Dynamic perfusion CT: what is normal myocardial blood flow?

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Coronary computed tomography angiography (CTA) is an established, reliable test for the anatomical diagnosis of obstructive coronary artery disease (CAD). However, although coronary CTA provides high sensitivity and a negative predictive value for detecting ≥50% diameter stenosis, it is limited in its ability to diagnose myocardial ischaemia. Since the discrepancies between the anatomical severity of a lesion and its haemodynamic significance are common, functional evaluation of intermediate stenoses is recommended for therapeutic decisions.1 Adding myocardial CT perfusion (CTP) imaging to CTA provides an opportunity for combined evaluation of coronary anatomy and functional significance of coronary stenosis.2,3

Myocardial CTP imaging is based on the assessment of contrast attenuation in the myocardium, which is proportional to tissue concentration of iodinated contrast agent. Myocardial CTP imaging can be performed on two ways.4 Static CTP imaging is based on acquisition of an image of the myocardium during the approximate peak of the contrast bolus that enables qualitative evaluation of differences in enhancement between hypoperfused and normally perfused myocardium. Dynamic CTP is based on repetitive acquisition of images before and during the first pass of a contrast bolus that enables the construction of time–attenuation curves of the myocardium and a reference artery. Mathematical modelling is applied to calculate myocardial blood flow (MBF) in absolute units, i.e. mL per gram of tissue per minute (mL/g/min). Experimental and clinical studies have validated quantification of MBF by CTP during vasodilator stress for the detection of flow-limiting stenosis defined by abnormal fractional flow reserve (FFR).4–6

AbsOLUTE quantification of MBF has potential to improve diagnostic accuracy of perfusion imaging and stratification of patient’s risk when compared with conventional, qualitative analysis.7–9 Reduced quantitative MBF during vasodilator stress can uncover global, diffuse ischaemia due to multivessel disease, which may appear completely normal by conventional analysis due to homogeneous reduction in perfusion. Quantitative analysis of regional stress MBF can also improve assessment of vessel-specific ischaemia in patients with extensive CAD. Furthermore, quantitative analysis provides an opportunity to detect microvascular dysfunction and document the effects of risk factor modification on that. Importantly, reduced coronary flow reserve (CFR), i.e. ratio of maximal quantified MBF during stress to MBF at rest, has been shown to be a powerful predictor of cardiac mortality in patients with suspected CAD both in the presence and absence of regional perfusion abnormalities.10

In this issue of European Heart Journal – Cardiovascular Imaging, Ho et al.11 describe MBF measured by dynamic CTP imaging at rest and during vasodilator stress in 35 asymptomatic individuals without obstructive CAD on CTA, calcium score of <100 and low (<10%) 10-year risk for MI or cardiac death based on the Framingham risk score. In this low-risk group, average rest MBF was 0.74 mL/g/min, stress MBF 1.35 mL/g/min, and CFR 1.86. There was significant heterogeneity of flow with the highest MBF in the lateral wall and a transmural MBF gradient with the higher MBF in the endocardial than in the epicardial wall. In a historical control group of 35 patients with previously documented CAD, stress MBF was 1.1 mL/g/min and CFR 1.3. The use of tube current modulation and 80 kV tube voltage resulted in the average radiation dose of 13 mSv from the rest–stress scan.

Definition of normal range of MBF and CFR is an important step for clinical application of quantitative CTP, which makes the study by Ho et al. important. As expected, the stress MBF and CFR values in low-risk individuals were higher than in the cohort of patients with documented CAD.11 The MBF values are in line with previous studies using dynamic CTP in symptomatic patients with suspected CAD.4–6 The average stress MBF in these studies varied between 1.05 and 1.23 mL/g/min in the myocardium subtended by non-significant stenosis and was <0.75–0.78 mL/g/min in the areas subtended by significant stenosis defined by abnormal FFR. State-of-the-art technology, including a 128-slice dual-source CT scanner, standard stress protocol, and parametric deconvolution method for flow quantification, was used in the study of Ho et al.11 However, analysis is based on manual definition of the regions of interest and evaluation of re-test reproducibility of MBF is problematic due to radiation exposure associated with repeated scans. In the future, standard imaging and analysis protocols will be important to make quantitative CTP imaging available to more widespread use. However, technical advances in the field have been rapid and re-evaluation of normal values is likely needed with new scanner technology.

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Surprisingly, the study by Ho et al. or earlier studies with one recent exception\textsuperscript{12} have not compared CTP MBF values against positron emission tomography (PET), which is an established technique for non-invasive quantification of MBF. In healthy volunteers, PET perfusion studies have shown average rest flow of 0.84 mL/g/min, stress flow of 3.16 mL/g/min, and CFR of 4.11.\textsuperscript{18} Using \textsuperscript{15}O-water PET perfusion imaging, stress MBF of $<2.4$ mL/g/min and CFR $<2.5$ were the best cut-off values for the detection of significant stenosis defined by quantitative angiography and FFR.\textsuperscript{18} Comparing with these values, it looks obvious that significant underestimation of MBF occurs during high-flow state by CTP imaging. This may be partly related to differences in patient characteristics, but technical factors related to modelling of contrast agent kinetics, image quality, and temporal resolution may play a role.

Several single-centre studies and a multicentre study have shown feasibility of CTP imaging for the detection of obstructive CAD.\textsuperscript{2,3} These studies have been mainly based on qualitative, visual analysis of the images. The transition from semi-quantitative to quantitative analysis of MBF involves mathematical data modelling that depends on accurate determination of tracer input function and myocardial tracer concentration over time. Therefore, the quantitative data are also prone to artefacts. New scanner technology may help to optimize the balance between radiation dose, temporal resolution, and image quality during dynamic CTP imaging. Future studies will show whether quantitative CTP imaging can provide similar diagnostic benefits that have been observed with other imaging modalities, and whether the benefits outweigh the higher radiation dose of dynamic CTP imaging.

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References