Diagnostic coronary angiography: past, present and future

Since its introduction, diagnostic coronary angiography has been considered the gold standard for detecting coronary artery stenosis and offers direct and immediate progression to percutaneous coronary intervention. Because drug-eluting stents are costly and associated with rare but significant late complications their appropriate use is vital. However, the two-dimensional nature of fluoroscopic imaging means that visual estimation of lesion severity can be inaccurate and poorly reproducible, particularly in moderate lesions (Fischer et al, 2002). Confounding factors limiting accuracy include vessel tortuosity, overlap of structures and the effects of lumen shape, while after intervention, a hazy broadened silhouette may overestimate the actual gain in lumen size (Topol and Nissen, 1995). The introduction of fractional flow reserve and intracoronary imaging tools has helped to offset these limitations and allowed a detailed, objective appreciation of disease significance and morphology.

The past

Although cardiac catheterization was being used to measure cardiac haemodynamics throughout the 1940s, diagnostic coronary angiography was not discovered until almost 20 years later. While attempting to inject radiocontrast into a patient's left ventricle, the American physiologist F Mason Sones Jr accidentally injected radiocontrast directly into the right coronary artery (Sones and Shirey, 1962). The patient immediately went into asystole requiring a precordial thump to restore sinus rhythm. Despite this, the resulting images of the patient's coronary circulation were far superior to anything seen before and led to the development and widespread clinical use of diagnostic coronary angiography.

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The present

The COURAGE trial established that revascularization of stenotic lesions that induce ischaemia improves patients' functional status and outcomes (Shaw et al, 2008). However, there can be marked disparity between the degree of coronary stenosis and the functional significance of a lesion, with almost 10% of patients with acute coronary syndrome showing non-critical stenosis on diagnostic coronary angiography.

Fractional flow reserve is a measure of the physiological significance of a stenotic artery and can be determined during coronary angiography by calculating the ratio of distal coronary artery pressure to aortic pressure. A fractional flow reserve value of less than 0.8 identifies ischaemia-inducing stenotic lesions with over 90% accuracy (Pijls et al, 1996). Because each artery is analysed separately, fractional flow reserve can provide more specific information with better spatial resolution than myocardial perfusion studies.

While revascularization of stenotic lesions shown by fractional flow reserve to induce ischaemia improves patients' outcomes, the benefit of revascularization of non-ischaemic lesions is less clear. The DEFER trial revealed that medical management of stenotic lesions shown by fractional flow reserve to not induce ischaemia reduces mortality and incidence of future myocardial infarction compared to routine stenting (Pijls et al, 2007).

The FAME study has subsequently shown that routine measurement of fractional flow reserve in patients with multi-vessel coronary artery disease undergoing percutaneous coronary intervention significantly reduces major adverse events (Tonino et al, 2009). As such, incorporation of fractional flow reserve into diagnostic coronary angiography has become the new gold standard in the physiological assessment of coronary artery stenosis. Its introduction has heightened the judicious use of coronary stenting, thereby improving clinical outcomes and potentially decreasing health-care costs.

The discrepancy between stenosis severity and degree of ischaemia by fractional flow reserve emphasizes the importance of factors other than stenosis in lesion-specific ischaemia. High-risk anatomical plaque features such as plaque burden, thin cap fibroatheroma, positive arterial remodelling, necrotic cores, spotty calcifications and macrophage infiltration are fundamental to the pathology of acute coronary syndrome and sudden cardiac death (Virmani et al, 2006).

Intracoronary imaging tools, predominantly intravascular ultrasound and optical coherence tomography, help the interventional cardiologist determine these high-risk plaque features, in addition to determining optimal stent size and minimizing the complications associated with percutaneous coronary intervention.

Intravascular ultrasound uses ultrasound waves produced by a catheter-mounted transducer and radiofrequency-based technology to determine positive arterial remodelling and plaque composition and identify vulnerable plaques. A meta-analysis of over 19 000 patients across eleven studies showed that intravascular ultrasound-guided stent insertion was associated with reduced mortality, major adverse cardiac events and stent thrombosis compared to angiography alone (Zhang et al, 2012).

In contrast, optical coherence tomography uses near-infrared light and Fourier domain spectral imaging to provide both cross-sectional views for detailed plaque study and longitudinal and lumen profile views for determining stent length. Three-dimensional reconstruction is also possible and can be used in assessing bifurcation lesions and in optimizing percutaneous coronary intervention results. Although clinical outcome data for optical coherence tomography are limited, percutaneous coronary intervention with angiography and optical coherence tomography guidance reduces rates of cardiac death, myocardial infarction and repeat revascularization compared to percutaneous coronary intervention under angiography guidance alone (Prati et al, 2012).

Future technological adaptions in intracoronary imaging such as micro-optical coherence tomography and photo acoustic imaging are currently underway. These are likely to further advance our understanding of the coronary disease process and the response to revascularization.

The future?

Numerous non-invasive functional imaging modalities are used to assess coronary artery disease, such as stress echocardiography, cardiac magnetic resonance and myocardial perfusion scintigraphy. These modalities assess wall motion abnormalities or regional differences in coronary flow reserve as surrogate markers for ischaemia. As such they cannot discriminate between specific vessels that cause ischaemia or accurately isolate targets for revascularization. Conversely, coronary computed tomography angiography is highly accurate in excluding high-grade coronary stenosis, but is less precise in predicting functionally significant lesions. However, recent developments in computational fluid dynamics have enabled calculation of a computed tomography-estimated fractional flow reserve which may provide a novel, non-invasive method of determining suitable lesions for revascularization.

While initial research into computed tomography-estimated fractional flow reserve by the DISCOVER-FLOW study showed promise in predicting functionally significant lesions (Koo et al, 2011), enthusiasm was dampened by the results of the DeFACTO trial which showed poor specificity and failure to meet the pre-specified primary end points (Min et al, 2012).

Following refinements in computed tomography-estimated fractional flow reserve technology and physiological modelling, the NXT trial has shown that computed tomography-estimated fractional flow reserve provides high diagnostic accuracy in identifying physiologically significant stenoses compared to invasively measured fractional flow reserve (Nørgaard et al, 2014).

Meanwhile computed tomography identification of adverse plaque characteristics, such as aggregate plaque volume, positive remodelling and low attenuation plaques, can be used to predict functionally significant lesions (Park et al, 2015). As such future technological advances in coronary computed tomography angiography may allow combined computed tomography-estimated fractional flow reserve and detailed anatomical assessment of lesion characteristics, thereby enabling detection and haemodynamic evaluation of coronary artery disease in a non-invasive manner.

Conclusions

Traditional diagnostic coronary angiography fails to differentiate those lesions which are functionally significant and is unable to look beyond the lumen at high-risk anatomical plaque features. As such, it is mostly limited to total or subtotal occlusions or primary percutaneous coronary intervention. The incorporation of fractional flow reserve and intracoronary imaging tools has offset these limitations and allows a detailed, objective appreciation of disease significance and morphology. The emergence of non-invasive imaging modalities which can predict functionally significant lesions and detect high-risk anatomical plaque features represents the future in the diagnosis of coronary artery disease and the identification of suitable targets for revascularization. **BJHM**

KEY POINTS

- Fractional flow reserve is an accurate tool in identifying functionally significant coronary lesions and the subsequent decision whether to opt for medical management or revascularization.
- Intracoronary imaging tools, such as intravascular ultrasound and optical coherence tomography, help determine high-risk plaque features, optimize stent deployment and minimize complications following percutaneous coronary intervention.
- Ongoing research into computed tomography-derived fractional flow reserve and identification of adverse plaque characteristics may provide a novel, non-invasive method of determining functionally significant coronary lesions.

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