by the parietal pericardium. Paracardial adipose tissue originates from the primitive thoracic mesenchyme and is supplied by the pericardiophrenic artery, a branch of the internal thoracic artery. EAT is defined as adipose tissue situated within the pericardium. EAT originates from the splanchnopleuric mesoderm (such as the mesenteric and omental fat deposits), and the vascular supply is from coronary arteries. Conceptually, EAT is more interesting than paracardial adipose tissue because of the close anatomic relationship between EAT and the myocardium. EAT also includes pericoronary fat situated around the coronary arteries, which may even be more appealing due to its very close proximity to the coronary arteries, suggesting a role for the development of coronary atherosclerosis. So far there is no general consensus as to which of these fat deposits should be studied, but most reports are about EAT, and few also report about the peri-coronary fat deposits.^{1,2} EAT is metabolically active visceral fat, and the quantity of EAT is correlated with the metabolic syndrome (a waist circumference, hypertriglyceridemia, and hyperglycemia), cardio-metabolic risk factors, and coronary atherosclerosis.² EAT is distributed asymmetrically around the heart, and the fat is deposited mainly at the atrioventricular and interventricular grooves, around the major coronary arteries and free wall of the right ventricle, and the apex of the left ventricle. EAT can be measured by magnetic resonance imaging or echocardiography, but recently computed tomography (CT) has emerged as a robust, 3-dimensional, high-resolution imaging technique that reliably identifies EAT. CT allows quantification of EAT by manually tracing the pericardium on cross-sectional CT images. Within the traced region, the adipose tissue is identified by voxels that have a range of -190 to -30 HU. Automated computer-assisted methods allow quantification of epicardial fat tissue measurements.

The measurements are presented as regional fat thickness (mm), as cross-sectional area (cm²), and as a volume (cm³). EAT volume is reported as ranging from 68 to

124 cm³. The volume of EAT accounts for approximately 15% to 20% of the total cardiac volume and covers approximately 80% of the total cardiac surface. EAT accounts for roughly 1% of the total body fat mass. EAT volume is higher in patients with a high body mass index (BMI) than in patients with a low BMI. The mean EAT thickness measured at several sites, including the free right ventricular wall, left ventricular anterior wall, and grooves was 5.3 ± 1.6 mm.¹ The measurement of regional fat thickness around the coronary arteries is useful because it may reflect region-specific fat characteristics that may affect coronary atherosclerosis. The mean coronary perivascular adipose tissue thickness is 10.9 ± 1.9 mm in patients referred for invasive coronary angiography. CT scanning allows for the identification of coronary calcium, obstructive disease of the coronary arteries, and pericardial fat. Thus, CT scanning permits the establishment of a potential relationship between EAT and the quantity of coronary calcium and the magnitude of the coronary plaque burden, which may then be linked to the occurrence of adverse coronary events. In this issue of *Clinical Cardiology*, Iwasaki et al reported on the relationship between EAT, the calcium score, and the severity of coronary atherosclerosis.³ They studied 197 patients who underwent CT calcium scoring and 64-slice CT coronary angiography. In all of these patients they carefully measured the volume of EAT using a dedicated off-line postprocessing program. They found a significant correlation between the volume of EAT and the magnitude of the calcium score. In patients with EAT <100 mL, the calcium score was significantly lower than the score in patients with EAT volume >100 mL (175 ± 395 vs 384 ± 782 ($P = 0.0016$)). The presence of severe coronary artery disease (CAD) ($\geq 50\%$ diameter stenosis) was also significantly higher in patients with EAT volume >100 mL compared to patients with EAT volume <100 mL (40.2% vs 22.7% ($P = 0.008$)). The amount of EAT was significantly higher in patients with a high calcium score (>400) and severe coronary artery obstructive disease.

This study confirms and extends earlier studies that also demonstrated a positive relationship between EAT and the severity of CAD. The pathophysiologic significance of EAT in the development of coronary atherosclerosis is gradually evolving, and it is thought that peri-vascular adipose tissue adjacent to the coronary vessel wall may enable diffusion or transportation via the vaso vasorum of proinflammatory cytokines and adipokines produced by the adipocytes that may enhance the development of coronary atherosclerosis. It has been shown that these cytokines and adipokines are expressed and secreted at

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a higher level in the adipose tissue of patients with CAD than in patients without CAD.² Indirect evidence for the atherogenic role of EAT is given by the fact that the absence of peri-vascular coronary fat, as occurs in coronary segments with myocardial bridges or segments with intramyocardial course, is associated with the absence of coronary atherosclerosis. Furthermore, preliminary studies have reported that EAT is associated with incident coronary heart disease, independent of BMI and cardiac risk factors, and the occurrence of adverse coronary events, suggesting that EAT is one of the factors contributing to coronary atherosclerosis.^{4,5} However, further studies are needed to unravel the pathophysiologic mechanisms of EAT. Large-sized studies should indicate that EAT is independently and incrementally associated with coronary atherosclerosis and is not confounded by the effects of abdominal adipose tissue and thus with obesity-associated systemic effects.

So far only cross-sectional studies have shown that the amount of EAT volume as well as the thickness

of peri-vascular adipose tissue are associated with CAD. Long-term studies are lacking that establish whether EAT is an independent predictor of adverse coronary events.

Finally, the standardization of EAT thickness and cross-sectional or volume measurements obtained by CT are necessary to allow comparison of the studies.

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