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A Novel Noninvasive Technology for Treatment Planning Using Virtual Coronary Stenting and Computed Tomography-Derived Computed Fractional Flow Reserve

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Objectives This study sought to determine whether computational modeling can be used to predict the functional outcome of coronary stenting by virtual stenting of ischemia-causing stenoses identified on the pre-treatment model.

Background Computed tomography (CT)-derived fractional flow reserve (FFR) is a novel noninvasive technology that can provide computed (FFR_{CT}) using standard coronary CT angiography protocols.

Methods We prospectively enrolled 44 patients (48 lesions) who had coronary CT angiography before angiography and stenting, and invasively measured FFR before and after stenting. FFR_{CT} was computed in blinded fashion using coronary CT angiography and computational fluid dynamics before and after virtual coronary stenting. Virtual stenting was performed by modification of the computational model to restore the area of the target lesion according to the proximal and distal reference areas.

Results Before intervention, invasive FFR was 0.70 ± 0.14 and noninvasive FFR_{CT} was 0.70 ± 0.15. FFR after stenting and FFR_{CT} after virtual stenting were 0.90 ± 0.05 and 0.88 ± 0.05, respectively ($R = 0.55$, $p < 0.001$). The mean difference between FFR_{CT} and FFR was 0.006 for pre-intervention (95% limit of agreement: –0.27 to 0.28) and 0.024 for post-intervention (95% limit of agreement: –0.08 to 0.13). Diagnostic accuracy of FFR_{CT} to predict ischemia (FFR $\leq$0.8) prior to stenting was 77% (sensitivity: 85.3%, specificity: 57.1%, positive predictive value: 83%, and negative predictive value: 62%) and after stenting was 96% (sensitivity: 100%, specificity: 96% positive predictive value: 50%, and negative predictive value: 100%).

Conclusions Virtual coronary stenting of CT-derived computational models is feasible, and this novel noninvasive technology may be useful in predicting functional outcome after coronary stenting. (Virtual Coronary Intervention and Noninvasive Fractional Flow Reserve [FFR]; NCT01478100) (J Am Coll Cardiol Intv 2014;7:72–8) © 2014 by the American College of Cardiology Foundation

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Revascularization of coronary artery stenoses that induce ischemia can improve the functional status and clinical outcome of patients with coronary artery disease (1,2). Measurement of fractional flow reserve (FFR) during invasive coronary angiography is the gold standard for the diagnosis of ischemia-causing stenoses and can enhance clinical decision making and reduce healthcare costs (3,4). Coronary computed tomographic angiography (cCTA) is a commonly used noninvasive test that can provide accurate anatomical information on coronary artery disease (5,6). Previous studies, however, have shown that stenosis severity interpreted on cCTA does not match well with functional severity evaluated by invasive FFR (7).

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Recently, application of computational fluid dynamics technology to cCTA images has enabled computation of coronary artery blood flow and pressure, and calculation of lesion-specific FFR without the need for an invasive procedure (8). FFR can be computed from typically acquired cCTA scans without any additional image acquisition, modification of cCTA protocols, or administration of medications. Previous studies (9,10) suggest that computation of FFR from cCTA (FFR_{CT}) can identify patients with functionally significant coronary lesions prior to invasive cardiac catheterization. The same computational modeling technology allows for modification of the coronary flow model to eliminate an ischemia-causing stenosis, thus enabling "virtual stenting" of a coronary lesion. The resulting re-calculation of coronary blood flow and FFR_{CT} can, in turn, serve to predict hemodynamic effect of coronary stenting in a lesion-specific manner. Such prediction of revascularization benefit (or lack thereof) may be a useful tool for patient or lesion selection and treatment planning prior to invasive procedures.

The purpose of this study is to determine whether virtual stenting of coronary stenoses identified on CT-based computational models can predict functional status of coronary lesions after stenting using measured FFR as the reference standard.

Methods

Study design and population. At 3 centers, 44 patients who had functionally significant coronary stenoses (35 men, mean age 65 years) with available pre-intervention cCTA and pre- and post-intervention FFR were enrolled. All patients were stable adults ≥18 years with suspected or known coronary artery disease who had undergone cCTA, were identified as having a ≥50% stenosis in a major coronary artery (≥2.0 mm diameter), and who underwent clinically indicated invasive coronary angiography with FFR measurement. Coronary calcium scoring was not performed at the time of cCTA, although no patient was excluded based on the upper threshold of qualitative coronary calcification, heart rate, or body mass index. Performance and timing of the invasive coronary angiography or FFR was at the discretion of the treating physician, but study cases were limited to those in which cCTA and invasive angiography was performed within 45 days without an intervening coronary event. The study protocol was approved by the institutional review boards of each participating center and all patients gave written informed consent.

cCTA and invasive coronary procedures. Each center performed cCTA in accordance with the Society of Cardiovascular Computed Tomography guidelines on performance of cCTA using a variety of different CT scanner platforms (Lightspeed VCT, GE Healthcare, Milwaukee, Wisconsin; Somatom Sensation and Definition CT, Siemens, Forchheim, Germany; Brilliance 256 and 64, Philips, Surrey, United Kingdom; Aquilion One and 64, Toshiba, Otawara, Japan). cCTA were performed by retrospective electrocardiographic helical or prospective electrocardiography-triggered methods. Oral metoprolol was administered for any patient with a heart rate ≥65 beats/min. Immediately before image acquisition, 0.2 mg sublingual nitroglycerin was administered. During the cCTA acquisition, 80 to 140 cc of iodinated contrast was injected followed by a 50-cc saline flush. Contrast timing was performed to optimize uniform contrast enhancement of the coronary arteries. The scan parameters were as follows: 64/256/320 × 0.5/0.625/0.750 mm collimation; tube voltage 100 or 120 mV; effective 400 to 650 mA. Dose reduction strategies—including electrocardiogram-gated tube current modulation and reduced tube voltage—were employed whenever feasible.

Abbreviations and Acronyms

cCTA = coronary computed tomographic angiography

FFR = fractional flow reserve

FFR_{CT} = computed fractional flow reserve from coronary computed tomographic angiography

LAD = left anterior descending

TIMI = Thrombolysis In Myocardial Infarction

Coronary angiography and percutaneous coronary intervention were performed by standard techniques. The revascularization strategy, including the size of balloon and coronary stent, was left to the discretion of the operators. FFR was measured using a 0.014-inch pressure-monitoring guidewire (Pressure Wire Certus, St. Jude Medical Systems, Uppsala, Sweden) with the pressure sensor at the same location before and after coronary stenting. Maximal hyperemia was induced with a continuous intravenous infusion of adenosine at the rate of 140 μg/kg/min. FFR was calculated as the ratio of the mean distal pressure to the mean aortic pressure during maximal hyperemia. An FFR ≤0.8 was considered diagnostic of lesion-specific ischemia. FFR was measured in a blinded fashion, without knowledge of FFR_{CT} values.