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Editorial

Redefining cardiovascular risk stratification: The evolving role of coronary CTA

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ABSTRACT

Coronary computed tomography angiography (CCTA) has evolved far beyond its initial role as an anatomical imaging modality. Today, it serves as a versatile, multiparametric tool for cardiovascular risk assessment. This progress has been driven by advances in plaque characterization, non-invasive functional assessment, coronary inflammation imaging, and artificial intelligence (AI). CCTA enables clinicians not only to detect obstructive coronary artery disease but also to evaluate total plaque burden and high-risk plaque characteristics, such as low-attenuation components and positive remodeling. The addition of fractional flow reserve derived from CCTA (FFR-CT) offers myocardial ischemia assessment without the need for invasive testing. More recently, the perivascular fat attenuation index (FAI) has emerged as a promising marker of coronary inflammation, highlighting patients who may have residual inflammatory risk despite non-obstructive disease. AI-driven tools, including models like AI-QCTISCHEMIA, now allow for automated and accurate plaque analysis and ischemia prediction. The advent of photon-counting detector CT (PCD-CT) complements these advancements by improving spatial resolution and visualization of vulnerable plaque. These developments are reshaping the role of CCTA in clinical practice—from a diagnostic test to an integrated platform for individualized cardiovascular prevention and management.

Over the last decade, coronary computed tomography angiography (CCTA) has progressed from a method primarily used to exclude obstructive coronary artery disease (CAD) into a versatile imaging modality that informs comprehensive cardiovascular risk assessment.[1,2] Clinicians have increasingly shifted from focusing solely on luminal narrowing to considering the underlying biology of atherosclerosis and the broader implications of coronary plaque behavior.

This progression has been driven by a confluence of innovations. Advances in plaque characterization, developments in non-invasive functional imaging, the ability to visualize coronary inflammation, and the integration of artificial intelligence (AI) have collectively redefined what CCTA can offer in clinical practice.[1] These tools have positioned CCTA as more than just a diagnostic test; it now serves as an integrative modality for risk stratification and preventive planning.

Beyond Narrowing: Quantifying Plaque Burden and Vulnerability

A foundational advancement was the ability of CCTA to visualize and characterize coronary atherosclerotic plaque beyond simple stenosis measurement.[3] Growing evidence shows that luminal narrowing is an incomplete and often insufficient surrogate for cardiovascular risk.[4] The SCOT-HEART trial was instrumental in supporting this paradigm shift. In its five-year follow-up, clinicians who received CCTA data, particularly regarding non-obstructive disease, were more likely to initiate appropriate preventive therapies, resulting in a significant reduction in coronary death and non-fatal myocardial infarction.[5]

The concept of high-risk plaque (HRP) has emerged from such studies. CCTA can identify HRP features such as low-attenuation plaque (LAP), positive remodeling, and spotty calcification, which are linked to vulnerable plaque biology.[6] In SCOT-HEART, patients exhibiting HRP features had a threefold increased risk of coronary death or myocardial infarction, independent of clinical risk factors. Notably, those with both obstructive lesions and HRP features had over a tenfold increase in event rates compared to individuals with normal arteries.[7]

Extending Insight: Hemodynamic and Inflammatory Evaluation

A. Hemodynamic Assessment with FFR-CT

While anatomical information remains essential, it does not always capture the physiological significance of a coronary lesion. The development of fractional flow reserve derived from CCTA (FFR-CT) addressed this limitation of anatomical imaging by enabling assessment of myocardial ischemia. Using computational fluid dynamics applied to standard CCTA datasets, FFR-CT non-invasively calculates pressure gradients across coronary lesions, with values of 0.80 or lower indicating significant ischemia.[8]

The PLATFORM trial provided early clinical validation of this approach. Among patients referred for invasive coronary angiography (ICA), a diagnostic strategy combining CCTA with FFR-CT significantly reduced the proportion of patients undergoing ICA without obstructive disease, from 73% to 12% , without compromising outcomes.[9] The ADVANCE registry further supported these findings, demonstrating that patients with negative FFR-CT results had very low event rates and rarely required revascularization.[10] Collectively, these studies have established

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FFR-CT as a valuable tool for guiding decisions regarding invasive evaluation and intervention.

B. Imaging Coronary Inflammation: Perivascular Fat Attenuation Indeks

One of the most notable recent advancements in coronary imaging is the ability to non-invasively assess vascular inflammation, a critical contributor to plaque destabilization and rupture. The perivascular fat attenuation index (FAI) serves as a novel biomarker that captures inflammation-induced changes in the adipose tissue surrounding coronary arteries, based on the principle that inflamed vessels influence the phenotype of adjacent perivascular fat through paracrine signaling.[11]

The prognostic value of FAI was highlighted by the CRISP-CT study, which included nearly 4,000 patients and demonstrated that elevated FAI levels were independently associated with a markedly increased risk of fatal cardiovascular events. Notably, this association was independent of traditional risk factors, coronary calcium burden, luminal stenosis, and even high-risk plaque characteristics. These findings suggest that FAI reflects a unique and biologically active axis of risk not captured by conventional imaging parameters. By enabling the identification of patients with residual inflammatory risk, FAI has introduced a new dimension to personalized cardiovascular risk assessment and holds promise in guiding future anti-inflammatory therapeutic strategies.[11]

The Role of Artificial Intelligence in Modern CCTA

The ability to integrate and interpret multiparametric data from CCTA has been made possible by advances in artificial intelligence. AI tools now provide automated quantification of plaque characteristics and coronary stenosis, with AI-guided quantitative CT (AI-QCT) achieving diagnostic accuracy comparable to expert readers and invasive modalities such as intravascular ultrasound.[12] Automation has reduced the time and labor involved in CCTA interpretation, making comprehensive analysis feasible in routine clinical workflows.[13]

Importantly, AI models are not limited to automation but increasingly support advanced diagnostic capabilities in cardiovascular imaging. One example is AI-QCT$_{ISCHEMIA}$, an FDA-approved AI-based algorithm that integrates a comprehensive set of quantitative features, including plaque characteristics, stenosis severity, and vascular morphology, derived from CCTA to predict myocardial ischemia. It has demonstrated diagnostic performance equivalent to, or exceeding, that of FFR-CT in identifying functionally significant CAD.[14] Its clinical integration marks a pivotal step toward broader implementation of AI-guided, CCTA-based strategies for non-invasive ischemia assessment.

A Technological Leap Forward: Photon-Counting CT

Advances in CT scanner hardware are also contributing to the growing clinical value of CCTA. Photon-counting detector CT (PCD-CT) introduces higher spatial resolution and spectral imaging capabilities. This enables more precise assessment of plaque morphology, reduces artifacts such as calcium blooming, and improves reproducibility in evaluating LAP and other HRP features.[15] When paired with AI analytics, PCD-CT may further improve the identification of rupture-prone plaques, such as thin-cap fibroatheromas, marking a potential breakthrough in preemptive cardiovascular care.

Conclusion

The role of CCTA has evolved from an anatomical diagnostic tool to a central pillar in personalized cardiovascular prevention. Its ability to characterize plaque burden and morphology, assess physiological significance, visualize vascular inflammation, and incorporate AI-based analysis has redefined its clinical utility as an integrative imaging modality.

This evolution supports a new approach to cardiovascular care, one that moves from reactive management of events to proactive, individualized strategies guided by detailed imaging biomarkers. CCTA now enables clinicians to evaluate not only coronary anatomy but also the biological and functional aspects of atherosclerotic disease. As a result, CCTA is emerging not only as a diagnostic modality but also as a prognostic tool, capable of guiding targeted preventive strategies and influencing long-term cardiovascular outcomes.

Conflict of Interest

There is no conflict of interest.

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