Challenges of Cardiac Computed Tomography for Anatomic and Functional Evaluation of Coronary Artery Disease

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Abstract

Cardiac computed tomography is a widespread and noninvasive diagnostic tool in clinical practice. Computed tomographic angiography provides anatomic images of the coronary artery trees, as well as detects, characterizes and quantifies coronary plaques, which has important implication in cardiac diagnosis, risk stratification and management. Unfortunately, computed tomographic angiography tends toward overestimation of coronary stenoses and may encourage unnecessary invasive angiography. Computed tomography-derived fractional flow reserve, combing anatomic and functional information, is a useful physiological test for the detection and exclusion of ischemic lesions, and has the potential of being a reliable gatekeeper to the pathway of invasive angiography. However, cardiac computed tomography has its own limitations: poor temporal resolution, numerous artifacts, large radiation exposure, contrast-induced nephropathy, and hypothetical models. Future possibilities should focus on the methods to overcome these limitations.

Keywords: Computed Tomography; Fractional Flow Reserve; Myocardial Ischemia; Coronary Artery Disease.

Although noninvasive diagnostic tools for cardiovascular diseases have expanded with innovations in magnetic resonance imaging, molecular radionuclide imaging and perfusion echocardiography, cardiac computed tomography continues to advance along with other imaging modalities and has been gaining widespread application in clinical practice [1]. As multi-slice computed tomography (MSCT) has rapidly evolved from 4-detector row systems in 1998 to the latest 256-slice and 320-slice CT systems, great progresses have been made in gantry rotation speed, spatial resolutions and reconstruction techniques, which contribute to lowing radiation exposure and contrast volume, improving image quality and achieving high diagnostic accuracy for evaluation of coronary artery disease (CAD) [2-3].

Anatomic Evaluation of CAD

Coronary computed tomographic angiography (CCTA) provides anatomic images for the coronary artery trees. Systematic reviews and meta-analysis have confirmed that the negative predictive value of post-64 MSCT is as high as 95-98%, indicating it as a cost- and time-effective alternative to conventional coronary angiography for ruling out significant CAD [4-5]. In addition, MSCT can be used to detect, characterize and quantify non-obstructive coronary plaque, which has important implication in cardiac risk stratification and management [6]. Studies have demonstrated that CCTA provides prognostic information for predicting adverse cardiac events in patients with suspected or known CAD [7,8]. A predictive score combining CCTA parameters with clinical information significantly improves prediction compared with well-established clinical risk scores [9].

Unfortunately, CCTA remains much lower in quality and is suboptimal for diagnostic and interventional purposes when compared with conventional angiography. Despite of the excellent spatial resolution (isotropic voxel 0.5×0.5×0.5 mm3 or 0.6×0.6×0.6mm3 for post-64 MSCT), the main technological challenge of CCTA is the poor temporal resolution (165-175ms for post-64 MSCT), which is still significantly inferior to that of conventional angiography (20ms). [2] Although prospective ECG gating is used to overcome the limitation of poor temporal resolution, patients with

rapid heart rate, atrial fibrillation and frequent premature beat are not recommend to receive CCTA [1]. The other challenges for CCTA includes calcium-induced blooming artefact, quantum statistical noise, large radiation exposure and contrast-induced nephropathy [10]. Due to these limitations, the positive predictive values of CCTA varied a lot (from 64% to 95%) [11]. CCTA assessment of coronary stenoses tends toward overestimation, since only a minority of lesions with CCTA-identified severe stenosis are found to be ischemia causing [12]. Widespread application of CCTA may encourage unnecessary invasive angiography [10].

Physiological evaluation of CAD

For patients with no to mild myocardial ischemia, medical therapy is recommended while revascularization is associated with increased mortality. Thus, the presence and extent of myocardial ischemia is a key to decision-making for revascularization. Fractional flow reserve (FFR) is thought to be a gold standard for invasive assessment of coronary ischemic lesions. Studies demonstrate that FFR-guided percutaneous coronary intervention (PCI) is superior to angiography-guided PCI and medical therapy [13-15]. With recent advances in computational fluid dynamics and image-based modeling, computed tomography-derived fractional flow reserve (FFRCT), which combines anatomic and functional information, can be gathered from CCTA without the need for additional imaging, acquisition protocol and medication [16]. FFRCT assesses non-invasively the ratio of flow across a stenosis to putative flow in the hypothetical absence of a stenosis, and is a useful physiological test for assessment of coronary lesions that cause ischemia. The recently reported prospective multicenter DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve) study, the DeFACTO (Determination of Fractional Flow Reserve by Anatomic Computed Tomographic Angiography) trial and the NXT (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps) Trial demonstrated that FFRCT was associated with improved diagnostic accuracy versus measures of CCTA stenosis severity, and is a viable alternative to invasive FFR for the detection and exclusion of ischemic lesions [17-19]. FFRCT has the potential of being a reliable gatekeeper to the pathway of invasive angiography.

However, heterogeneities among studies exists. The specificity of FFRCT in DeFACTO study (56%~67%) is lower than those in NXT Trial and DISCOVER- FLOW study (61%~85%). FFRCT has its own limitations. Numerous artifacts (calcification, motion, ladder, misregistration) may affect the image quality and interpretability. Additional limitations of FFRCT relate to assumptions in the physiological models that is "simulated" but not "real". These models include patient- and population-specific data. The amount of viable myocardium subtended by the epicardial coronary branch harboring the stenosis, the coronary microvascular resistance based on vessel size, and the reductions in resistance in response to adenosine-mediated hyperemia vary among patients and influence the value of FFRCT.[20]

Future possibilities for cardiac computed tomography should focus on the methods to overcome these limitations. The indications for application of cardiac computed tomography must be specified based on the terms of whether they lead to the greatest benefit and whether the risk may be greater than the benefit.[2] The ultimate gold of cardiac computed tomography is to enable appropriate clinical decision making.

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