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EDITORIAL

Computed tomography angiography-derived microvascular resistance: is less always more?

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Approximately 40% of patients with non-obstructive epicardial coronary artery disease (CAD) present with associated coronary microvascular dysfunction (CMD) and/or coronary vasospasm[1]. Despite its high prevalence and clinical relevance, this condition remains largely underdiagnosed, with affected patients experiencing impaired quality of life, recurrent hospitalisations, and adverse cardiovascular outcomes. According to the latest European Society of Cardiology (ESC) Guidelines on chronic coronary syndromes (CCS), the comprehensive evaluation of patients with angina/ischaemia and non-obstructive coronary arteries (ANOCA/INOCA) requires invasive coronary angiography (ICA) with direct haemodynamic assessment – using thermodilution or Doppler techniques – and pharmacological vasomotor testing[2]. Non-invasive diagnostic modalities may also aid in identifying ANOCA/INOCA through the measurement of coronary flow reserve (CFR); however, these approaches require the prior exclusion of obstructive epicardial CAD[2]. Consequently, a substantial unmet diagnostic need persists in the non-invasive evaluation of CMD.

Coronary computed tomography (CT) angiography (CCTA) is a practical, widely available non-invasive modality for the exclusion of epicardial CAD. The integration of CCTA-derived fractional flow reserve (FFR) has further enhanced its diagnostic specificity and physiological interpretability[3]. Nevertheless, whether CCTA – alone or supplemented by additional functional assessment – can reliably identify CMD in a fully non-invasive manner remains an open and clinically relevant question.

In this issue of EuroIntervention, Deng et al report the validation of a non-invasive index of microvascular resistance (IMR) derived from CCTA, referred to as IMR_{CT}[4]. The study analysed 216 vessels from 176 patients, demonstrating a strong correlation between IMR_{CT} and invasively measured IMR (r=0.71, 95% confidence interval: 0.62-0.76; p<0.001) and an overall diagnostic accuracy of approximately 80% at both the vessel and patient levels. A discordance rate of 18.1% was observed between invasive and CCTA-derived IMR values when using the standard threshold of 25. The calculation of IMR_{CT} relies on a vascular deformation-based flow estimation approach, where changes in vessel geometry during the cardiac cycle are used to estimate resting coronary blood flow (CBF). By adjusting boundary conditions, resting CBF is scaled to represent hyperaemic flow, which is then incorporated into computational fluid dynamics simulations to derive IMR_{CT}.

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The authors should be commended for conducting this important external validation study of IMR_{CT}; this work represents an important step toward the CT-based physiological assessment of CMD, expanding the diagnostic potential of non-invasive coronary imaging.

However, several aspects of the study warrant further discussion. First, an intrinsic limitation of the method lies in the use of bolus thermodilution as the reference technique. Because the proposed approach relies on CBF estimation from CCTA, the use of mean transit time as a surrogate for flow may have introduced a degree of variability. In this context, continuous thermodilution might have provided more precise and reproducible data[5,6]. In addition, changes in boundary conditions during the computational modelling process may

further contribute to variability in CBF estimation and, consequently, in IMR_{CT} calculation[7].

Second, the method defines CMD solely on the basis of IMR, which reflects hyperaemic microvascular resistance and therefore overlooks the CFR component that is central to the diagnostic framework for CMD assessment, and currently captures only the structural and resistance-related components of microvascular dysfunction. The microvascular resistance reserve (MRR) represents an index specifically targeted to microvascular resistance, independent of epicardial stenosis, and thus expresses the true vasodilatory capacity of the coronary microcirculation[8]. Incorporating CT-derived physiological tools capable of estimating this index could further enhance the diagnostic performance of CCTA in CMD detection.

Third, it should be acknowledged that vasoreactivity cannot be estimated from CT-based techniques, which is a crucial component of the comprehensive CMD diagnostic algorithm for identifying vasospastic and endothelial dysfunction-related phenotypes[2].

Finally, CT-derived morphological characteristics can complement CT-derived physiological metrics in the detection of CMD. Previous CCTA-based studies have demonstrated that patients with CMD tend to exhibit smaller epicardial vessels and a lower coronary volume-to-myocardial mass ratio, primarily due to a significant reduction in total coronary vessel volume[9]. These structural alterations limit the capacity of the coronary vasculature to meet myocardial metabolic demand. This important aspect was not considered in the present analysis, although integrating morphological and physiological CT-derived data could enhance the accuracy and pathophysiological insight of CMD assessment.

Considering the above-mentioned issues, it is evident that we are still far from adopting CT as a standalone diagnostic tool for CMD. Nonetheless, there remains considerable potential for CT-derived microvascular assessment. The key question to ask is what we should expect from such a tool. To address this, it is useful to recall the evolution and clinical impact of CCTA and CT-derived FFR (FFR_{CT}) in the assessment of CAD. In a large, nationwide investigation evaluating the impact of FFR_{CT} on the United Kingdom's healthcare system, adding FFR_{CT} to CCTA resulted in a relative reduction of 14% in cardiovascular mortality and of 8% in all-cause mortality, with a parallel 5% reduction in ICA, while percutaneous coronary interventions increased by up to 8%[10].

Translating these findings to CT-derived microvascular assessment, such a tool should be viewed as a screening modality complementary to ICA and invasive functional testing, which remain the cornerstone of the ANOCA/INOCA diagnostic algorithm. Consequently, a screening test should prioritise sensitivity over specificity, since confirmatory invasive testing inherently provides higher diagnostic specificity. With a patient-level sensitivity of 81.5% and specificity of 80.2%, IMR_{CT} may represent a promising non-invasive screening approach for identifying patients who would benefit from further invasive investigation for CMD, particularly given its potential to provide a comprehensive evaluation of all coronary arteries.

Nevertheless, larger, multicentre validation studies are warranted, as the relatively small proportion of patients with CMD in the current cohort (5.1% with structural CMD, 4.5% with functional CMD, and 23% with isolated IMR elevation) may have led to a modest overestimation of diagnostic performance.

The bottom line is that CCTA is rapidly evolving; computational fluid dynamics and post-processing algorithms are progressively enabling comprehensive functional assessment of both the macro- and microcirculation. Whether therapeutic decisions should rely solely on CT-derived physiological metrics remains uncertain, but CCTA-based physiology may soon serve as a first-line screening strategy to more effectively identify patients who are likely to benefit from targeted invasive investigation.

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Conflict of interest statement

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