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CT myocardial perfusion imaging: ready for prime time?

Richard A. P. Takx [1] · **Csilla Celeng** [1] · **U. Joseph Schoepf** [2,3]

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Abstract
The detection of functional coronary artery stenosis with coronary CT angiography (CCTA) is suboptimal. Additional CT myocardial perfusion imaging (CT-MPI) may be helpful to identify patients with myocardial ischaemia in whom coronary revascularization therapy would be beneficial. CT-MPI adds incremental diagnostic and prognostic value over obstructive disease on CCTA. It allows for the quantitation of myocardial blood flow and calculation of coronary flow reserve and shows good correlation with ^{15}O-H_2O positron emission tomography and invasive fractional flow reserve. In addition, patients prefer CCTA/CT-MPI over SPECT, MRI and invasive coronary angiography. CT-MPI is ready for clinical use for detecting myocardial ischaemia caused by obstructive disease. Nevertheless, the clinical utility of CT-MPI to identify ischaemia in patients with non-obstructive/microvascular disease still has to be established.

Key Points
- *CT-MPI can improve the positive predictive value of CCTA for lesion-specific ischaemia.*
- *CT-MPI adds incremental prognostic value over CCTA for major adverse cardiac events.*
- *CT-MPI correlates with ^{15}O-H_2O PET.*
- *CT-MPI/CCTA shows high overall patient satisfaction.*

Keywords Perfusion · Computed tomography · Coronary artery disease · Ischaemia · Patient satisfaction

✉ U. Joseph Schoepf
schoepf@musc.edu

1 Department of Radiology, University Medical Center Utrecht, Utrecht, The Netherlands

2 Division of Cardiovascular Imaging, Department of Radiology and Radiological Science, Medical University of South Carolina, Charleston, SC, USA

3 Heart and Vascular Center, Medical University of South Carolina, Ashley River Tower, 25 Courtenay Drive, Charleston, SC 29425-2260, USA

Editorial

Coronary CT angiography (CCTA) is an excellent non-invasive test for ruling out obstructive coronary artery disease (CAD) [1]. Nevertheless, the positive predictive value of CCTA for identifying myocardial ischaemia is suboptimal [1, 2]. More importantly, CCTA as an *a priori* anatomical imaging test shares with invasive coronary angiography (ICA) the limitations for accurately gauging the haemodynamic relevance of a lesion; furthermore, severe anatomical narrowing does not necessarily imply the presence of functionally significant stenosis [3].

The role of CT-myocardial perfusion imaging (MPI) in obstructive CAD

CT myocardial perfusion imaging (CT-MPI) has emerged as a non-invasive imaging method for the detection of myocardial ischaemia [4]. Currently, three different approaches are available to perform CT-MPI: conventional CT-MPI (i.e. snapshot perfusion), dynamic perfusion CT-MPI and dual-energy CT-MPI (DECT-MPI) [5]. These different techniques have shown good diagnostic performance [6, 7]. Nevertheless, dynamic and DECT-MPI seem to have a better sensitivity, likely due to the ability to detect more subtle perfusion defects [8, 9]. Cury et al. [10] showed in a multicentre study that regadenoson CT-MPI was in good agreement with SPECT for detecting reversible ischaemia. Results from a sub-analysis of the CORE320 (Combined Non-invasive Coronary Angiography and Myocardial Perfusion Imaging Using 320 Detector Computed Tomography) study [11] demonstrated superior diagnostic accuracy of CT-MPI compared to SPECT for predicting obstructive CAD on ICA. Nevertheless, ICA is a suboptimal test to establish the hemodynamic severity of significant stenosis [12]. In a recent meta-analysis, CT-MPI demonstrated a high diagnostic accuracy for identifying haemodynamically significant myocardial perfusion defects determined by ICA in combination with fractional flow reserve (FFR), with comparable results to magnetic resonance imaging (MRI) [7]. The combination of CT-MPI with CCTA allows for anatomical and functional evaluation of CAD [13, 14]. The addition of CT-MPI to obstructive lesions on CCTA (e.g. ≥ 50 % stenosis degree) appears to be of incremental value for the diagnosis of myocardial ischaemia as determined by invasive FFR [4]. One multicentre registry evaluated the prognostic value of dynamic CT-MPI [15] for major adverse cardiac events in 144 patients during a follow-up period up to 18 months; the authors observed that also in prognostication the addition of CT-MPI to obstructive stenosis on CCTA results in an incremental prognostic value, which remained when correcting for clinical risk factors. Furthermore, a clear trend in increase in hazard ratio was observed with an increase in the number of territories with perfusion defects. These results are congruent with studies combing SPECT with CCTA [16, 17]. Van Rosendael et al. [18] demonstrated not only that those with a normal stress CT-MPI had a low occurrence of major cardiovascular events at 12 months, but also that adding CT-MPI to obstructive disease on CCTA results in lower referral rates for ICA and revascularisation.

CT-MPI in non-obstructive CAD and microvascular disease

CT-MPI allows for the quantitation of myocardial blood flow (MBF) and calculation of coronary flow reserve (CFR) [19, 20]. Abnormal measures can be suggestive for the presence of epicardial and/or microvascular CAD [21]. At least 10–30 % of patients with angina pectoris undergoing ICA have no significant stenosis, and among those 50–65 % are believed to have coronary microvascular dysfunction [22–25]. The recognition of microvascular dysfunction and the potentially underlying myocardial ischaemia is, however, often delayed due to the ‘hidden nature’ of the disease. Williams et al. evaluated the diagnostic performance of ‘snapshot’ adenosine stress CT-MPI [26]. Part of the study population (22 out of 51) was compared to ^{15}O-H_2O positron emission tomography (PET). ^{15}O-H_2O allows for free diffusion (100 % extraction fraction) and is linearly correlated with myocardial uptake [27, 28]. However, its use is mainly limited to research since it requires an on-site cyclotron due to the short half-time of the tracer. In their study, Williams et al. [26] demonstrated that CT myocardial attenuation (measured in Hounsfield units) during hyperaemia correlates with MBF as measured by ^{15}O-H_2O PET. The observed difference in ^{15}O-H_2O uptake between no CAD and non-obstructive CAD under hyperaemic conditions shows potential to detect microvascular disease. In addition, CT-MPI/CCTA demonstrated a good positive predictive value of 90 % on a patient level compared to ICA/FFR. With regard to gender, women are more prone to have non-obstructive CAD compared to men; the WISE (Women's Ischemia Syndrome Evaluation) study showed that 81 % of women referred for ICA have no or non-obstructive CAD [29]. At a 10-year follow-up cardiovascular death or myocardial infarction occurred in 6.7 % of women with minimal CAD (i.e. ≤ 20 % diameter reduction) and in 12.8 % of women with non-obstructive CAD (i.e. > 20 %, but < 50 % narrowing) [30]. Due to the relatively high occurrence of events in patients with non-obstructive CAD, the incorporation of CT-MPI to clinical decision-making can be of great importance for better identification of myocardial ischaemia.

Patient satisfaction and radiation dose

A recent study by Feger et al. [31] observed high patient satisfaction for CT (including CT-MPI) and found that patients prefer it over SPECT, MRI and ICA. In detail, half of the patients preferred the combined CT-MPI/CCTA approach, with only 2 % of patients giving preference to stress MRI. Furthermore, the use of (semi)-automated quantification of CT-MPI data provides substantially reduced analysis times, making it feasible to integrate quantitative CT-MPI into clinical workflow [32]. A concern with CT-MPI is the associated increase in radiation exposure of patients. In a review, Danad et al. [9] calculated an average radiation exposure of 5.9 mSv (range 1.9–15.7) for snapshot CT-MPI and 9.2 mSv (range 3.8–12.8) for dynamic CT-MPI. Nevertheless, when using low-kV protocols dynamic CT-MPI is feasible at 4–6 mSv [33, 34]. Adenosine is usually well tolerated by patients, though the administration is of concern for patients with advanced heart block or asthma, and patients should avoid caffeine intake 24 h before testing [35]. The recent introduction of third generation DSCT and dual layer CT systems is expected to further increase the role of CT-MPI with highly accurate iodine quantification [36]. Furthermore, data from the SPECIFIC (Dynamic Stress Perfusion CT for Detection of Inducible Myocardial Ischemia) trial, which aims to determine the diagnostic accuracy of CT-MPI compared with invasive FFR in patients with suspected or known CAD (ClinicalTrials.gov Identifier: NCT02810795) is expected to give more insight into the role of dynamic CT-MPI.

Conclusion

CT-MPI is a proven method for detecting myocardial ischaemia caused by obstructive CAD, is associated with high patient satisfaction, and has been shown to be ready for clinical use in this setting. Recent research shows that perfusion imaging has incremental prognostic value over stenosis degree on CCTA. In addition, it has the potential to identify ischaemia caused by non-obstructive CAD and microvascular disease. Nevertheless, the future clinical utility of CT-MPI to identify the extent of ischaemia in patients with non-obstructive/microvascular CAD still has to be established.

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Compliance with ethical standards

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Methodology Editorial

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