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CT Assessment of Myocardial Perfusion and Fractional Flow Reserve

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ABSTRACT

Coronary computed tomography angiography (CTA) offers a non-invasive method to detect coronary plaque and stenosis. However, to date, CTA has been most useful as a method of ruling out coronary artery disease (CAD) among patients with low to intermediate pretest probability of significant CAD. The reduced specificity of CTA for detecting physiologically significant stenosis is a known limitation of this technique, particularly since some patients require additional functional testing following CTA. Therefore, intense interest has focused on the development of methods to determine the functional significance of anatomical lesions identified by CTA. This article will discuss two emerging methods: stress myocardial perfusion imaging using CT, or CT perfusion, and computer simulation of fractional flow reserve.

Coronary computed tomography (CT) angiography (CTA) emerged in the 1990s as an experimental non-invasive method of diagnosing coronary artery disease (CAD).[1] Due to rapid evolution and technological advances in multi-detector CT as well as image reconstruction methods, CTA quickly gained clinical acceptance as a diagnostically accurate[2,3] anatomic test with important prognostic value.[4] However, to date, CTA has been most useful as a method of ruling out CAD among patients with low to intermediate pretest probability of significant CAD.[5] The reduced specificity of CTA for detecting physiologically significant stenosis continues to be a concern, particularly since some patients require additional functional testing following CTA.

The rationale for evaluating ischemia

Even though the degree of stenosis is one of the factors that partially predicts the presence or absence of lesion specific ischemia, the association between coronary anatomy and ischemia is poor. For instance, patients can have no ischemia in presence of significant stenosis (NIPSS) and presence of ischemia with no severe stenosis (PINSS).[6,7] An ideal coronary diagnostic test would possess the ability to accurately assess the burden of atherosclerosis as well as to determine the physiological consequence of anatomical lesions by determining the presence and severity of ischemia. Therefore, intense interest has focused on the development of methods

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Abbreviations and Acronyms

ALARA = as low as reasonably achievable (radiation exposure)

CAD = coronary artery disease

CT = computed tomography

CTA = computed tomography angiography

CTP = computed tomography perfusion

FFR = fractional flow reserve

FFR_{CT} = computer simulation of fractional flow reserve based upon computed tomography

ICA = invasive coronary angiography

MACE = major adverse cardiac outcomes

MDCT = multi-detector computed tomography

NIPSS = no ischemia in presence of significant stenosis

MPI = myocardial perfusion imaging

MRI = magnetic resonance imaging

PINSS = presence of ischemia with no severe stenosis

SPECT = single photon emission computed tomography

to determine the functional significance of anatomical lesions identified by CTA.

Coronary angiography has been used as clinical gold standard for detecting CAD for the past few decades and the degree of anatomical stenosis has shown to have a powerful prognostic value.[8,9] However, treatment strategies based on angiographic findings and severity of anatomical stenosis alone do not result in reduction of major adverse cardiac outcomes (MACE) compared to optimal medical therapy (OMT).[10] Unlike anatomy driven treatment strategies, physiology based treatment strategies have been shown to be associated with improved outcomes.[11–16] While most non-invasive techniques for detecting ischemia provide a global assessment of myocardial blood flow (MBF), invasive assessment with fractional flow reserve (FFR) offers a lesion specific measure of ischemia determined by calculating the ratio of flow across a lesion to a flow at maximum hyperemia in a presumable absence of stenosis. The fractional flow reserve versus angiography for guiding percutaneous coronary intervention (FAME) and FAME 2 studies demonstrated that FFR guided therapy is superior to both angiography guided therapy and OMT, respectively.[13–16]

This article will discuss two emerging methods of using cardiac CT to assess ischemia: stress myocardial perfusion imaging using CT, or CT perfusion (CTP), and computer simulation of fractional flow reserve (FFR_{CT}).

CT myocardial perfusion imaging

CT scans of canine hearts undergoing stress CTP demonstrated in 2007 that CTP derived quantitative perfusion correlated well with myocardial perfusion determined by microspheres.[17] The first reports of CTP as technically feasible and accurate in human clinical studies were reported in two separate studies by Blankstein and George in 2009.[18,19] Since that time, the diagnostic accuracy of CTP has been studied in comparison to a variety of reference standards, including myocardial perfusion imaging (MPI) by single photon emission CT (SPECT) or magnetic resonance imaging (MRI), invasive or noninvasive angiographic stenosis, and invasive FFR.[20–26]

CTP protocols

In order to assess both coronary anatomy and myocardial ischemia using CTP, two separate CT acquisitions are required: one for vasodilator induced stress MPI and one for rest MPI and coronary CTA. However, a current challenge for the field of CTP is a lack of standardized approaches for image acquisition and post-processing. While close attention to heart rate is required for the rest acquisition, heart rate control is not as stringent for stress perfusion MPI since the coronaries will not be interpreted on this study. A delay ranging from 10 to 30 minutes is currently employed between acquisitions to allow for CT contrast washout and/or reversal of the effects of the pharmacological vasodilator used. For the stress perfusion, peak hyperemia may be achieved with adenosine, dypyridamole, or regadenoson. Regadenoson has the benefit of not requiring a continuous intravenous infusion pump since it is administered as a single injection that results in several minutes of hyperemia. A clinical example of CTP is demonstrated in Fig 1.

A common question is whether to employ a stress–rest perfusion protocol or a rest–stress protocol. Investigators have used either protocol with similar clinical result, but for practical workflow a rest–stress protocol would have the advantage that only patients who are identified to have a possible stenosis would then undergo stress perfusion imaging. Routine use of stress and rest CTP along with CTA for all patients is unlikely to be cost-effective since only approximately one third[4] of patients currently referred to CTA have possible stenosis. Fig 2 illustrates the general protocol for stress–rest (top panel) and rest–stress for CTP.

Nearly any modern scanner with 64 or more detectors can accurately evaluate CT MPI, although there are unique considerations for each specific CT platform. First of all is the z-axis coverage, which is mostly determined by the number of detectors. While the first reported CT MPI studies used 64 multi-detector CT (MDCT) platforms, which require image acquisition over multiple heart beats, the use of this technique results in myocardial contrast enhancement that is not homogeneous due to the slight differences in acquisition time of each slab. Such temporal differences are usually not significant enough to impair a qualitative assessment of CTP, but may be problematic when quantitative techniques are used or when assessing for differences in contrast opacification gradients. With 320 MDCT, sufficient z-axis coverage allows for a single beat acquisition that provides more homogeneous MPI data.

Another important consideration is the estimated effective radiation dose delivered to the patient. Most patients who would clinically benefit from the additive information of CT MPI are older and have CAD and therefore the affect of medical radiation exposure upon lifetime risk of malignancy will be negligible. However, public health guidelines including recommendations of the American Heart Association[27] recommend to reduce