

## Letters

### Combined CT Techniques to Assess Functionally Significant Coronary Stenoses



The study by Wong et al. (1) revealed that transluminal attenuation gradient (TAG) by 320-detector row computed tomography + computed tomography angiography (CTA) and computed tomography perfusion (CTP) + CTA provided comparable diagnostic accuracy for functional assessment of coronary artery stenosis. However, several limitations and biases need to be acknowledged.

First, a TAG cutoff of  $-15.1$  Hounsfield units (HU)/10 mm was retrospectively determined from receiver-operating characteristic curve analysis in a previous study (2), which may lead to overestimation of its predictive value. For CTA, 70% has been proven to be a better cutoff for discriminating ischemia-causing stenosis (3), whereas a stenosis of  $\geq 50\%$  was classified as functionally significant in this study, which would bias the results.

Second, 30 of 127 vessels were excluded from the analysis because of the intramyocardial course of the left anterior descending artery, branch or small vessel, calcified disease, and significant artifact, which would artificially and significantly increase the apparent clinical performance. To reflect its real-world diagnostic performance, uninterpretable test results should also be included in the analysis (4). Also, the CTP was performed with intravenous adenosine infusion; although TAG was measured from resting state, pharmacologic stress TAG should be considered the counterpart in comparison with CTP.

Last, we do admit that TAG obtained by the 320-detector row computed tomography (CT) had a higher sensitivity (71% vs. 47.5%) as compared with TAG assessment on 64-detector row CT (5) by enabling near isophasic, single-beat imaging of the entire coronary tree. However, the high demand for multidetector CT scanners may limit its widespread clinical use. As acknowledged by the authors, CTA had a sensitivity of 89% (1). The integration of TAG and CTA may be the solution for low sensitivity of

TAG without increasing the detector row of the CT scanner, which yielded to a comparable diagnostic accuracy (area under receiver-operating characteristic curve = 0.809 vs. 0.848) on 64-detector row compared with 320-detector row CT.

It would be important to have additional well-designed studies with larger sample sizes before the final clinical application of TAG.

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#### REPLY: Combined CT Techniques to Assess Functionally Significant Coronary Stenosis



We thank Dr. Dai and colleagues for their thoughtful comments regarding our paper (1). Previous studies have shown that coronary stenosis  $\geq 50\%$  on computed tomography angiography (CTA) has good diagnostic accuracy for detecting coronary artery stenosis as well as predicting cardiovascular outcome

(2). The high sensitivity and negative predictive value of CTA is well described. In order for computed tomography (CT) to emerge as a “1-stop shop” that provides not only anatomical but also functional assessment of coronary artery stenosis, adjunct CT methods, such as transluminal attenuation gradient (TAG320) and adenosine stress computed tomography perfusion (CTP), described in our paper attempted to improve the specificity of CT. The TAG320 cut-off value of  $-15.1$  Hounsfield units/10 mm was not retrospectively derived in this study, but was instead prospectively chosen on the basis of the results of our initial experience (3). Although TAG320 was measured in the resting state, the diagnostic accuracy, particularly when combined with CTA, was encouraging (AUC = 0.844). It would be of significant interest to evaluate the diagnostic accuracy of TAG320 in conjunction with pharmacologic stress such as CTP. However, CTA imaging performed during adenosine infusion increases heart rate, and the likelihood of artefact caused by heart motion could affect the performance of TAG320. Besides heart motion artefact, analysis of TAG320 is also impacted by calcified and small vessels. It is anticipated that further technical refinements that allow TAG320 assessment of cross-sectional Hounsfield units sampling at 1-mm intervals and exclusion of calcified segments may reduce the percent of excluded vessels. Acknowledging these limitations of CTA and TAG320, CTP resulted in the successful evaluation of 97% of vessels in this study. We speculate that a future practical approach may be to explore a calcium score threshold that would render CTA and TAG320 uninterpretable, leading to CTP being performed upfront in certain patients. The isophasic, single-beat imaging of the entire coronary tree afforded by a 320-detector row CT contributes to the improved diagnostic accuracy of TAG320 compared with

64-detector row CT. We agree that integration of TAG and CTA on 64-detector row CT would be ideal. Further studies are required to evaluate whether correction of contrast opacification in the coronary artery to corresponding descending aortic opacification to correct for timing-dependent perturbation of coronary contrast delivery associated with multiple heart imaging will improve the diagnostic accuracy of TAG in 64-detector row CT. We agree that, before the application of TAG in clinical practice, larger multi-center studies to assess its diagnostic accuracy and prognostic value are required.

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