Epicardial adipose tissue: friendly companion or hazardous neighbour for adjacent coronary arteries?

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This editorial refers to ‘Peri-coronary epicardial adipose tissue is related to cardiovascular risk factors and coronary artery calcification in post-menopausal women’† by A.M. de Vos et al. on page 777

Visceral adiposity has been increasingly recognized as a marker for cardiovascular risk and metabolic syndrome, including glucose intolerance, hypertension, dyslipidaemia, hyperinsulinaemia, and atherosclerosis. The pathophysiology may be explained by its action as an endocrine and paracrine organ with various biological and metabolic functions, including a reservoir for several atherogenic inflammatory cytokines.1,2 Visceral adipose tissue expresses numerous genes for secretory proteins, and several biologically active molecules secreted from adipose tissue (adipocytokines) may have important roles in the development of atherosclerotic diseases.

Epicardial adipose tissue (EAT) is a particular form of visceral adipose tissue deposited around the heart and found in considerable quantities around subepicardial coronary arteries. EAT shares a common embryological origin with abdominal adipose tissue. Apart from the anatomical description, there is growing evidence about the physiological and metabolic importance of EAT, especially in the association of cardiovascular risk profiles and the pathogenesis of atherosclerotic coronary artery disease (CAD). Earlier studies in cadavers showed that the weight of dissected epicardial fat is correlated with the heart weight, and that coronary atherosclerotic plaque tends to be more prominent on the arterial side in contact with EAT deposits.3 Other studies have shown that EAT supplies free fatty acids for myocardial energy production and synthesizes cytokines. Data from animal studies suggested that the rate of fatty acid synthesis is significantly greater in EAT than in any other depots of the body.4,5 Additionally, EAT of patients with significant CAD has been shown to be a source of several inflammatory mediators and exhibited significant inflammatory responses, independent of body mass index or diabetes.6 Our group has previously shown that interatrial septum thickness, that is essentially determined by the amount of EAT, correlates with the presence and severity of CAD by angiogram.7 EAT measured either on the right ventricle or the amount surrounding the whole heart is significantly related to waist circumference, diastolic blood pressure, left ventricular mass, high level of insulin, whole-body glucose uptake, and the severity of CAD assessed by coronary angiography.8–12

All these findings suggest that EAT plays a role in the development of coronary atherosclerosis via the association with conventional coronary risk factors and also through direct endocrine and paracrine effects. This hypothesis was suspected many years ago based on studies demonstrating the absence of atherosclerosis in human intramyocardial, but not epicardial, coronary arteries.13,14 Segments of coronary arteries lacking EAT or separated from it by a bridge of myocardial tissue appear to be protected against the development of atherosclerosis. The mechanism for this selective natural protection of intramural coronary artery may be due to the absence of adipose tissue in the myocardium as compared with epicardial coronary arteries. The concept of ‘outside-to-inside’ cellular cross-talk has recently been postulated, in that inflammatory mediators outside the coronary artery, such as pericardial and adventitial inflammation, may contribute to intimal atherosclerotic lesions.6,15 There is no fibrous fascial layer between EAT and its adjacent coronary arteries to impede diffusion of free fatty acids and adipokines. The close anatomical relationship between EAT and the adjacent coronary artery permits local paracrine interactions between these structures. Despite there being several studies suggesting the potential role of EAT in the development of CAD, the exact mechanism requires further investigation.

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de Vos et al. evaluated the relationship between peri-coronary EAT and cardiovascular risk factors and coronary artery calcification in 573 healthy post-menopausal women selected from participants in the PROSPECT study. The authors examined the particular location of EAT directly surrounding the coronary arteries, which provided a better understanding of the concept of ‘outside-to-inside’ cellular cross-talk as the mechanism of action of adipocytes as an endocrine and paracrine gland in the local growth of atherosclerotic CAD. The maximal thickness of EAT surrounding each of the three major coronary arteries and coronary calcification was assessed using multidetector computerized tomography (CT). The main findings of this study in post-menopausal women are the significant relationship between EAT directly surrounding the coronary arteries and several vascular risk factors, and the lack of an independent association between EAT and body mass index. The authors also found that peri-coronary EAT is related to coronary calcification, but the association disappeared after controlling for waist circumference as a measure of abdominal obesity. This study provides important information to improve our understanding of the possible causal role of EAT in the local development of CAD. This study is also the first to determine the association between EAT and coronary atherosclerosis analysing major coronary arteries and the adjacent EAT for each coronary territory.

Although there is growing evidence supporting the hypothesis of the direct contribution of EAT surrounding coronary arteries to the development of atherosclerotic CAD, some issues remain to be clarified.

First, it is now more evident that EAT is strongly associated with abdominal visceral adiposity. The fact that the association between EAT and coronary calcification disappeared after adjusting for measures of central obesity should not be quickly interpreted as a ‘lack of association’ between EAT and coronary disease. It is very likely that abdominal visceral fat and EAT are statistically colinear, because both represent measures of total visceral fatness. With the current data, we cannot know if the main pathogenic factor linked to CAD is EAT, abdominal obesity, or total visceral fatness. Playing the devil’s advocate, it could even be said that the overwhelming evidence supporting the association between central obesity and CAD could be explained by the fact that patients with central obesity have larger deposits of EAT, and not the other way around. Whether EAT is only a marker of abdominal visceral adiposity or abdominal visceral adiposity is a surrogate of a pathogenic cardiac adipose tissue is still to be determined.

The second issue that remains to be clarified is whether EAT provides incremental information for risk prediction. So far, all the studies testing the association between EAT and coronary disease have been cross-sectional, so it remains unknown how EAT measurement will improve the predictive value of standard cardiovascular risk scores such as the Framingham or PROCAM. However, even before long-term longitudinal studies can be designed to test the potential role of EAT to predict cardiovascular disease, the scientific community needs first to decide what is the best way to quantify EAT. The measurement of EAT is not straightforward, regardless of the method used. Several non-invasive imaging techniques have been employed in the quantitative assessment of EAT, such as transthoracic echocardiography, multidetector CT, and magnetic resonance imaging (MRI). Among these, transthoracic echocardiography is the method most widely available in clinical centres and is the technique used in most of the studies assessing the association between EAT and CAD. However, the ability to quantify EAT with echocardiography is modest compared with the use of CT. Echocardiography is highly dependent on the acoustic windows and may not give an adequate window of EAT surrounding all cardiac segments and chambers. Multidetector CT has advantages of high temporal and spatial resolution, and three-dimensional views of the heart and its epicardial surface. MRI has been considered the gold standard for the measurement of visceral adiposity. Additionally, there might be different implications for measuring the volume of EAT content vs. only two-dimensional measurements of thickness. The current study shows that regional measurement of EAT is also important, instead of using a single value for total cardiac fatness.

Finally, because the amount of EAT appears to be independent of body mass index, according to this and other previous studies, it is possible that a patient could have a completely normal body weight and large amounts of EAT. Therefore, if EAT proves in the future indeed to cause CAD, we may coin a new condition called ‘cardiac obesity’ to identify those with normal weight and a fatty heart. Because visceral fat deposition can be reversed with increased physical activity and caloric restriction, the use of a new label to identify patients at risk could eventually be used as an extra tool to promote lifestyle changes to prevent cardiovascular disease.

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References
Cardiac lipoma diagnosed by cardiac magnetic resonance imaging

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A 62-year-old man experienced a transient ischaemic attack. He underwent a transthoracic echocardiogram to rule out the presence of embolic source. It showed a 10 mm mass with broad attachment to the left side of the inter-ventricular septum. Diagnosis of cardiac myxoma, sessile thrombus, and localized hypertrophic cardiomyopathy were considered. He was then referred for a cardiac magnetic resonance imaging (MRI) study for further characterization of the mass.

Cardiac MRI showed a solitary, well-defined, spherical mass arising from the endocardial surface of the mid-anterior septum. No other masses were present. On cardiac short-axis T1-weighted fast spin-echo MRI, the mass was hyperintense (Panel A). On T1-weighted fast spin-echo with fat suppression sequence, the mass appeared hypointense (arrowhead) (Panel B). After administration of gadolinium-DTPA, first-pass perfusion imaging showed the mass was poorly perfused relative to normal myocardium (arrowhead) (Panel C). On late contrast-enhanced images, the mass did not uptake contrast (image not shown). On short-axis steady-state free precession cine MRI, the mass was slightly hyperintense showing a dark rim with the adjacent blood (Panel D). Regional wall motion was normal in all myocardial segments. All these MRI findings were compatible with a benign cardiac lipoma.

Primary tumours of the heart are rare. Approximately 75% of such tumours are benign and 25% are malignant. Most benign heart tumours are myxomas, and the majority of the rest are lipomas, papillary fibroelastomas, and rhabdomyomas. Cardiac lipomas account for 10% of all cardiac tumours. They are well-encapsulated tumours typically composed of mature fat cells. True cardiac lipomas are much less frequent than lipomatous hypertrophy of the interatrial septum, but they can occur in almost any location of the heart. Cardiac lipomas are generally incidental findings and in most cases require no treatment or surgical intervention. Cardiac lipomas can, however, cause arrhythmias, embolize, compress the coronary arteries, or obstruct flow within the heart. In these cases, surgical resection is recommended.

Our report highlights the importance of a comprehensive cardiac MRI approach that can provide the clinician not with only an accurate description of the imaging findings but also the etiological diagnosis.