European Heart Journal Supplements (2026) **28** (Supplement 5), v139–v142
The Heart of the Matter
https://doi.org/10.1093/eurheartjsupp/suag043

New cardiovascular risk factor and clinical surrogate: epicardial fat

Saima Mushtaq[1], Maria Elisabetta Mancini[1], Riccardo Maragna [1], Ettore Ventura[1], and Gianluca Pontone[1,2]*

[1]Department of Perioperative Cardiology and Cardiovascular Imaging, Centro Cardiologico Monzino IRCCS, Milan 20134, Italy; and [2]Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan 20134, Italy

KEYWORDS
Coronary computed tomography angiography; Coronary artery disease; Fat attenuation index; Pericoronary adipose tissue attenuation

Coronary computed tomography angiography (CCTA) has become a cornerstone in the non-invasive evaluation of coronary artery disease (CAD). Beyond defining stenosis severity, CCTA enables detailed quantification of total atherosclerotic burden, plaque composition, and imaging markers of plaque vulnerability. Recent advances—including artificial intelligence (AI)-enhanced algorithms—now allow automated and highly reproducible plaque phenotyping, with major implications for risk stratification and therapeutic monitoring. Concurrently, imaging of pericoronary adipose tissue has introduced novel biomarkers of vascular inflammation, particularly the Fat Attenuation Index and pericoronary adipose tissue attenuation. These indices independently predict adverse cardiovascular events beyond traditional risk factors. Serial imaging studies further demonstrate that lipid-lowering and anti-inflammatory therapies modulate plaque biology, promoting regression or stabilization. Integration of coronary plaque analytics, adipose tissue biology, and AI-driven risk prediction is redefining preventive cardiology and enabling increasingly individualized management strategies.

Introduction

Coronary computed tomography angiography (CCTA) has evolved from a tool primarily used to identify haemodynamically significant stenosis into a modality capable of comprehensive atherosclerotic phenotyping.[1–4] Contemporary CCTA provides robust quantification of plaque volume, delineates calcified and non-calcified components, and identifies imaging signatures associated with high-risk lesions, such as low-attenuation plaque, positive remodelling, spotty calcification, and the napkin-ring sign.[4]

The parallel emergence of artificial intelligence (AI)-based analytic platforms has further accelerated the ability to assess plaque characteristics at scale and to monitor atherosclerotic progression longitudinally with high reproducibility.[5]

Beyond luminal and plaque morphology, CCTA now allows assessment of peri-vascular and epicardial adipose depots. Biomarkers such as Fat Attenuation Index (FAI) and PCAT attenuation offer non-invasive surrogates of coronary inflammation, a central driver of atherogenesis and plaque destabilization.[6] PCAT, situated in direct anatomical continuity with the coronary adventitia, undergoes compositional shifts in response to vascular inflammatory signalling and thus serves as a sensitive imaging readout of inflammatory activity.[6]

This review synthesizes contemporary evidence on the role of PCAT as an emerging cardiovascular biomarker, with emphasis on its association with

*Corresponding author. Tel: 0258002574, Fax: 0258002281, Email: gianluca.pontone@ccfm.it

plaque vulnerability, its prognostic value, and technical considerations relevant to its measurement.

CCTA-based plaque assessment

CCTA offers accurate quantification of atherosclerotic burden with substantial agreement with intravascular ultrasound. Plaque volumes derived from CCTA independently predict coronary events across both lesion-level and patient-level analyses.[1–4]

The coronary artery calcium score remains a powerful long-term risk marker; however, it is limited by its inability to identify non-calcified plaque—often the substrate for acute coronary syndromes. CCTA therefore provides superior clinical insight by integrating anatomic, compositional, and morphologic information.[1,2]

High-risk plaque features on CCTA include:

- positive remodelling
- spotty calcification
- low-attenuation plaque
- napkin-ring sign

The presence of two or more of these features identifies a vulnerable plaque phenotype closely associated with increased risk of major adverse cardiovascular events.[7]

Pathophysiology of PCAT

PCAT is composed of metabolically active adipocytes contiguous with the coronary arterial wall. This anatomic proximity facilitates bidirectional paracrine signalling.[6] PCAT releases pro-inflammatory mediators that promote endothelial dysfunction, oxidative stress, and plaque instability. Conversely, inflammatory signalling from the arterial wall induces a shift in PCAT composition—characterized by reduced lipid content, increased water content, and higher CT attenuation.

Because adipose CT attenuation becomes less negative as inflammation increases, both FAI and PCAT attenuation serve as sensitive markers of vascular inflammatory activity. Landmark trials, including CRISP-CT and SCOT-HEART, demonstrate that elevated FAI or PCAT attenuation predicts incident cardiovascular events independently of stenosis severity or plaque phenotype.[6,7]

Figure 1 shows a CCTA of a coronary segment with HRP characteristics (low attenuation plaque, napkin rink sign and spotty calcification) and an example of quantitative analysis of plaque and highly inflamed pericoronary fat.

PCAT, CAD, and plaque vulnerability

PCAT attenuation around the right coronary artery (RCA) is the most validated measurement site and demonstrates graded increases across the spectrum of CAD severity. Patients with myocardial infarction consistently exhibit higher PCAT attenuation than those with stable CAD, and both exceed values observed in individuals without CAD.

In CRISP-CT ($n = 3912$), FAI > −70.1 HU was strongly associated with cardiac mortality and improved risk prediction beyond established clinical algorithms.[8]

PCAT attenuation correlates tightly with non-calcified and low-attenuation plaque—key substrates of acute coronary syndromes—while showing minimal association with extensively calcified plaque, which generally reflects a more stable phenotype.[7]

PCAT also appears responsive to therapeutic modulation. Statin therapy has been associated with favourable changes in PCAT characteristics, though effects of emerging anti-inflammatory agents remain under investigation.[8,9]

PCAT in non-coronary cardiovascular disease

Emerging evidence implicates PCAT in disease processes beyond CAD. In atrial fibrillation (AF), inflammatory and adipose infiltration within epicardial fat contribute to atrial fibrosis and arrhythmogenic substrate formation. PCAT attenuation independently predicts AF recurrence following catheter ablation.[10,11]

In heart failure—particularly heart failure with preserved ejection fraction—epicardial fat may exert mechanical constraint on the left ventricle and promote neurohormonal activation. Preclinical studies suggest that dysfunctional perivascular adipose tissue loses vasodilatory and anti-contractile properties, though PCAT itself has not yet been systematically evaluated across heart failure phenotypes.

Evaluation of PCAT

Cardiac CT is currently the only validated non-invasive modality capable of accurately quantifying PCAT. Adipose tissue typically ranges from −190 to −30 HU; less negative values indicate smaller adipocytes and heightened inflammatory activity. Although PCAT and total epicardial fat volume are correlated, PCAT shows the strongest association with coronary plaque burden, consistent with its intimate anatomical relationship to the arterial wall.[6]

However, heterogeneity in PCAT definitions, segmentation approaches, and analytic methods remains substantial. Most studies define PCAT as adipose tissue within a radial distance equal to the vessel diameter, typically measured along a 40-mm segment of the proximal RCA. Standardized protocols are not yet established.

Factors influencing PCAT measurement

a. Technical parameters

PCAT attenuation is sensitive to CT acquisition parameters, particularly tube voltage, reconstruction kernel, and scanner model. Variations in tube voltage alone can shift attenuation values by >10 HU. Although observer reproducibility is generally good, formal test–retest reliability studies are lacking. Image

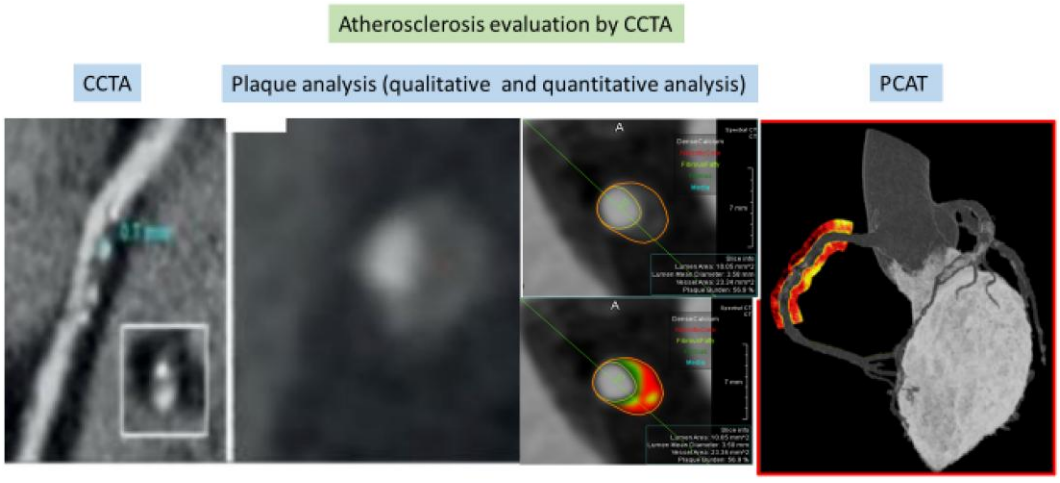

Figure 1 Coronary computed tomography angiography (CCTA) showing a coronary artery segment with multiple high-risk plaque features, including low-attenuation plaque, the napkin-ring sign, and spotty calcifications. The panel also illustrates an example of quantitative plaque assessment and pericoronary adipose tissue (PCAT) analysis, demonstrating markedly inflamed pericoronary fat surrounding the diseased vessel segment.

Table 1 Factors influencing PCAT measurement

Factor	Summary description	Implications for measurement
Technical parameters	Beam energy; reconstruction algorithm; scanner model; tube voltage; differences in software; body habitus; image quality and artifacts (partial-volume effects, motion, calcifications).	Potential alterations exceeding 10 HU; risk of poor reproducibility; possible overestimation or underestimation of inflammation; need for standardized protocols and thin-slice reconstructions.
Measurement site	Variability depending on the vessel assessed; the RCA provides the most stable site and has the greatest adipose volume, whereas LAD and LCx measurements may be less reliable.	RCA PCAT is predictive of cardiovascular events; measurement in a single vessel may not capture overall coronary inflammation; potential failure to detect stenotic segments in other territories.
Impact of plaque	Higher PCAT in the presence of non-calcified or mixed plaque; no correlation with calcified plaque. Variability stems from the dynamic nature of both pericoronary adipose tissue and plaque.	Suggests plaque vulnerability rather than stable disease; possible test–retest variability; discrimination may improve with advanced radiomics techniques (still experimental).

quality, patient habitus, motion artefacts, and coronary calcifications further influence accuracy.[12]

b. Measurement location

Anatomic site markedly affects PCAT values. The proximal RCA provides reproducible measurements due to consistent anatomy and substantial surrounding adipose tissue. RCA-based PCAT has demonstrated stronger associations with myocardial infarction and mortality relative to LAD or LCx, though findings vary across studies and software platforms.[8]

c. Influence of plaque

PCAT attenuation is consistently higher adjacent to non-calcified or mixed plaques and correlates poorly with heavily calcified lesions. This supports PCAT as a biomarker of active inflammation rather than chronic plaque stabilization. Physiological variability and dynamic adipose–plaque interactions may limit reproducibility in serial assessments.[6,8]

Table 1 summarizes the main factors that influence the measurement of PCAT.

FAI and CaRi-heart: clinical translation

The Fat Attenuation Index (FAI) quantifies perivascular inflammation by characterizing spatial changes in adipose tissue attenuation. Because inflammatory remodelling alters adipocyte density and morphology, FAI provides a sensitive surrogate of vascular inflammatory activity independent of stenosis severity or the presence of obstructive CAD.[13]

CaRi-Heart, an AI-supported platform, integrates FAI measurements with demographic, clinical, and plaque-based information to generate individualized estimates of fatal cardiac risk. Trained on large international datasets, CaRi-Heart offers harmonized FAI scoring and personalized nomograms that enable more accurate risk reclassification and inform early, targeted management—including anti-inflammatory strategies where appropriate.

Conclusions

PCAT attenuation is an emerging imaging biomarker with significant potential to identify residual inflammatory risk and bridge the gap between subclinical inflammation and clinical atherosclerotic disease. Detecting elevated PCAT attenuation in patients without obstructive CAD may allow earlier initiation of targeted medical therapy and support the identification of high-risk subgroups for future trials involving anti-inflammatory agents such as canakinumab or colchicine.[14–16]

However, widespread clinical adoption requires standardized quantification protocols, prospective validation of reproducibility, and clear consensus on optimal measurement sites. The mechanistic link between inflammation and PCAT attenuation, although biologically plausible, warrants confirmation through prospective imaging–histopathology studies and integration with circulating inflammatory biomarkers.

PCAT represents one of the most promising non-invasive biomarkers of coronary inflammation available through CCTA. By merging biological and morphological insights, PCAT offers a path towards increasingly personalized cardiovascular risk assessment, pending further prospective validation.

Funding

No funding.

Conflict of interest: None declared.

Data availability

No new data were generated or analysed in support of this research.

Disclaimer

This paper was originally published in the Italian language as ‘Nuovo fattore di rischio e surrogato clinico: il grasso epicardico’, in the Volume degli Atti del Congresso “Conoscere e Cuare il Cuore 2026”, published by Centro per la Lotta contro l’Infarto for distribution at the CCC Conference. This paper was translated by Dr. Mario Albertucci, representative of the CLI Foundation, and republished with permission.

References

1. Stone GW, Maehara A, Lansky AJ, de Bruyne B, Cristea E, Mintz GS *et al.* A prospective natural-history study of coronary atherosclerosis. *N Engl J Med* 2011;**364**:226–235.
2. Papadopoulou S-L, Neefjes LA, Garcia-Garcia HM, Flu W-J, Rossi A, Dharampal AS *et al.* Natural history of coronary atherosclerosis by multislice computed tomography. *JACC Cardiovasc Imaging* 2012;**5**:S28–S37.
3. Al Rifai M, Ahmed AI, Alahdab F, Al-Mallah MH. Clinical utility of coronary artery computed tomography angiography-what we know and What’s new? *Prog Cardiovasc Dis* 2022;**75**:12–20.
4. Yamaji K, Kanenawa K, Morofuji T, Nishikawa R, Imada K, Kohjitani H *et al.* Serial optical coherence tomography assessment of coronary atherosclerosis and long-term clinical outcomes. *J Am Heart Assoc* 2024;**13**:e034458.
5. Dawson LP, Lum M, Nerleker N, Nicholls SJ, Layland J. Coronary atherosclerotic plaque regression: JACC state-of-the-art review. *J Am Coll Cardiol* 2022;**79**:66–82.
6. Antonopoulos AS, Sanna F, Sabharwal N, Thomas S, Oikonomou EK, Herdman L *et al.* Detecting human coronary inflammation by imaging perivascular fat. *Sci Transl Med* 2017;**9**:eaal2658.
7. Williams MC, Kwiecinski J, Doris M, McElhinney P, D’Souza MS, Cadet S *et al.* Low-attenuation noncalcified plaque on coronary computed tomography angiography predicts myocardial infarction: results from the multicenter SCOT-HEART trial (Scottish computed tomography of the HEART). *Circulation* 2020;**141**:1452–1462.
8. Oikonomou EK, Marwan M, Desai MY, Mancio J, Alashi A, Hutt Centeno E *et al.* Non-invasive detection of coronary inflammation using computed tomography and prediction of residual cardiovascular risk (the CRISP CT study): a post-hoc analysis of prospective outcome data. *Lancet* 2018;**392**:929–939.
9. Williams MC, Moss AJ, Dweck M, Adamson PD, Alam S, Hunter A *et al.* Coronary artery plaque characteristics associated with adverse outcomes in the SCOT-HEART study. *J Am Coll Cardiol* 2019;**73**:291–301.
10. Venteclef N, Guglielmi V, Balse E, Gaborit B, Cotillard A, Atassi F *et al.* Human epicardial adipose tissue induces fibrosis of the atrial myocardium through the secretion of adipo-fibrokines. *Eur Heart J* 2015;**36**:795–805a.
11. Nerlekar N, Muthalaly RG, Wong N, Thakur U, Wong DTL, Brown AJ *et al.* Association of volumetric epicardial adipose tissue quantification and cardiac structure and function. *J Am Heart Assoc* 2018;**7**:e009975.
12. Ma R, Ties D, Van Assen M, Pelgrim GJ, Sidorenkov G, van Ooijen PMA *et al.* Towards reference values of pericoronary adipose tissue attenuation: impact of coronary artery and tube voltage in coronary computed tomography angiography. *Eur Radiol* 2020;**30**:6838–6846.
13. Matyas B, Benedek I, Rat N, Blindu E, Gerculy R, Rosca A *et al.* Redefining cardiovascular risk evaluation: employing the CaRi-Heart validated FAI-score in patients screened with SCORE2 and CAD-RADS 2.0 techniques. *Eur Heart J* 2024;**45**:ehae666.171.
14. Budoff MJ, Bhatt DL, Kinninger A, Lakshmanan S, Muhlestein JB, Le VT *et al.* Effect of icosapent ethyl on progression of coronary atherosclerosis in patients with elevated triglycerides on statin therapy: final results of the EVAPORATE trial. *Eur Heart J* 2020;**41**:3925–3932.
15. Perez de Isla L, Diaz-Diaz JL, Romero MJ, Muñiz-Grijalvo O, Mediavilla JD, Argüeso R *et al.* Alirocumab and coronary atherosclerosis in asymptomatic patients with familial hypercholesterolemia: the ARCHITECT study. *Circulation* 2023;**147**:1436–1443.
16. Fiolet ATL, Lin A, Kwiecinski J, Tutein Nolthenius J, McElhinney P, Grodecki K *et al.* Low-dose colchicine on pericoronary inflammation and coronary plaque composition in chronic coronary disease: a subanalysis of the LoDoCo2 trial. *Heart* 2025;**111**:1156–1163.