Local Epicardial Adipose Tissue Deposits and Left Ventricular Diastolic Function in Patients With Preserved Left Ventricular Ejection Fraction

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Extrabdominal fat deposits, including epicardial adipose tissue (EAT) as well as intra-abdominal visceral adiposity, are now considered as markers of cardiovascular risk, and EAT is regarded as metabolically active fat anatomically adjacent to the myocardium and coronary arteries. EAT volume (EATV) and visceral adipose tissue are increased in obese patients and correlate with the presence of coronary artery disease (CAD), independent of the traditional CAD risk factors such as age, hypertension, diabetes mellitus, and smoking. Furthermore, excessive accumulation of EAT imposes a paracrine or mechanical burden on the coronary microcirculation and myocardium, and the EATV is reported to be an independent predictor of left ventricular (LV) remodeling and LV diastolic dysfunction (LVDD). The EATV also correlates with the left atrial diameter, an indirect structural parameter of LVDD. These previous studies have focused on full-volume quantification of EAT and its effect on coronary atherosclerosis or myocardial function. However, whether local EAT accumulation is linked to LV diastolic parameters and, if so, the mechanisms by which regional EAT results in LVDD remain unclear.

In this issue of the Journal, Maimaituxun et al provide the first report on the relationship between local EAT depots and LVDD in Japanese patients with suspected coronary artery disease. The possible pathways by which epicardial adipose tissue (EAT) deposits result in left ventricular (LV) diastolic function in patients with preserved LV ejection fraction are shown in the figure. Local EAT deposits may directly inhibit mitral annular motion reflected in echocardiographic parameters (lateral e’ and E/e’), and then LV diastolic function in patients with preserved LV ejection fraction.

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CAD and preserved LV ejection fraction (LVEF). LVDD in patients with normal LVEF (≥50%) is defined as a combination of 4 items: (1) average E/e’ ≥14, (2) septal e’ velocity <7 cm/s or lateral e’ velocity <10 cm/s, (3) tricuspid regurgitation velocity >2.8 m/s, and (4) left atrial volume index (LAVI) >34 mL/m², based on the 2016 ASE/EAE/EACI guideline. Among the various echocardiographic parameters, local EAT thickness surrounding the left circumflex artery (EAT_LCX) and the LV wall (EAT_LV) strongly correlated with LVDD diagnosis (lateral e’ and lateral E/e’), suggesting that local fat depots are directly linked to mitral annular motion and LVDD diagnosis. And, among the various EAT measures, only EAT_LCX provided a significant cutoff for predicting LVDD, indicating that an increase in EAT_LCX could be a pathophysiologic indicator of LVDD (Figure). The potential mechanisms underlying the direct correlation between EAT and LVDD remain to be elucidated, but may involve mechanical and paracrine processes. Mechanically, atrial enlargement correlates with impaired diastolic filling in obese patients. The LAVI (a marker of atrial enlargement) is associated with the LV mass index (LVM), EATV index, and EAT_LCX, which suggests that impairment of the restoring LV force and active LV relaxation, partially affected by local EAT accumulation, but not an impaired lengthening load (LA dysfunction), could cause LVDD. Notably, the LVM correlated with LVDD diagnosis (septal e’ and septal E/e’), but not with lateral e’ and lateral E/e’, independent of EAT_LCX. On the other hand, EAT_LCX correlated well with lateral e’ and lateral E/e’ but not with septal e’ or septal E/e’. Taken together, the authors suggest that local EAT deposits (EAT_LCX), independent of LV remodeling (hypertrophy), are associated with LVDD diagnosis through impairment of lateral mitral annulus motion. Aging was associated positively with EAT_LCX and EAT_LV and negatively with septal and lateral e’ and E/e’. However, EAT_LCX showed a borderline significance for LVDD in both the <65 and ≥65 age groups, suggesting a role of EAT accumulation independent of aging. Conversely, paracrine processes could manifest through EAT accumulation. Adipose tissue is a source of several bioactive molecules that might directly influence the myocardium. Accumulated EAT, as compared with non-accumulated EAT, contains high levels of various adipocytokines, and therefore its pro-inflammatory characteristics could cause pathophysiological conditions such as coronary atherosclerosis and LVDD. Furthermore, under metabolic and cardiovascular disease conditions, EAT can expand, becoming hypoxic and dysfunctional and recruiting inflammatory cells, which leads to reductions in protective cytokines and increases in detrimental cytokines, resulting in impaired cardiac function (Figure). This increased weight probably also leads to a mechanical burden on cardiac muscle expansion and further deteriorates LV relaxation in LVDD patients. Excessive levels of EAT may also lead to myocardial triglyceride accumulation that negatively effects LV overload and hypertrophy or cardiac lipotoxicity.

This study has potential limitations that should be noted. It was cross-sectional in design and conducted at a single center with a relatively small number of patients. In addition, the patients were all Japanese, so the relevance of this study to other ethnic populations requires further research. Finally, the study did not consider the effect of patients’ medications or lifestyles on EAT measures.

In conclusion, local EAT accumulation was linked to LV diastolic parameters in patients with preserved LVEF, and further study is warranted to clarify whether local EAT depots are functionally linked to clinical manifestations of LVDD.

Disclosures

The authors declare no conflicts of interest.

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