EDITORIAL

Epicardial Adipose Tissue — A New Biomarker of Cardiovascular Risk

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Epicardial adipose tissue (EAT) has emerged as a new imaging-derived biomarker expressing the risk of cardiovascular disease. The role of epicardial thickness in predicting cardiovascular risk has been recently described in patients with subclinical atherosclerosis, diabetes mellitus, renal failure and different diseases characterized by an increased inflammatory status.[1] The characteristics of pericoronary fat depot are very distinct from those of other fat depots in the body. In a recently published study, it has been shown that only pericoronary fat was associated with the presence of coronary plaques, while other fat depots such as periaortic, or extracardiac, were not.[2] At the same time, an increased volume of pericoronary fat was associated with systemic release of inflammatory biomarkers.[2]

EPICARDIAL ADIPOSE TISSUE AND CORONARY ARTERY DISEASE

The association between EAT and coronary artery disease (CAD) has been proved by a multitude of studies that demonstrated that the volume of EAT is significantly higher in patients with CAD and is an effective indicator of future cardiovascular risk.[3] However, as yet, it has not been clarified whether increased EAT determines an augmented inflammation via releasing inflammatory markers into the systemic circulation, or the increased inflammation present in cardiovascular diseases results in increased EAT. EAT is considered nowadays to represent a significant source of pro-inflammatory cytokines that are released into the systemic circulation, and the relation between pro-inflammatory biomarkers and CAD has been well documented in various studies.[4]

However, a recent follow-up study demonstrated that while EAT and coronary artery calcium were significantly correlated with the level of systemic inflammatory markers such as IL-2, IL-4, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, IL-15, IL-17, IFN-gamma, TNF-alfa, hs-CRP and others at baseline, these biomarkers were not predictive of an increase in EAT or CAD.[5]

EPICARDIAL ADIPOSE TISSUE AND PATIENT VULNERABILITY

Another issue under debate relates to the role of EAT in expressing the vulnerability of patients with coronary artery disease. No study so far has compared the prognostic role of EAT in stable versus unstable patients. Hajsadeghi *et al.* proved that increased EAT predicts MACE rates independent of other conventional risk factors, in patients with CAD.[6] It has been shown that increased EAT is associated with the presence of high-risk, vulnerable plaques in the coronary arteries, indicating that EAT could represent a new marker of vulnerability. Therefore, an increased EAT could show the risk of developing an acute coronary event, probably via an inflammatory-related mechanism, as it is well documented that inflammation plays a significant role in plaque formation, progression, and rupture. EAT proved to be closely and directly related to the severity of coronary lesions, at the same time being an inde-

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pendent risk factor for CAD.[7] even if EAT volume proved to add no significant information relating to the functional significance of a coronary artery stenosis.[8]

IMAGING TECHNIQUES FOR ASSESSMENT OF EAT

Various imaging techniques have been proposed for the evaluation of EAT. The most useful and reliable one is Computed Tomography (CT), a technique that allows precise quantification, not only of EAT volume but also of the amount of pericoronarian EAT or the determination of the density of this tissue. Moreover, EAT density, as shown by CT, has been proposed as a useful marker of a risk of future cardiovascular events. A recent study indicated that the density of pericoronal adipose tissue was associated with increased EAT and body mass index, with a concomitant decrease in pericoronary adipose tissue density with increasing distance from the vessel and from the proximal to distal segments of the LAD.[9]

A significant advantage of CT evaluation is the possibility of providing complex information related to EAT volume, at the same time as giving an accurate assessment of plaque vulnerability, by the identification of susceptibility markers, present in coronary plaques.

Magnetic Resonance Imaging has been proposed for the evaluation of EAT. However, its use is limited by its poorer ability to diagnose coronary artery diseases, compared to Angio CT.

A recent study using single-photon emission computed tomography (SPECT) demonstrated an increased regional accumulation of epicardial fat, present in areas with reversible perfusion defects, compared to the areas with normal perfusion.[10]

Despite the advantages provided by these cutting-edge techniques, echocardiography remains an easily accessible method that may be used for routine examination of patients with coronary artery disease, including the assessment of the EAT. In a very recent study, an initial thickness of EAT of more than 7 mm was shown to be a significant predictor of MACE, death, revascularization, and myocardial infarction.[11] However, echocardio-graphy can only determine the diameter of EAT, while CT provides the advantage of more reliable quantification and at the same time, an assessment of plaque vulnerability.

EPICARDIAL ADIPOSE TISSUE IN POST INFARCTION DIABETIC PATIENTS

In a Korean population, EAT thickness was independently associated with the incidence of diabetes (OR 3.26, 95% CI = 1.17–9.12).[12] A study published in this issue of JCE indicates that the thickness of EAT is highly correlated with an increased inflammatory post-infarction status, in patients with AMI and type II diabetes, and represents a significant risk factor for severe impairment of ventricular function in the post-infarction phase.[13] In this study, the diabetic patients with increased epicardial fat volumes presented a lower EF, marked enlargement of the ventricular cavities and the development of ventricular remodeling at six months, as compared to those with lower values of EFT, and also as compared to the non-diabetic patients. The results suggest that there is a link between an increased inflammatory response, an enlarged EAT and the remodeling process, in patients with diabetes and myocardial infarction. Interestingly, the study indicates significant differences in EAT volume between diabetic patients who developed post-infarction ventricular remodeling versus those who did not. This difference was not observed in non-diabetic patients, suggesting that the presence of diabetes could play a significant role in the inflammatory-mediated process and the increased susceptibility of patients in the post-infarction period.

At the same time, the study demonstrated a significant correlation between systemic values of hsCRP, a biomarker characterizing an increased inflammatory status, and EAT, especially in diabetic patients, identifying EAT (OR: 6.11, p = 0.01) and serum levels of hsCRP (OR: 4.09, p = 0.03) as powerful independent predictors of left ventricular remodeling in diabetic patients, thus proving the role of inflammation-mediated pathways in increasing patient vulnerability. The study underlines that a routine quantification of epicardial fat thickness, by simple echocardiographic evaluation performed in the first days after infarction, may significantly help to identify patients more exposed to the risk of ventricular remodeling and heart failure following the infarction. These results could be further extrapolated in future algorithms to determine vulnerable patients using complex risk assessment tools.

SUMMARY

Overall, it may be concluded that epicardial adipose tissue is present in a larger volume in patients with coronary artery disease compared to those without coronary atherosclerotic involvement. Moreover, the larger the amount of epicardial adipose tissue, the greater the medium and long term vulnerability of these patients. The study pre-

sented in this issue of the journal (Rat *et al.*) demonstrates that the thickness of the epicardial adipose tissue in diabetic patients with acute myocardial infarction correlates with an increased amount of inflammatory markers in the acute phase and with a poorer prognosis in the medium term. Various imaging techniques are increasingly used to evaluate this parameter. So far it is unclear if EAT produces inflammatory effectors or is only associated with them. However, it is clear that the volume of epicardial adipose tissue is a candidate for inclusion in the risk score when evaluating coronary patients.

CONFLICT OF INTEREST

Nothing to declare.

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