EDITORIAL

The Epicardium as a Mirror of Metabolism: from Visceral Fat to Heart Failure with Preserved Ejection Fraction

El epicardio como espejo del metabolismo: de la grasa visceral a la insuficiencia cardíaca con fracción de eyección preservada

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For a long time, adipose tissue was considered a passive energy store. Today we know that it is a highly dynamic endocrine and paracrine organ, capable of communicating with multiple tissues through a complex molecular language. In the heart, this conversation occurs in close proximity: epicardial adipose tissue (EAT), which rests directly on the myocardium without an intermediate anatomical barrier shares its blood supply, oxygenation, and metabolic fate. (1,2)

The study published in this issue of the Argentine Journal of Cardiology, "Epicardial Fat and Its Relationship with Cardiac Morphological Alterations and Markers of Diastolic Dysfunction," provides valuable local evidence. (3) In a cohort of patients with type 2 diabetes without overt cardiovascular disease, the authors demonstrate that increased EAT thickness—as measured by echocardiography—is associated with a higher prevalence of diastolic dysfunction criteria. This finding transforms the epicardium: it ceases to be an anatomical curiosity to become an accessible biomarker of early cardiometabolic risk. (1,4)

In essence, EAT is visceral fat, sharing its embryological origin and its inflammatory and hormonal circuits. Under overeating, insulin resistance, and mitochondrial dysfunction conditions, EAT expands, infiltrates, and loses its anti-inflammatory profile, releasing proatherogenic cytokines, leptin, angiotensinogen, and microRNAs. (5,6) Thus, the heart is literally surrounded—and affected—by its own metabolic environment. (7)

In line with this evidence, Milton Packer has in recent years proposed a transformative pathophysiological model . In his most recent work, "The Adipokine Hypothesis of Heart Failure with a Preserved Ejection Fraction: A Novel Framework to Explain Pathogenesis and Guide Treatment", (8) he postulates that the expansion of visceral adipose tissue is not only a marker but also the upstream trigger that drives a cascade of endothelial dysfunction, systemic inflammation, and myocardial stiffness. (8-11) According to this hypothesis, alterations in the secretion of proinflammatory and antifibrotic adipokines modify nitric oxide signaling and the myocyte´s ability to sustain oxidative phosphorylation. Consequently, heart failure with preserved ejection fraction (HFpEF) emerges as a systemic disease whose epicenter is not in the heart, but in adipose tissue. (8,11)

In this context, the epicardium acts as a local messenger of this global disorder. Its expansion exerts a mechanical compressive effect on the ventricle, and also releases mediators that interfere with myocardial bioenergetics, reduce mitochondrial biogenesis, and stimulate the activation of cardiac fibroblasts. (2,6) Clinical observation and molecular physiology are intertwined: the hypertrophied epicardium becomes a visible mirror of altered metabolism, anticipating the transition from silent metabolic phenotype to overt heart failure. (5,7,8)

This metabolic process also interacts with classical hemodynamic mechanisms. Hypertension and activation of the renin-angiotensin-aldosterone axis perpetuate wall stress, inflammation, and myocardial fibrosis. (7,9) In HFpEF, aldosterone not only retains sodium but also induces mitochondrial dysfunction and epicardial remodeling, integrating the hormonal component into the inflammatory and metabolic framework that defines this entity. (7,11)

One of the great merits of the Argentine study

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lies in restoring the value of echocardiography as a practical tool for quantifying EAT. Although magnetic resonance imaging or computed tomography allow for more accurate volumetric characterization, epicardial thickness measured in the right parasternal long axis correlates strongly with total EAT burden and myocardial stiffness. (1,4) In this study, a threshold of 5 mm was associated with a sharp increase in the prevalence of diastolic dysfunction and multiple adverse echocardiographic criteria. (1,3) It could be said that the heart receives inflammation before symptoms.

Perhaps the most encouraging message from this line of research is its potential for reversibility. Epicardial fat is a dynamic tissue that responds to metabolic changes. Trials with GLP-1 (glucagon-like peptide-1) receptor agonists and SGLT2 (sodium-glucose cotransporter 2) inhibitors have shown significant reductions in epicardial volume within a few months, accompanied by improvements in diastolic function and functional capacity. (6,7) Therefore, EAT could become a dynamic therapeutic biomarker, sensitive to the impact of pharmacological and lifestyle interventions. (5,7,8)

The study here discussed marks a milestone in local research. Beyond its limitations—small sample size and cross-sectional design—it demonstrates that it is possible to generate robust evidence on cardiometabolic pathophysiology from our own centers. According to Packer´s hypothesis HFpEF is not a disease of the heart, but of the metabolism that the heart suffers from.

In this new cardiology of the tissue, the epicardium emerges as a witness of and participant in metabolic imbalance. Measuring, understanding, and modifying it could be one of the keys to preventing HFpEF in the 21st century. (7-9,11)

Conflicts of interest

None declared

(See authors conflicts of interest forms on the website).

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