PERSPECTIVE PEER REVIEWED

New imaging modalities in coronary artery disease

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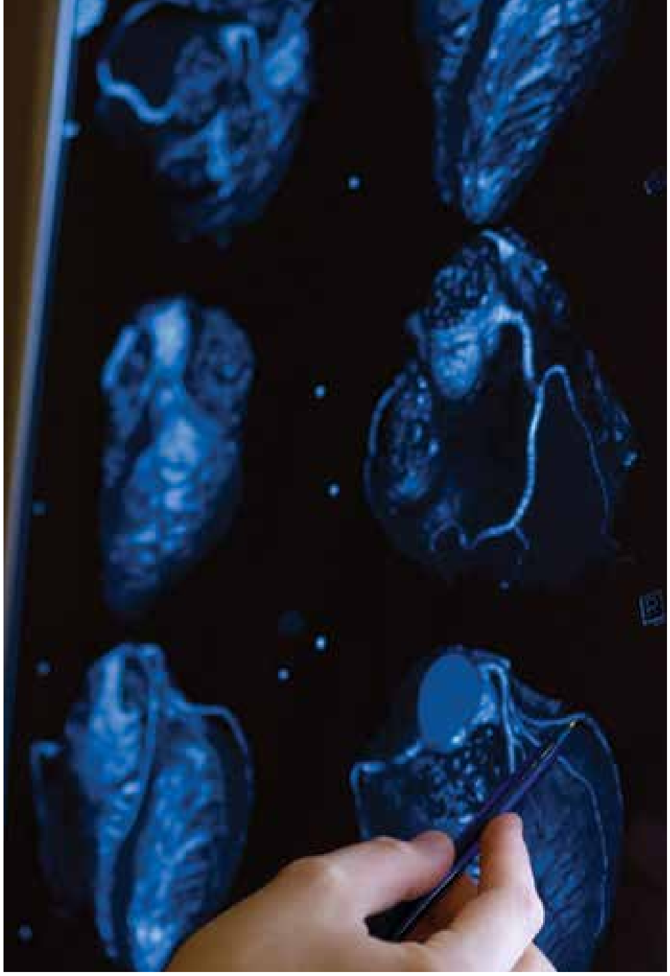
Cardiac imaging remains one of the most powerful tools in the diagnosis and management of coronary artery disease. Novel imaging modalities are expected to further enhance diagnosis and treatment of coronary atherosclerosis.



Key points

- **There is a growing focus on characterising coronary lesions beyond angiographic features.**
- **Coronary computed tomographic angiography is a noninvasive imaging technique traditionally used to identify anatomically significant coronary lesions and coronary anatomy before surgical intervention.**
- **Advances in catheter-based intracoronary imaging techniques now offer unprecedented views of coronary anatomy and pathology.**
- **Optical coherence tomography has provided a deeper understanding of plaque morphology, progression of atherosclerosis and poststenting outcomes.**

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Over the past several decades, the advent of cardiac imaging has greatly changed the diagnosis and management of patients with ischaemic heart disease. Generally, there is growing focus on characterising coronary lesions beyond angiographic features. For example, innovative advances in noninvasive modalities are increasingly being used to better delineate functionally, rather than only anatomically, significant coronary lesions. Similarly, concurrent developments in invasive imaging now provide an unprecedented view of coronary plaques, with the potential to identify disease at earlier stages and improve preventive management.

In this brief review, we provide a glimpse of novel invasive and noninvasive imaging techniques as they transition into the clinical realm. It is important for GPs to be aware of these emerging modalities, particularly their roles in diagnosis and implications for the long-term management of patients with coronary artery disease (CAD).

Coronary lesions: anatomical versus functional significance

Traditionally, coronary imaging by invasive angiography has relied on the operator's visual assessment of atherosclerotic lesions. Although this approach has been moderately successful, visual estimation of the degree of stenosis may be unreliable, particularly in the evaluation of intermediate lesions (50 to 70% stenosis). An accurate estimation is important because the decision to proceed with angioplasty or stenting often hinges on a percent diameter stenosis (%DS) of more than 70%.

Furthermore, anatomical measures (such as %DS) have also been shown to correlate poorly with functionally significant stenosis – that is, a flow obstruction that results in myocardial ischaemia.[1] This is partly due to the fact that standard x-ray angiography provides a two-dimensional image of a complex three-dimensional lesion. Therefore, a lesion that appears significant from one angle may not actually cause myocardial ischaemia; the reverse may also be true in some cases, hence the interest in identifying functionally significant coronary obstructions.

Fractional flow reserve (FFR) is the gold standard technique to identify functionally significant lesions. This invasive catheter-based technique involves measuring coronary blood pressure proximal and distal to a stenosis at baseline and during induced hyperaemia (stress conditions). In a healthy artery without stenosis, the ratio of distal to proximal pressure (Pd/Pa) should be one. However, in an artery with stenosis, distal blood pressure decreases; an FFR value (Pd/Pa) of 0.8 or less is the generally accepted cut-off value for significant lesions and, therefore, for intervention.

Although FFR-guided intervention has been definitively shown to improve outcomes, it is an invasive procedure that carries a small, but real, procedural risk and also an economic cost. Innovations in noninvasive imaging are bringing 'virtually-derived' FFR into the clinical domain, and have the potential to alter the landscape of diagnosing CAD.

Noninvasive imaging to identify functionally significant lesions

Coronary computed tomographic angiography

In addition to a detailed history and physical examination, an electrocardiogram and echocardiogram coupled with physiological testing still form the basis for assessment of patients with ischaemic heart disease. However, emerging noninvasive imaging modalities such as coronary computed tomographic angiography (CCTA) are transforming the accuracy and precision of diagnosing significant atherosclerotic lesions.

CCTA is a noninvasive imaging technique that has traditionally been used to identify anatomically significant coronary lesions and coronary anatomy before surgical intervention. The most widely available 64-slice CT scanners have a spatial resolution of about 600 μm. Although this resolution is not nearly as good as invasive imaging modalities (as discussed below), it allows relatively accurate noninvasive assessments of plaque morphology in addition to luminal imaging in appropriately selected patients (Figure 1). The development of the 320-slice and 640-slice CT scanners means patients are exposed to a lower total amount of radiation, but these machines are not yet widely available.

Further recent advances in CCTA methods include dual-energy CT imaging and the noninvasive assessment of FFR.

Fractional flow reserve CT

Briefly, FFR-CT results are computationally derived by solving fluid dynamic equations governing the flow of blood in three-dimensional reconstructions of the patient's coronary arteries. One strength of this method is that it does not require additional imaging, radiation, contrast or medications beyond standard CCTA protocols. Seminal studies such as the Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve (DISCOVER-FLOW) study[2] and the Determination of Fractional Flow Reserve by Anatomic Computed Tomographic Angiography (DeFACTO) trial have demonstrated improved diagnostic accuracy, sensitivity and specificity of FFR-CT for functionally significant coronary lesions compared with CCTA alone.[2,3] The computational nature of FFR-CT requires certain assumptions to be made in order to solve the equations governing fluid motion, but it is expected that methodological refinements will continue to improve the accuracy of FFR-CT. Additionally, FFR-CT was recently approved for clinical use by the US Food and Drug Administration and its availability is likely to increase.

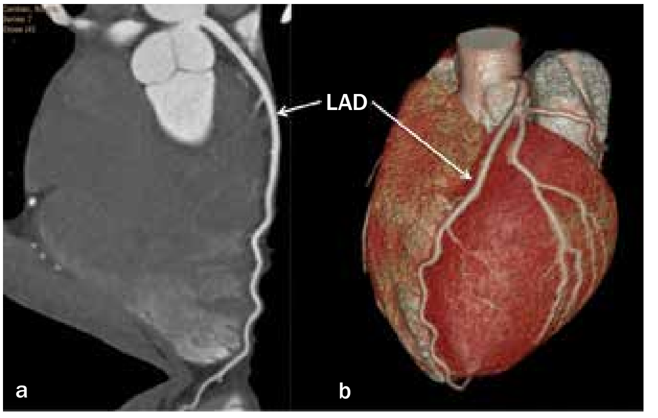

Figure 1. A 45-year-old man with a history of hypertension and smoking presented with exertional chest pain. During exercise stress testing, he experienced chest pain but ECG was equivocal. Stress echocardiography was similarly nondiagnostic as target heart rate was not achieved. The patient therefore had a coronary computed tomographic angiography (CCTA) that showed no coronary lesions. (a, left). CCTA image showing the left anterior descending (LAD) coronary artery free of stenosis. (b, right). Three-dimensional reconstruction of the CCTA.

Dual-energy CT

Dual-energy CT (DECT) is another recent advance in CCTA modalities. DECT relies on the observation that additional information can be gathered from integrating the differential tissue and contrast penetration patterns of high- and low-energy x-ray frequencies. This information has been used to map the tissue distribution of iodinated contrast through the cardiac cycle, thus providing myocardial perfusion assessment on par with single positron emission CT and MRI perfusion imaging.[4,5] Early clinical studies utilising DECT have been promising, but larger randomised trials are needed before widespread clinical uptake is possible.

Ultimately, legitimate concerns about radiation and false-positive results persist. Therefore, in all likelihood, the main use of CCTA modalities will remain the ruling out of disease in stable patients with a low to intermediate pre-test probability of CAD or in patients with a sufficiently unclear or conflicting presentation. CCTA

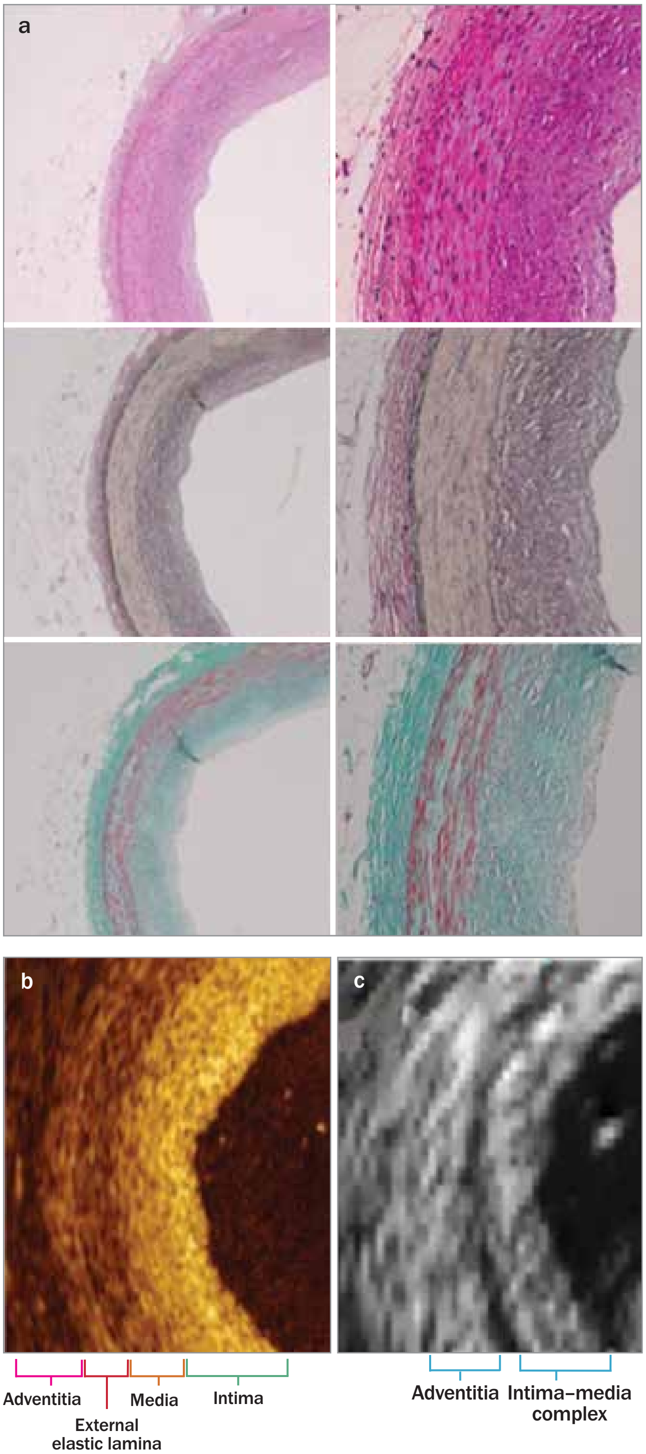

Figure 2. With a resolution 10-fold greater than ultrasound, optical coherence tomography (OCT) permits detailed interrogation of the superficial coronary artery wall. (a, top six images). Histological staining of the coronary artery (three different stains shown). (b, bottom left). OCT of a section demonstrating near-histological distinction of arterial wall tissue layers. (c, bottom right). The same coronary segment visualised by intravascular ultrasound.

modalities are generally not appropriate in patients with a high pre-test probability of CAD – that is, those with a clear presentation of stable cardiac ischaemia, acute coronary syndrome or ST-elevation myocardial infarction.

Invasive imaging to characterise plaque morphology and stent positioning

Although coronary angiography remains the gold standard invasive imaging modality in interventional cardiology, advances in catheter-based intra-coronary imaging techniques now offer unprecedented views of coronary anatomy and pathology. This, therefore, allows for new possibilities in diagnosis and treatment.

Intravascular ultrasound

Intravascular ultrasound (IVUS) utilises a catheter-based probe that emits ultrasound frequencies and detects scattered signals, which are then processed into two-dimensional cross-sectional images of the arterial lumen and wall. IVUS has a maximum optical resolution of 100 to 150 μm and an axial penetration depth of up to 8 mm. IVUS has been used clinically and in research settings to detect atherosclerotic plaques and arterial wall pathology.

Optical coherence tomography

Optical coherence tomography (OCT), a more recently developed light-based analogue of IVUS, offers a resolution one order of magnitude higher than IVUS (10 to 15 μm) at the expense of a limited axial depth penetration of 2 to 3 mm. So, although IVUS provides visualisation of deeper wall pathology, OCT provides superior lumen and intimal assessment (Figure 2). OCT has an excellent safety profile and has been histologically validated. Since its introduction into clinical and research practice, OCT has provided a deeper understanding of plaque morphology, progression of atherosclerosis and poststenting outcomes.

OCT can be used to accurately delineate plaque morphology by identifying various components of atheromas, including lipid and macrophage-rich collections, fibrous tissue, calcium and necrotic areas (Figure 3).[6] Depending on the overall composition and morphology, plaques can be characterised as having a low or high risk of rupture. Most significantly, OCT-derived plaque morphology is increasingly viewed as a possible surrogate marker of disease progression and overall risk of future cardiovascular events. If validated, lesion morphology may improve risk stratification and further inform general patient management strategies.

OCT can also be used to visualise acute thrombus, thereby aiding the interventionalist in optimising the lesion before stent placement. A recent study of patients presenting with acute coronary syndrome showed that certain patients with large thrombus burden as detected by OCT benefited from deferred stenting and continued thrombolytic therapy.[7] In a significant proportion of these patients (38%), stenting was altogether unnecessary after successful thrombolytic therapy. This is a highly significant finding, as avoidance of stenting abrogates the need for antiplatelet therapy and eliminates the risk of potentially catastrophic events such as stent thrombosis.

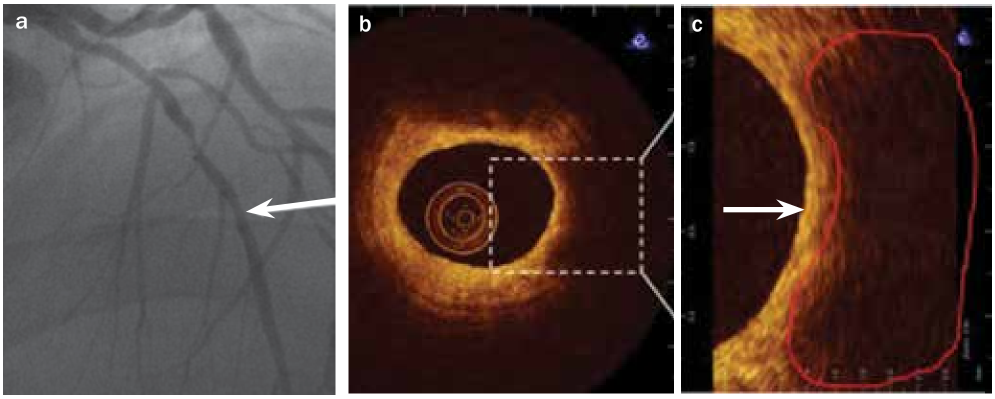

Figure 3. Optical coherence tomography (OCT) is used to identify a thin-cap fibroatheroma (TCFA), a high-risk plaque vulnerable to rupture. (a, left). Standard coronary angiography shows a visually insignificant, slight narrowing of the artery (arrow). (b, middle). OCT imaging of this region identifies a high-risk TCFA. (c, right). A close view of this plaque demonstrates a thin fibrous cap (arrow) and an underlying lucent area consistent with a lipid-rich atheroma.

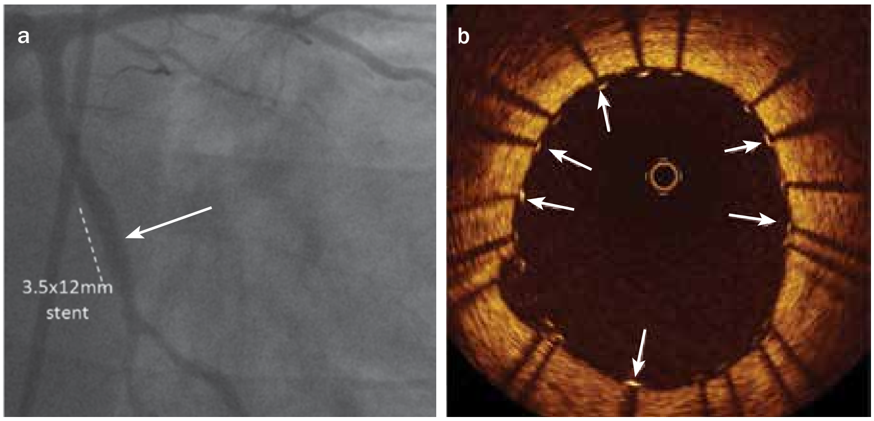

Figure 4. Angiography and optical coherence tomography (OCT) show a stent deployed within an artery. (a, left). Angiographic result following implantation of a stent in the left circumflex artery (arrow). (b, right). OCT imaging of the stented segment showed that stent struts (arrows) were well-apposed to the vessel wall. In cases of stent malapposition detected by OCT, interventionalists can redilate the stent to reduce malapposition.

In patients requiring stent placement, OCT has also been used to assess the quality of stent deployment, as inadequately positioned stents have been associated with late stent failure.[8] For instance, OCT is used to identify stent malapposition, in which stent struts are not in contact with the vessel wall, a feature that may predispose to stent thrombosis (Figure 4). Evidence continues to mount suggesting that OCT-guided intervention improves overall outcomes for patients compared with standard x-ray angiography-based intervention.[9]

Conclusion

Novel coronary imaging modalities serve as the basis for increasingly versatile techniques in the diagnosis of anatomically and functionally significant CAD. CCTA and techniques such as FFR-CT are promising avenues for noninvasive diagnosis of coronary disease when applied to the appropriate patient in the appropriate clinical setting. OCT represents a vast leap forward in intracoronary imaging due to its high resolution, and is expected to play a larger role not only in the diagnosis and prognostication of CAD, but also optimisation of procedural results and poststenting outcomes. **CT**

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COMPETING INTERESTS: None.