Comparison of Diagnostic Value of a Novel Noninvasive Coronary Computed Tomography Angiography Method Versus Standard Coronary Angiography for Assessing Fractional Flow Reserve

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Noninvasive fractional flow reserve (FFR) from coronary computed tomography angiography (cCTA) correlates well with invasive FFR and substantially improves the detection of obstructive coronary artery disease. However, with current algorithms, computed tomography (CT)–based FFR is derived off-site in an involved time-consuming manner. We sought to investigate the diagnostic performance of a novel CT-based FFR algorithm, developed for time-efficient in-hospital evaluation of hemodynamically indeterminate coronary lesions. In a blinded fashion, CT-based FFR was assessed in 67 coronary lesions of 53 patients. Pressure guidewire–based FFR <0.80 served as the reference standard to define hemodynamically significant stenosis and assess the diagnostic performance of CT-based FFR compared with standard evaluation of cCTA (luminal diameter stenosis of ≥50%). We recorded the time needed for derivation of CT-based FFR. On a per-lesion and per-patient basis, CT-based FFR resulted in a sensitivity of 85% and 94%, a specificity of 85% and 84%, a positive predictive value of 71% and 71%, and a negative predictive value of 93% and 97%, respectively. The area under the receiver operating characteristic curve on a per-lesion basis was significantly greater for CT-based FFR compared with standard evaluation of cCTA (0.92 vs 0.72, p = 0.0049). A similar trend, albeit not statistically significant, was observed on per-patient analysis (0.91 vs 0.78, p = 0.078). Mean total time for CT-based FFR was 37.5 ± 13.8 minutes. In conclusion, the CT-based FFR algorithm evaluated here outperforms standard evaluation of cCTA for the detection of hemodynamically significant stenoses while allowing on-site application within clinically viable time frames. © 2014 Elsevier Inc. All rights reserved. **(Am J Cardiol 2014;114:1303–1308)**

The diagnosis of coronary artery disease (CAD) is noninvasively accomplished with coronary computed tomography angiography (cCTA) by assessing coronary artery anatomy and direct visualization of atherosclerotic plaque.[1] This method also provides potential benefit via detection of nonobstructive coronary lesions before they develop hemodynamic significance and progression to clinical end points, chiefly major adverse cardiac events.[2] However, particularly with intermediate coronary artery lesions, the differentiation of flow-limiting stenoses remains a limitation of cCTA. To add physiological information to anatomic cCTA data, multiparametric imaging protocols are currently being developed, including computed tomography (CT) myocardial perfusion imaging and CT-based derivation of fractional flow reserve (FFR).[3,4] Initial approaches applied a CT-based FFR algorithm off-site using computations on a parallel supercomputer to solve complex Navier-Stokes equations for simulation of coronary hemodynamics.[5] We sought to investigate the diagnostic value of a novel CT-based FFR prototype algorithm, developed for time-efficient and in-hospital application without data transfer, to detect lesion-specific ischemia in coronary artery stenoses, as confirmed by invasive FFR.

Methods

Using a retrospective study design, we investigated patients with suspected or known coronary artery disease who had undergone clinically indicated cCTA, coronary catheter angiography (CCA), and FFR from September 2008 to February 2014 in a non-emergent setting. Exclusion criteria were defined as time between procedures exceeding 3 months, interprocedural major adverse cardiac events (cardiac death, nonfatal myocardial infarction, or revascularization), severely reduced left ventricular function, previous coronary artery bypass surgery, stent placement in the

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See page 1308 for disclosure information.

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http://dx.doi.org/10.1016/j.amjcard.2014.07.064

Table 1
Patient characteristics (n = 53)

Parameter	Mean ± Standard Deviation or Frequency (%)
Age (years)	61.2 ± 12.0
Men	34 (64%)
Height (cm)	173.2 ± 10.8
Weight (kg)	87.0 ± 21.2
Body-mass index (kg/m^2)	28.9 ± 6.5
Caucasian	44 (77%)
African American	13 (23%)
Hypertension*	31 (54%)
Diabetes mellitus	18 (32%)
Hyperlipidemia†	31 (54%)
Current smoker	8 (14%)
Prior percutaneous coronary intervention	9 (16%)
Prior coronary bypass surgery	0 (0%)
Left ventricular ejection fraction (%)	58.3 ± 9.3
Systolic blood pressure (mm Hg)	136.2 ± 15.7
Diastolic blood pressure (mm Hg)	71.8 ± 9.3
Heart rate (beats per minute)	70.2 ± 12.6
Aspirin	31 (54%)
Clopidogrel	10 (18%)
β blocker	30 (53%)
Statin	35 (61%)
Angiotensin converting enzyme inhibitor	23 (40%)
Calcium-channel blocker	10 (18%)

* Defined as blood pressure >140 mm Hg systolic, >90 mm Hg diastolic, or use of antihypertensive medication.

† Defined as a total cholesterol level of >200 mg/dl or use of antilipidemic medication.

Table 2
Procedural results (number of narrowing = 67)

Coronary Catheter Angiography	Frequency (%)
Luminal stenosis ≥50%	44 (66%)
Luminal stenosis ≥70%	21 (31%)
FFR <0.80	20 (30%)
No. of stenoses of interest per location	
Left anterior descending coronary artery	41 (61%)
Left circumflex coronary artery	15 (22%)
Right coronary artery	11 (16%)
Coronary Computed Tomography Angiography	**Value or Frequency (%)**
Agatston score, mean ± standard deviation*	778.4 ± 731.1
Range*	0–2547
No. of patients ≥400*	19 (36%)
Luminal stenosis ≥50%	55 (82%)
Luminal stenosis ≥70%	27 (40%)
Intermediate grade luminal stenosis (30%–70%)	39 (58%)
CT-based FFR <0.80	24 (36%)

* Agatston score was obtained in 46 patients.

vessel containing the lesion of interest, bifurcation stenosis types D to G (SYNTAX score classification[6]), severe stenosis of the proximal left main and/or the proximal right coronary artery, total chronic occlusion, and nondiagnostic quality of the cCTA data set. The responsible institutional review board for human research approved the present study. The need for written informed patient consent was waived for this retrospective study.

In all subjects, selective CCA had been performed in our cardiac catheterization laboratory as per current guidelines.[7] Multiple projections were obtained of each major coronary artery (left main, left anterior descending, left circumflex, and right coronary artery). CCA projection angles were adjusted on an individual patient basis depending on the cardiac orientation. Based on the CCA examination, luminal stenosis was visually graded by an experienced interventional cardiologist. FFR interrogation was conducted at the time of CCA if a stenosis was suspected to cause ischemia. As described previously,[8] a dedicated pressure-monitoring guidewire was advanced distal to a lesion of interest, and the exact position of the sensor was recorded before assessing FFR. Hyperemia was induced by intravenous administration of adenosine at a rate of 140 μg/kg per min. FFR was derived as the ratio of mean coronary pressure distal to the stenosis and mean aortic pressure at the time of pharmacologically induced hyperemia. A threshold of <0.80 was considered to indicate hemodynamic significance of stenoses.

All cCTA examinations were acquired using first- and second-generation dual-source CT scanners (Somatom Definition and Somatom Definition Flash; Siemens Healthcare, Forchheim, Germany) according to the guidelines of the Society of Cardiovascular Computed Tomography.[9] To minimize radiation exposure, the cCTA acquisition technique was selected on an individual basis with adaptation of the acquisition to heart rate, heart rhythm, and body mass index of each patient. Retrospective electrocardiographic gating with tube current modulation, prospective electrocardiographic triggering, and prospective high-pitch electrocardiographically triggered spiral acquisition were used. A volume of 50 to 80 ml of iodinated contrast material was injected at a rate of 4 to 6 ml/s, immediately followed by a 50-ml saline bolus. The parameters of the cCTA protocol were tube current-time product, 350 to 650 mAs; tube potential, 80 to 120 kVp; gantry rotation time, 0.28 to 0.33 seconds. All data sets were reconstructed at a section thickness of ≤0.75 mm, with an increment of 0.4 mm. Image reconstruction was performed using filtered back projection and a dedicated vascular kernel (B26f). Standard cCTA interpretation was performed by an observer with 7 years of experience in evaluating cCTA studies. The percent luminal diameter stenosis of each lesion of interest was visually determined using transverse CT sections and curved multiplanar reformats along the vessel centerline on a dedicated analysis platform (SyngoVia, Siemens). A qualitative image rating of the cCTA data sets was conducted by an experienced observer using a 5-point Likert scale (1 = nondiagnostic; 2 = diagnostic despite impairment by image noise, artifacts, and/or low contrast opacification; 3 = moderate image noise with sufficient intraluminal visibility, artifacts may be present; 4 = good vessel contrast in the absence of major artifacts, low image noise; and 5 = excellent, no diagnostic limitations).

CT-based FFR computation was performed on regular cCTA data sets without the need for additional imaging, modification of the acquisition protocol, or administration of pharmacologic stress agents. A software research prototype (Siemens cFFR, version 1.4; Siemens Healthcare, currently not commercially available) installed on a regular workstation