Assessing Cardiometabolic Risk Through Epicardial Adipose Tissue Imaging

Kenneth Chan[1] MRCP, Evangelos K. Oikonomou[2,3] MD DPhil

1. Acute Multidisciplinary Imaging & Interventional Centre, British Heart Foundation (BHF) Centre of Research Excellence, Division of Cardiovascular Medicine, Radcliffe Department of Medicine, NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, UK
2. Section of Cardiovascular Medicine, Department of Internal Medicine, Yale School of Medicine, New Haven, CT, USA
3. Cardiovascular Data Science (CarDS) Lab, Yale School of Medicine, New Haven, CT, USA

Word count: 1126

References: 12

Figure(s): 1

Correspondence to:

Dr Kenneth Chan, Acute Multidisciplinary Imaging & Interventional Centre (AMIIC), University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU

e-mail: kenneth.chan@cardiov.ox.ac.uk

Epicardial adipose tissue (EAT) is a unique visceral fat depot located between the myocardium and the visceral pericardium. In the absence of a separating fascial layer, it lies in direct contact with the underlying myocardial tissue and shares the coronary microcirculation.(1) Beyond providing mechanical protection and acting as a local energy reservoir, EAT exhibits a transcriptomic and secretory profile distinct from that of other adipose depots and has emerged as a metabolically active tissue with important cardiometabolic implications.(2) Under physiological conditions, EAT exerts cardioprotective effects through fatty acid buffering, thermogenic activity, and secretion of anti-inflammatory adipokines. In contrast, in states of obesity and cardiometabolic dysfunction, EAT undergoes pathological remodelling characterized by adipocyte hypertrophy, immune cell infiltration, fibrosis, and a shift toward a pro-inflammatory and pro-fibrotic secretome.(3) Accumulating evidence implicates both quantitative expansion and qualitative alteration of EAT in the pathogenesis of coronary artery disease(4), atrial fibrillation(5), and heart failure with preserved or reduced ejection fraction(3,6). (**Figure**) Cardiac computed tomography (CT) and magnetic resonance imaging provide high spatial resolution, enabling non-invasive quantification and phenotypic characterisation of EAT, while emerging artificial intelligence–based segmentation techniques facilitate automated, high-throughput analysis.(5) As coronary CT angiography is increasingly placed as a first-line investigation for anatomical assessment of coronary artery disease, concurrent evaluation of EAT offers an opportunity to capture the biological and cardiometabolic milieu surrounding the coronary arteries. Integrating EAT metrics into routine imaging workflows may therefore enhance cardiovascular risk stratification by providing complementary information beyond luminal stenosis and plaque morphology alone.(7)

In this issue of JACC: Cardiovascular Imaging, Filtz et al (8) provide valuable insight into the temporal influence of EAT and coronary artery disease burden by analysing serial CCTA performed at an interval of ≥2 years from the PARADIGM registry. Consistent with prior observations (4), higher baseline EAT volume was cross-sectionally associated with greater overall atherosclerotic plaque burden, particularly lipid-rich, noncalcified plaque components.(4) The present study extends these findings by demonstrating that elevated EAT volume is associated not only with baseline disease severity but also with accelerated plaque progression over time, which in turn leads to adverse clinical outcomes.(8) Individuals in the highest tertile of EAT volume exhibited significantly greater plaque progression, as well as rapid plaque progression defined as an annual increase in atheroma volume ≥1%. Although patients with rapid plaque progression were older and carried a higher burden of traditional cardiovascular risk factors, EAT volume remained independently associated with plaque progression after adjustment for age, sex, body mass index, and established risk factors. These findings highlight the contribution of residual cardiometabolic risk beyond conventional measures, and the translational value of EAT quantification in refining cardiovascular risk stratification.

To determine the clinical utility of EAT in risk prediction, it is essential to define the threshold at which EAT volume confers detrimental cardiovascular effects. Volumetric EAT values associated with adverse phenotypes vary widely across cohort studies. In studies measuring EAT volume from CCTA, patients with high-risk plaque characteristics consistently had higher EAT volumes, with a mean difference of approximately 10-40 cm^3 compared with those without high-risk plaque, .(4) Several studies have identified discriminatory thresholds for atherosclerotic risk in the range of ~100–130 cm^3 for the detection of high-risk plaque features or thin-cap fibroatheroma.(4) Similarly, volumetric

EAT has been linked to diastolic dysfunction, with patients exhibiting impaired relaxation demonstrating approximately 20-40 cm^3 greater EAT volume than those with normal diastolic function.(3,6) These findings suggest that EAT volumes exceeding roughly 100–130 cm^3 may reflect a maladaptive cardiometabolic milieu associated with both atherosclerotic vulnerability and myocardial dysfunction, though it is important to highlight that most studies generally did not report indexed values to anthropometric measurements such as body surface area (BSA).

Furthermore, the relationship between EAT and cardiovascular disease may not be strictly linear. Notably, in populations with reduced left ventricular ejection fraction, lower EAT volumes have been observed compared with individuals with preserved systolic function, supporting the concept of an “EAT paradox”, whereby very low EAT volume in cachectic heart failure states may reflect adverse remodelling and poor prognosis.(9) Thus, both excessive and markedly reduced EAT volumes may carry clinical significance. Defining an optimal, perhaps sex-specific EAT range, appropriately indexed for BSA, that balances physiological and pathological effects remains an important unmet need. Establishing standardised optimal EAT volumetrics will be critical for facilitating clinical interpretation and integrating EAT quantification into cardiovascular risk stratification frameworks.

Beyond volumetric expansion, the interaction between EAT and the cardiovascular system is likely more complex than size alone. EAT undergoes qualitative remodelling characterized by immune cell infiltration, adipocyte hypertrophy, fibrosis, and shifts in its inflammatory and metabolic transcriptome, all of which may modulate local vascular biology independently of total fat volume.(2) Experimental and translational work has demonstrated that inflammatory signalling within perivascular adipose tissue can alter its lipid content and

extracellular matrix composition, leading to measurable changes in CT attenuation that reflect underlying biological activity rather than simple adiposity.(10,11) Importantly, these attenuation changes are spatially heterogeneous and closely linked to focal coronary inflammation at the tissue–vessel interface, supporting the concept that local fat phenotype, not just quantity, contributes to atherosclerosis.

Nevertheless, global EAT density, as assessed by mean CT attenuation in the present study, was not significantly associated with baseline plaque burden or subsequent plaque progression. One potential explanation is that averaged EAT attenuation may dilute spatially relevant inflammatory signals. While pericoronary adipose tissue attenuation has been shown to reflect localized inflammatory activity adjacent to the coronary wall, whole-depot EAT density represents a composite measurement across heterogeneous regions and may therefore lack sensitivity to detect focal metabolic activation. It is plausible that region-specific inflammatory remodelling was not adequately captured by global mean attenuation values. Advanced imaging approaches such as radiomic texture analysis may provide a more granular assessment of EAT microarchitecture, potentially offering indirect insight into its proteomic and secretory phenotype and improving the characterisation of biologically active epicardial fat beyond simple volumetric or density metrics.(11)

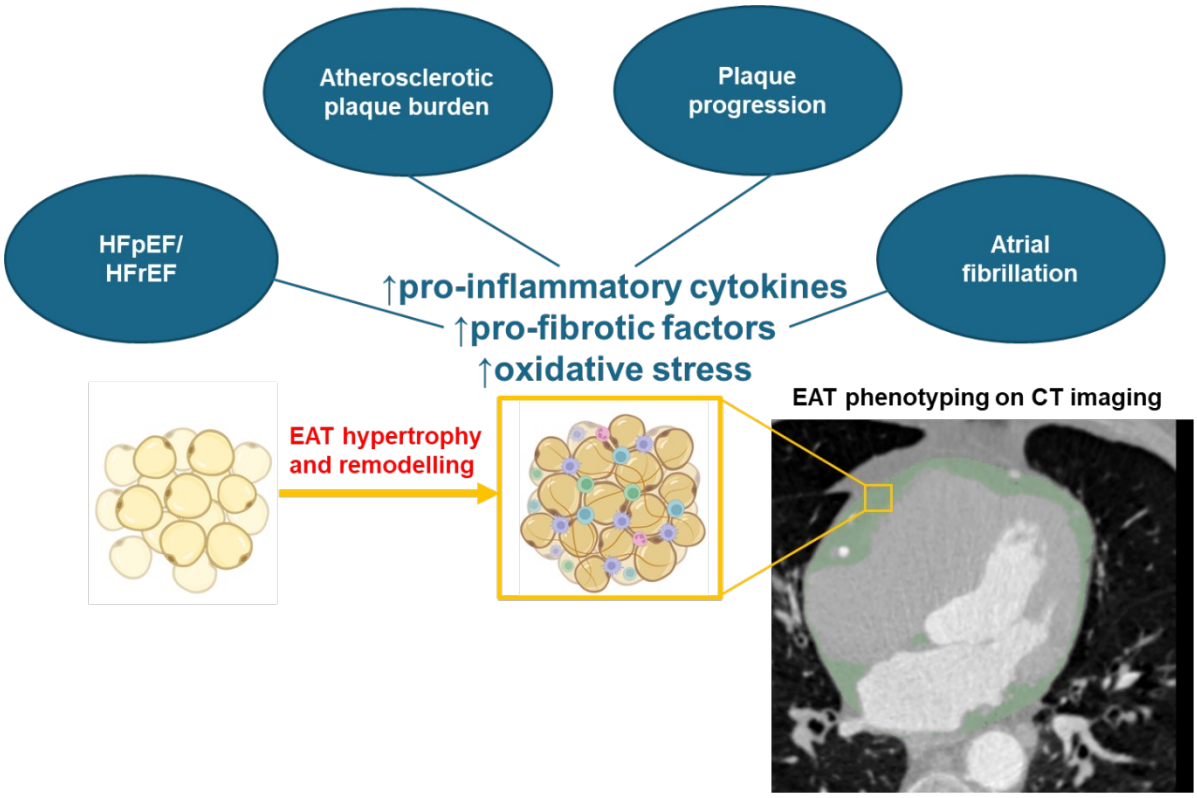
In summary, Filtz et al. demonstrate that greater EAT volume is independently associated with accelerated coronary plaque progression and adverse clinical outcomes. Emerging therapies, including glucagon-like peptide-1 receptor agonists (GLP-1RAs) and sodium–glucose co-transporter 2 (SGLT2) inhibitors, have been shown to favourably alter EAT volume and inflammatory phenotype.(9,12) This reinforces the prospect that EAT represents a potentially modifiable component of residual cardiometabolic risk. Together, the

present study supports a precision-based approach in which quantification and phenotyping of EAT could guide personalised strategies to address residual cardiometabolic risk and potentially attenuate progression of coronary atherosclerosis through targeted modulation of epicardial fat in cardiometabolic disease.

Funding support and author disclosures:

K.C. is supported by British Heart Foundation (FS/CRTF/24/24704). E.K.O. acknowledges research support through a Robert A. Winn Excellence in Clinical Trials Career Development Award and a Wiesman Award for Excellence in Early-Career ATTR Research from Cornerstone Medical Education (through Yale University). He is a co-founder of Evidence2Health LLC, a co-inventor in patent applications (18/813,882, 17/720,068, 63/508,315, 63/580,137, 63/619,241, 63/562,335) and granted patents (US12067714B2, US11948230B2, licensed through the University of Oxford to Caristo Diagnostics Ltd). He declares stock options with Caristo Diagnostics Ltd, a consultant agreement with Ensight-AI Inc, and has received honoraria from Clinical Education Alliance. He also serves as Associate Editor for European Heart Journal.

Figure: Influence of epicardial adipose tissue on cardiovascular disease.



CT, computed tomography; EAT, epicardial adipose tissue; HFpEF, Heart failure with preserved ejection fraction; HFrEF, Heart failure with reduced ejection fraction

References

1. Antoniades C, Tousoulis D, Vavlukis M et al. Perivascular adipose tissue as a source of therapeutic targets and clinical biomarkers. Eur Heart J 2023;44:3827-3844.
2. Iacobellis G. Epicardial adipose tissue in contemporary cardiology. Nat Rev Cardiol 2022;19:593-606.
3. Janssen-Telders C, Eringa EC, de Groot JR, de Man FS, Handoko ML. The role of epicardial adipose tissue remodelling in heart failure with preserved ejection fraction. Cardiovasc Res 2025;121:860-870.
4. Nerlekar N, Brown AJ, Muthalaly RG et al. Association of Epicardial Adipose Tissue and High-Risk Plaque Characteristics: A Systematic Review and Meta-Analysis. J Am Heart Assoc 2017;6.
5. West HW, Siddique M, Williams MC et al. Deep-Learning for Epicardial Adipose Tissue Assessment With Computed Tomography: Implications for Cardiovascular Risk Prediction. JACC Cardiovasc Imaging 2023;16:800-816.
6. Nerlekar N, Muthalaly RG, Wong N et al. Association of Volumetric Epicardial Adipose Tissue Quantification and Cardiac Structure and Function. J Am Heart Assoc 2018;7:e009975.
7. Mahabadi AA, Berg MH, Lehmann N et al. Association of epicardial fat with cardiovascular risk factors and incident myocardial infarction in the general population: the Heinz Nixdorf Recall Study. J Am Coll Cardiol 2013;61:1388-95.

8. Filtz A, Lorenzatti D, A S. Epicardial Adipose Tissue, Coronary Plaque Progression, and Major Adverse Cardiovascular Events: A Multicenter Study. JACC Cardiovasc Imaging 2026.
9. Banerjee M. Epicardial Fat Paradox and Differential Effects of GLP-1 Receptor Agonists Across Heart Failure Phenotypes. Circ Heart Fail 2023;16:e010966.
10. Antonopoulos AS, Sanna F, Sabharwal N et al. Detecting human coronary inflammation by imaging perivascular fat. Sci Transl Med 2017;9.
11. Oikonomou EK, Williams MC, Kotanidis CP et al. A novel machine learning-derived radiotranscriptomic signature of perivascular fat improves cardiac risk prediction using coronary CT angiography. Eur Heart J 2019;40:3529-3543.
12. Requena-Ibanez JA, Santos-Gallego CG, Rodriguez-Cordero A et al. Mechanistic Insights of Empagliflozin in Nondiabetic Patients With HFrEF: From the EMPA-TROPISM Study. JACC Heart Fail 2021;9:578-589.