Weight loss in obesity reduces epicardial fat thickness; so what?

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THE PHYSIOLOGICAL ROLES of human epicardial adipose tissue (EAT) are not well defined because this strategically located white adipose tissue (WAT) depot is difficult to access and study, and most of the information about it comes from humans with severe cardiac diseases undergoing open heart surgery or by implication from animal experiments (9, 10). Hypothetically, its functions include lipid storage for myocardial energy use, coronary artery mechanical buffering against arterial wave torsion, coronary artery vasomotion and remodeling, protection of the cardiac and coronary autonomic nerve supply, and expression and secretion of adipokines, a collective definition for WAT-derived hormones, growth factors, coagulation mediators, and pro- and anti-inflammatory cytokines (9–11).

Echocardiography (ECHO), computed tomography (CT), and magnetic resonance imaging (MRI) have been used to quantify EAT thickness or volume in healthy lean and obese subjects and in patients with coronary atherosclerosis (CAD) (1–5, 12). One rationale driving these studies is that EAT, itself visceral fat by definition, shares some common features with the more comprehensively studied mesenteric/omental visceral adipose tissue (VAT). Thus 1) each has the same intra-abdominal embryological derivation (10); 2) each depot’s mass increases in obesity (3, 5, 12); 3) the increase in size of one directly correlates with the other (4); and 4) their increases show significant independent associations with established cardiovascular risk predictors, such as high blood pressure, low blood high-density lipoprotein (HDL)-cholesterol, high triglycerides, and insulin resistance (3, 5, 12). Putatively, EAT might exhibit a proinflammatory adipokine profile in obesity like VAT and play a role in coronary atherogenesis (9, 10). Expansion of adipocytes with triglyceride is thought to be the trigger for increased expression and production of inflammatory cytokines such as TNF-α, monocyte chemotactant protein-1 (MCP-1), IL-1β, −6, and −8, and plasminogen activator inhibitor-1 (PAI-1), and decreased expression and production of leptin and vasoprotective adiponectin by the various cell types that constitute VAT (10). Importantly, there are no published data yet that demonstrate a VAT-like adipokine profile in EAT from obese humans. This primary metabolically mediated pathophysiological inflammatory response of VAT (and potentially of EAT) to fat loading must be distinguished from the secondary proinflammatory adipokine response in EAT overlying coronary atherosclerotic inflammation (9, 10).

In a study in the Journal of Applied Physiology, Kim et al. (8) report the novel finding, which is a significant addition to current knowledge in the field, that EAT thickness measured by ECHO over the free wall of the right ventricle (RV) of obese [mean body weight ~ 88 kg; body mass index (BMI) ~ 31 kg/m²] Japanese men was reduced after 3 mo of an aerobic exercise training program. Daily caloric intake was kept constant from the start to the end of the study so that the 3.6-kg body weight loss was explained by increased energy expenditure. Mean epicardial fat thickness decreased from 8.11 to 7.39 mm, a 0.72-mm statistically significant difference. Exercise training decreased blood pressure and VAT area, measured by CT scan, and increased insulin sensitivity. The percent reduction in EAT thickness from baseline was less than the percent decrease in VAT area from baseline. In another study (6), a greater percent reduction in EAT thickness relative to that in waist circumference occurred after 6 mo on a very low calorie (900 kcal/day) diet. This suggests that the method used to attain weight loss may be responsible for relative differences in fat loss in EAT and VAT seen in the two studies.

The study of Kim et al. (8) investigated exercise training with isocaloric intake. This can be compared and contrasted with the results of two other studies summarized in Table 1 that also used ECHO to measure RV EAT thickness before and after weight loss induced by bariatric surgery (12) or by supervised caloric restriction without exercise (6). The number of patients in each group was small and heterogeneous. There was variability in mean pretreatment thickness and in the decrease in posttreatment thickness, possibly due to ethnicity rather than to adiposity. Thus morbidly obese South Florida patients [body wt, 154 kg; BMI, 54 kg/m²] (12) had less initial EAT thickness than the mildly obese Japanese men [body wt, 88 kg; BMI, 31 kg/m²] (8) but approximately similar reductions of ~1 mm after weight loss. In contrast, the morbidly obese Caucasian Canadian patients [body wt, 154 kg; BMI, 45 kg/m²] (6) had the thickest EAT layer and the largest decrease of ~4 mm. A key observation (6) was the improvement in left ventricular (LV) mass and diastolic function, which correlated better with the decrease in EAT than in waist, suggesting that excess local fat around the heart is pathological. Notably, EAT mass correlates directly with intramyocardial triglyceride content (7), so the deleterious factor causing LV dysfunction (6, 7) might be cardiomyocyte triglyceride overload leading to lipidotoxic cardiomyopathy (10), rather than adipokine-mediated cardiomyocellular damage or physical constraints imposed on the myocardium by too much EAT.

So what does it mean if EAT thickness goes down after weight loss? If EAT expansion during the evolution of obesity proves to be proinflammatory and deleterious for myocardial and/or coronary function, then EAT shrinkage by weight loss may be therapeutically important. What future investigations can be devised to test this hypothesis? Human studies could be difficult to do because they should include larger numbers of people from different ethnic groups using circulating inflammatory or other biomarkers as yet undefined that specifically target EAT pathogenicity, and a radiological technique that measures EAT volume (see...
Experimental approaches using obese pigs or primates may give better insight but are more expensive than smaller obese rodents, which can prove unreliable (10, 11). A guinea pig under current investigation (11) has an epicardial fat layer that sits astride the aortic arch and base of the heart extending along epicardial coronaries in the atrioventricular grooves. In this model, the changes in EAT resulting from obesity and its effects on the myocardium and coronary arteries remain to be elucidated. The congenital absence of EAT in humans does not prevent atherogenesis (10). However, animal models of atherosclerosis might be useful to determine if and how EAT contributes to the progression of CAD once it has occurred.

In experienced hands, ECHO can reproducibly determine maximal EAT thickness over the free wall of the RV (5, 6, 12), but it has several limitations as an index of EAT mass (2, 3). EAT is a three-dimensional structure. ECHO measures EAT in two dimensions. EAT volume is more accurately quantitated at submillimeter resolution by CT (3) or MRI (2). The ECHO detection limit is 1 mm (10), which becomes important when differences between measurements are of this order of magnitude (see Table 1). ECHO is valuable to determine if and how EAT contributes to the progression of CAD once it has occurred.

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