Noninvasive Diagnosis of Ischemia-Causing Coronary Stenosis Using CT Angiography

Diagnostic Value of Transluminal Attenuation Gradient and Fractional Flow Reserve Computed From Coronary CT Angiography Compared to Invasively Measured Fractional Flow Reserve

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OBJECTIVES The aim of this study was to compare the diagnostic performance of coronary computed tomography angiography (CCTA)-derived computed fractional flow reserve (FFR<sub>CT</sub>) and transluminal attenuation gradient (TAG) for the diagnosis of lesion-specific ischemia.

BACKGROUND Although CCTA is commonly used to detect coronary artery disease (CAD), it cannot reliably assess the functional significance of CAD. Novel technologies based on CCTA were developed to integrate anatomical and functional assessment of CAD; however, the diagnostic performance of these methods has never been compared.

METHODS Fifty-three consecutive patients who underwent CCTA and coronary angiography with FFR measurement were included. Independent core laboratories determined CAD severity by CCTA, TAG, and FFR<sub>CT</sub>. The TAG was defined as the linear regression coefficient between intraluminal radiological attenuation and length from the ostium; FFR<sub>CT</sub> was computed from CCTA data using computational fluid dynamics technology.

RESULTS Among 82 vessels, 32 lesions (39%) had ischemia by invasive FFR (FFR ≤ 0.80). Sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratio of TAG (≤ −0.654 HU/mm) for detection of ischemia were 38%, 88%, 67%, 69%, 3.13, and 0.71, respectively; and those of FFR<sub>CT</sub> were 81%, 94%, 90%, 89%, 13.54, and 0.20, respectively. Receiver-operating characteristic curve analysis showed a significantly larger area under the curve (AUC) for FFR<sub>CT</sub> (0.94) compared to that for TAG (0.63, p < 0.001) and CCTA stenosis (0.73, p < 0.001). In vessels with noncalcified plaque or partially calcified plaque, FFR<sub>CT</sub> showed a larger AUC (0.94) compared to that of TAG (0.63, p < 0.001) or CCTA stenosis (0.70, p < 0.001). In vessels with calcified plaque, AUC of FFR<sub>CT</sub> (0.92) was not statistically larger than that of TAG (0.75, p = 0.168) or CCTA stenosis (0.80, p = 0.195).

CONCLUSIONS Noninvasive FFR computed from CCTA provides better diagnostic performance for the diagnosis of lesion-specific ischemia compared to CCTA stenosis and TAG. (J Am Coll Cardiol Img 2012;5:1088–96) © 2012 by the American College of Cardiology Foundation
Coronary computed tomography angiography (CCTA) is a noninvasive and accurate diagnostic tool to detect coronary artery disease (CAD), and is increasingly utilized in clinical practice. Diagnostic accuracy of 64-multidetector row CCTA has been validated in several multicenter trials, and the high negative predictive value establishes CCTA as an effective noninvasive alternative to invasive coronary angiography to rule out obstructive coronary artery stenosis (1,2). However, CAD stenosis by CCTA demonstrates an unreliable accuracy to define the lesion-specific ischemia (3). With a concern that widespread use of CCTA may result in excess referral of patients to invasive coronary angiography and unnecessary revascularization of nonischemic coronary lesions, several methods were developed and suggested to have the ability to evaluate for both anatomical and functional stenosis (4–6).

Transluminal attenuation gradient (TAG), defined as the linear regression coefficient between luminal attenuation and axial distance from the coronary ostium, is a novel concept that can evaluate the severity of coronary stenosis in CCTA, and has been validated against invasive coronary angiography (4,7). Computational fluid dynamics, as applied to CCTA images, enables prediction of blood flow and pressure in coronary arteries, and calculation of lesion-specific fractional flow reserve (FFR). The CCTA-derived computed FFR (FFR\textsubscript{CT}) was reported to have a high diagnostic performance for detection and exclusion of ischemia-causing stenosis (6). Both TAG and FFR\textsubscript{CT} can be computed from typically acquired CCTA scans without need of additional image acquisition or administration of medication, and were validated in 64-multidetector row CCTA (4,6). However, to date, the diagnostic value of these novel technologies has never been compared. In the present study, we aimed to compare the diagnostic performance of TAG and FFR\textsubscript{CT} derived from 64-multidetector row CT for the detection of lesion-specific ischemia, as determined by FFR performed at the time of invasive coronary angiography.

**METHODS**

**Patients.** From the prospective registry of the DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Non-Invasive Fractional Flow Reserve) study (6), 65 consecutive patients with suspected or known CAD who underwent CCTA, invasive coronary angiography, and FFR measurement in Seoul National University Hospital between October 27, 2009, and January 14, 2011, were included in this study. All patients were adults age \( \geq 18 \) years, had CCTA with \( \geq 50\% \) stenosis in a major coronary artery (\( \geq 2.0 \) mm diameter), and underwent clinically indicated invasive coronary angiography with FFR measurement. Patients with CCTA images that were determined as nonevaluable for FFR\textsubscript{CT} or TAG by each core laboratory were excluded. The institutional review board committee had approved this study.

**Protocol for CCTA and noninvasive coronary artery analysis by CCTA.** The CCTA was performed using a 64-detector row CT scanner (Somatom Definition, Siemens, Forchheim, Germany; Brilliance 64, Philips, Best, the Netherlands) (8). Oral metoprolol was administered for any patient with a heart rate \( \geq 65 \) beats/min. Immediately before image acquisition, 0.2 mg sublingual nitroglycerin was administered. During acquisition, 80 ml of contrast (Iomeron 400, Bracco, Milan, Italy) was injected followed by a saline flush. Helical scan data was obtained with retrospective electrocardiography gating. Image acquisition was prescribed to include the coronary arteries, left ventricle, and proximal ascending aorta. The scan parameters were as follows:

**ABBREVIATIONS AND ACRONYMS**

- AUC = area under the curve
- CAD = coronary artery disease
- CCTA = coronary computed tomographic angiography
- FFR = fractional flow reserve
- FFR\textsubscript{CT} = fractional flow reserve computed from coronary computed tomography angiography
- LR\textsubscript{(-)} = negative likelihood ratio
- LR\textsubscript{(+)} = positive likelihood ratio
- NPV = negative predictive value
- PPV = positive predictive value
- ROC = receiver-operating characteristics
- TAG = transluminal attenuation gradient
64 × 0.625 mm/0.750 mm collimation, tube voltage 100 kV to 120 kV, tube current 340 mA/800 mA, rotation time 330/400 ms. Radiation dose reduction strategies were employed when feasible, and doses ranged from 3 mSv to 15 mSv.

The CCTAs were analyzed in blinded fashion by an independent core laboratory (CVCTA, San Francisco, California) in accordance with the SCCT guidelines on CTA interpretation (9). The CTA images were evaluated using 3-dimensional workstations (Vital Images, Minneapolis, Minnesota; Ziosoft, Redwood City, California). The CCTAs were visualized by any post-processing method, including axial, multiplanar reformats, maximum intensity projection, and cross-sectional analysis. Coronary segments were scored in a semi-quantitative manner using an 18-segment SCCT model. In each segment, atherosclerosis was defined as tissue structures >1 mm² that existed within the coronary artery lumen or adjacent to the coronary lumen that could be discriminated from pericardial tissue, epicardial fat, or vessel lumen itself. Coronary lesions were quantified and expressed on an ordinal scale as 0 (none; diameter stenosis = 0%), 1 (very mild; 1% to 24%), 2 (mild; 25% to 50%), 3 (moderate; 50% to 69%), or 4 (severe; 70% to 98%). Plaque composition was classified as noncalcified (<30% calcified plaque volume), partially calcified (30% to 70%), or calcified plaque (>70%) according to the volume of calcified component (>130 HU) in the plaque (4).

Invasive coronary angiography image acquisition and FFR performance. Selective invasive coronary angiography was performed by standard catheterization in accordance with the American College of Cardiology guidelines for coronary angiography (10). The FFR was performed in clinically indicated vessels. After administration of nitroglycerin, a pressure-monitoring guidewire (PressureWire Cer tus, St. Jude Medical Systems, Uppsala, Sweden; ComboWire, Volcano Corporation, San Diego, California) was advanced past the stenosis. Hyperemia was attained by administration of intravenous (140 μg/kg/min) adenosine (11). The position of the distal pressure sensor was recorded to enable the FFRCT to be calculated at the same point as invasive FFR measurement. The FFR was calculated by dividing the mean distal coronary pressure by the mean aortic pressure during hyperemia. The FFR was considered diagnostic of ischemia at a threshold of ≤0.80 (12).

TAG and FFRCT. The TAG was measured in blinded fashion by an independent core laboratory (Samsung Medical Center, Seoul, Korea) using a dedicated workstation (GE Advantage Workstation 4.3, GE Healthcare, Milwaukee, Wisconsin) (Fig. 1). Cross-sectional images perpendicular to the automatically determined long-axis vessel centerline were reconstructed for each major coronary artery. The following variables were measured at 5-mm intervals: from the ostium to the distal level where the vessel cross-sectional area fell below 2.0 mm² by area; lumen cross-sectional area (mm²), which served as the region of interest, lumen mean diameter (mm), and luminal radiological attenuation (HU). The contour of the region of interest and the vessel centerline were manually corrected if necessary, which was typically the case at the site of the bifurcations. If there was significant variation of any variable within a 5-mm vessel long-axis interval, the average of 3 randomly selected levels within the interval was used. The TAG was determined from the change in HU per 10 mm length of coronary artery, and defined as the linear regression coefficient between intraluminal radiologic attenuation (HU) and length from the ostium (mm).

The FFRCT was measured in blinded fashion by core laboratory scientists at HeartFlow, Inc. (Redwood City, California), as previously described (6). Three-dimensional models of the coronary tree and ventricular myocardium were reconstructed using custom methods applied to blinded CTA data for simulation of coronary flow and pressure (13). Total resting coronary flow and the microvascular resistance were calculated according to ventricular mass and the size of the feeding vessel, respectively (14–18). A lumped parameter model representing the resistance to flow during simulated hyperemia was applied to each coronary branch of the segmented CTA model. The FFRCT core laboratory scientists were instructed as to the location within a coronary artery where the FFR was reported by an independent scientist who interpreted both the CTA and invasive angiography and who was not involved in the CTA, invasive angiography, FFR, FFRCT, or TAG analyses.

Statistical analyses. Categorical variables are presented as frequencies and percentages, with continuous variables as mean ± SD. The correlation between each modality was evaluated using Pearson’s correlation coefficient. Receiver-operating characteristics (ROC) curve analysis was used to assess the performance of CTA stenosis grade, TAG, and FFRCT to detect ischemia-causing stenosis. The area under the ROC curve (AUC) was calculated for CTA stenosis, TAG, and FFRCT, and AUCs were compared by the DeLong method. With an optimal cutoff value derived from ROC
curve analysis, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio [LR(+)], and negative likelihood ratio [LR(−)] were calculated on a per-vessel basis and expressed with corresponding 95% confidence interval. Statistical significance was determined by a p value \( \leq 0.05 \). All analyses were performed with the SPSS 18.0 statistical package (SPSS, Inc., Chicago, Illinois).

**RESULTS**

The CCTA studies from 65 patients with invasive coronary angiography and FFR were evaluated. After excluding 3 patients (4.6%) with nonevaluable CCTA for TAG and 9 patients (13.8%) with nonevaluable CCTA for FFR, 53 patients (age 63 ± 9 years; male, 74%) and 82 coronary arteries were included in the final analysis. Baseline characteristics are listed in Table 1.

Among 82 coronary arteries, 29% (24 of 82) were calcified lesion, and 71% (58 of 82) were noncalcified or partially calcified lesion. A total of 32 vessels of 82 (39%) showed lesion-specific ischemia (FFR \( \leq 0.80 \)). The TAG was significantly lower in vessels with ischemia (0.230 ± 0.475 HU/mm, \( p = 0.029 \)) compared to vessels without ischemia (0.584 ± 0.800 HU/mm, \( p = 0.029 \)). The FFR was also significantly lower in vessels with ischemia (0.658 ± 0.136) compared to vessels without ischemia (0.876 ± 0.759, \( p < 0.001 \)).

![Figure 1. Anatomically Obstructive Stenosis With No Functional Ischemia](image)

Figure 1 illustrates the correlation between TAG, FFR, and invasive FFR. Whereas TAG showed modest correlation with invasive FFR (\( r = 0.379, p < 0.001 \)) (Fig. 2A), FFR showed strong correlation with invasive FFR (\( r = 0.703; p < 0.001 \)) (Fig. 2B). In addition, modest correlation was observed between TAG and FFR (\( r = 0.351; p = 0.001 \)) (Fig. 2C).

The ROC curves of CCTA stenosis grade, TAG, and FFR for diagnosis of lesion-specific...
ischemia (invasive FFR ≤0.80) are illustrated in Figure 3. The ROC curve analysis for TAG showed an AUC of 0.63 (p = 0.037) with an optimal cutoff value of 0.654 HU/mm, and resulted in 12 true positives (14.6%), 44 true negatives (53.7%), 6 false positives (7.3%), and 20 false negatives (24.4%) (Fig. 4A). Sensitivity, specificity, PPV, NPV, LR(+) and LR(−) of TAG were 37.5% (21.7% to 56.3%), 88.0% (75.0% to 95.3%), 68.8% (55.8% to 79.4%), 3.13 (1.30 to 7.49), and 0.71 (0.54 to 0.93) (Table 2). The ROC curve analysis for FFRCT demonstrated an AUC of 0.94 (p < 0.001) with an optimal cutoff value of 0.77, and resulted in 26 true positives (31.7%), 47 true negatives (57.3%), 3 false positives (3.7%), and 6 false negatives (7.3%) (Fig. 4B). Sensitivity, specificity, PPV, NPV, LR(+) and LR(−) of FFRCT were 90.6% (73.8% to 97.5%), 84.0% (70.3% to 92.3%), 87.3% (70.3% to 92.3%), 5.66 (2.97 to 10.79), and 0.11 (0.04 to 0.33).

In the overall vessels, the AUC for TAG was not significantly different compared to that for CCTA stenosis (0.73, p = 0.217), whereas the AUC for FFRCT (0.94) was significantly larger than that for CCTA stenosis (0.73, p < 0.001) and compared to that for TAG (0.63, p < 0.001) (Fig. 3). A ROC curve analysis was also performed in each subgroup with noncalcified or partially calcified plaque and calcified plaque (Fig. 5). In a subgroup with noncalcified or partially calcified plaque (n = 58), the AUC for FFRCT (0.94) was larger compared to that for TAG (0.63, p < 0.001) and to that for CCTA stenosis (0.70, p < 0.001). In a subgroup with calcified plaque (n = 24), the AUC for FFRCT (0.92) was not different from those for TAG (0.75, p = 0.168) and CCTA stenosis (0.80, p = 0.195).

**DISCUSSION**

The present study demonstrated that FFRCT had better correlation with invasive FFR compared to TAG and that the diagnostic accuracy of FFRCT was superior to TAG for the diagnosis of ischemia-causing lesions as determined by an invasive FFR.

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**Table 1. Baseline Characteristics (N = 53)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>63.1 ± 8.9</td>
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<tr>
<td>Male</td>
<td>39 (74%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>34 (64%)</td>
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<tr>
<td>Diabetes mellitus</td>
<td>16 (30%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>30 (57%)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>7 (13%)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>24.5 ± 2.4</td>
</tr>
<tr>
<td>History of coronary artery disease</td>
<td></td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Prior revascularization</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td>61.2 ± 5.0</td>
</tr>
<tr>
<td>Laboratory value</td>
<td></td>
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<tr>
<td>Hemoglobin, mg/dl</td>
<td>13.7 ± 1.7</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>40.7 ± 4.6</td>
</tr>
<tr>
<td>Creatinine, mg/dl</td>
<td>1.0 ± 0.2</td>
</tr>
</tbody>
</table>

Values are mean ± SD or n (%).

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**Figure 2. Correlation of TAG, FFRCT, and Invasive FFR**

(A) A modest correlation (γ = 0.379) is observed between transluminal attenuation gradient (TAG) and invasive fractional flow reserve (FFR), whereas (B) a strong correlation (γ = 0.703) is observed between coronary computed tomography angiography (CCTA)-derived FFR (FFRCT) and invasive FFR. (C) A modest correlation (γ = 0.351) is also observed between TAG and FFRCT.
The annual CCTA examinations is estimated to be 2.3 million in the United States alone (19). The consistently high sensitivity (94% to 99%) and NPV (97% to 99%) in persons without known CAD highlights the ability of CCTA to detect and exclude obstructive coronary artery stenosis (1,2). Conversely, comparatively low specificity (64% to 83%) and PPV (48% to 86%) underscores an excessive rate of false positive CCTA findings. Further, the anatomical assessment of a coronary stenosis as determined by CCTA correlates poorly with the hemodynamic significance of the stenosis. In a previous study of 79 patients undergoing CCTA and invasive angiography with FFR measurements, the sensitivity of CCTA by visual estimation to detect lesions with a FFR $\leq 0.75$ was $0.94 (0.86 - 0.98)$ and $0.63 (0.52 - 0.74)$ for TAG and CCTA stenosis grade, respectively. However, the area under the curve for CCTA stenosis grade was $0.73 (0.62 - 0.82)$ compared to $0.94 (0.86 - 0.98)$ for FFRCT, which is significantly larger.

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**Figure 3.** ROC Demonstrating AUC for CCTA Stenosis, TAG, and FFRCT for Discrimination of Lesions That Cause Ischemia in Overall Vessels

Area under the receiver-operating characteristics (ROC) curve (AUC) on a per-vessel level for ischemia (fractional flow reserve [FFR] $\leq 0.80$) by computation of coronary computed tomography angiography (CCTA)-derived FFR (FFRCT) is significantly larger than that of transluminal attenuation gradient (TAG) or CCTA stenosis grade. CI = confidence interval.

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**Figure 4.** Distribution of TAG and FFRCT Values According to Presence of Lesions That Cause Ischemia

Distribution of (A) transluminal attenuation gradient (TAG) and (B) coronary computed tomography angiography (CCTA)-derived FFR (FFRCT) values according to the presence of ischemia by FFR $\leq 0.80$ were illustrated with the number of true positive, true negative, false positive, and false negative discriminated by the cutoff value of TAG $\leq -0.654$ and FFRCT $\leq 0.77$. 

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high (94%), whereas the specificity to detect such lesion was poor (40%) (3). It is not unexpected because the diameter stenosis is a poor indicator of myocardial ischemia, even by invasive coronary angiography, and discrepancy between the severity of stenosis and a noninvasive stress test is not uncommon (20,21). Considering the role of CCTA as gatekeeper for invasive coronary angiography, these findings have raised concerns that false positive CCTA findings may precipitate unnecessary referral for invasive angiography and revascularization, accompanied by substantial cost to the patient and to the healthcare system.

Comprehensive noninvasive anatomical and functional imaging would be desirable to identify patients who are likely to benefit from invasive coronary angiography and revascularization (22). The TAG, defined as the gradient of intraluminal radiological attenuation, is a novel process that can evaluate the severity of coronary artery stenosis. In a previous study by Choi et al. (4), TAG was measured in 370 major coronary arteries by using 64-multidetector row CCTA. Compared to diameter stenosis on CCTA and invasive angiography, TAG decreased consistently and significantly with maximum stenosis severity; it was also significantly correlated with the velocity of coronary flow evaluated by TIMI (Thrombolysis In Myocardial Infarction) frame count. However, in the study, TAG was not compared to other functional studies, including

| Table 2. Diagnostic Performance of CCTA Stenosis, TAG, and FFRCT |
|------------------|------------------|------------------|
|                  | Per-Vessel Analysis (n = 82) |
|                  | CCTA Stenosis ≥70% (95% CI) | TAG < -0.654 HU/mm (95% CI) | FFRCT < 0.77 (95% CI) |
| Sensitivity       | 71.9 (53.0–85.6)    | 37.5 (21.7–56.3)    | 81.3 (63.0–92.1)    |
| Specificity       | 68.0 (53.2–80.1)    | 88.0 (75.0–95.3)    | 94.0 (82.5–98.4)    |
| PPV               | 59.0 (42.2–74.0)    | 66.7 (41.2–85.6)    | 89.7 (71.5–97.3)    |
| NPV               | 79.1 (63.5–89.4)    | 68.8 (55.8–79.4)    | 88.7 (76.3–95.3)    |
| LR(+)             | 2.25 (1.42–3.55)    | 3.13 (1.30–7.49)    | 13.54 (4.46–41.08)  |
| LR(−)             | 0.41 (0.23–0.73)    | 0.71 (0.54–0.93)    | 0.20 (0.10–0.41)    |

CCTA = coronary computed tomographic angiography; CI = confidence interval; FFRCT = fractional flow reserve computed from coronary computed tomography angiography; LR(+) = positive likelihood ratio; LR(−) = negative likelihood ratio; NPV = negative predictive value; PPV = positive predictive value; TAG = transluminal attenuation gradient.

Figure 5. ROC Demonstrating AUC for CCTA stenosis, TAG, and FFRCT for Discrimination of Lesions That Cause Ischemia in Vessels With Noncalcified or Partially Calcified Plaque and in Vessels With Calcified Plaque

(A) Area under the receiver-operating characteristic (ROC) curve (AUC) on a per-vessel level for ischemia (fractional flow reserve [FFR] ≤0.80) by computation of coronary computed tomography angiography (CCTA)-derived FFR (FFRCT) (pink line) is significantly larger than that of transluminal attenuation gradient (TAG) (green line) or CCTA stenosis grade (broken gray line) in vessels with noncalcified or partially calcified plaque. (B) In vessels with calcified plaque, the AUC for FFRCT was comparable to those for TAG and CCTA stenosis grade.
Ffr or myocardial perfusion imaging. Computation of Ffr from CCTA data (FFR_{CT}) provides a noninvasive method for identifying ischemia-causing stenosis. In the DISCOVER-FLOW study, the FFR_{CT} was computed in 159 major coronary arteries, compared to Ffr performed at the time of invasive angiography (6). The FFR_{CT} is well correlated with invasive Ffr, and showed high diagnostic performance for the detection and exclusion of coronary lesions that cause ischemia. Although CT myocardial perfusion imaging or other fusion images such as CT/positron emission tomography and CT/single-positron emission computed tomography also have the potential to assess the hemodynamic significance of an anatomical lesion, they require additional iodine contrast injection and radiation exposure, whereas FFR_{CT} or TAG can be computed from typically acquired CCTA scans without any modification of CCTA protocols, additional image acquisition, or administration of medication.

In the present study, TAG, and FFR_{CT} were measured in blinded fashion by independent core laboratories and compared to direct measurement of Ffr during invasive coronary angiography as a reference standard. For the detection or exclusion of lesion-specific ischemia, FFR_{CT} improved the diagnostic accuracy, as evidenced by a high AUC 0.94 compared to CCTA stenosis grade (AUC 0.73), although TAG could not (AUC 0.63). The most important difference was that FFR_{CT} was computed from simulated hyperemia, whereas TAG measured from the resting state. Although TAG was related not only to TIMI coronary flow but also to the stenosis severity (4,7), the ability to identify abnormal resting coronary flow in non-flow-limiting stenosis has limited value. In our study, an optimal cutoff value of TAG \( \leq -0.654 \text{ HU/mm} \) resulted in a high proportion of false negative (20 of 82, 24.4%), and consequently, worse sensitivity, NPV, and LR(−) (37.5%, 68.8%, and 0.71, respectively) even compared to those from CCTA stenosis with an optimal cutoff value of \( \geq 70\% \) (71.9%, 79.1%, and 0.41, respectively). The diagnostic value of TAG for the detection of ischemia-causing lesions is expected to be improved in conjunction with pharmacologic stress. However, at the same time, CCTA imaging performed during adenosine infusion increases heart rate, and the likelihood of artifact caused by heart motion could affect the performance of TAG. Future study is required to evaluate the feasibility and diagnostic value of stress TAG.

In this study, CCTA was performed with a 64-slice multidetector row CT scanner. It takes \( >1 \) cardiac cycle to cover the entire heart in the long axis of the patient, and intracoronary attenuation is not measured at the same time in the entire coronary tree. Lack of temporal uniformity might limit the diagnostic performance of TAG in the present study. Single-beat imaging with use of newly introduced newer scanners with wide-area coverage that can image the entire coronary tree at the same time instant during 1 cardiac cycle may improve the diagnostic performance of TAG.

Still, TAG might be useful in patients with imponderable coronary segments, such as severe coronary calcification or coronary stents. In a previous study by Choi et al. (4), the addition of TAG on visual estimate of CCTA resulted in reclassification from 1 class of stenosis severity to another in a significant number of vessels with calcified lesions, but not in noncalcified lesions. In the present study, the difference in the diagnostic accuracy between TAG and FFR_{CT} were narrower in calcified vessels compared to that in noncalcified or partially calcified vessels. However, it is not because of decline of diagnostic accuracy of FFR_{CT} in calcified vessels, but may possibly be due to improvement of diagnostic performance of TAG. Because the number of vessels with calcified plaque is limited in this study, further study with a larger number of patients is required to assess the diagnostic performance of TAG and FFR_{CT} according to the plaque characteristics.

Study limitations. First, this study was a single-center retrospective analysis of a prospectively enrolled cohort. The relatively small number of study subjects is another limitation. Moreover, patients who underwent clinically indicated invasive coronary angiography and Ffr as well as CCTA were enrolled in this study. Therefore, the ability to assess the diagnostic performance of FFR_{CT} and TAG in all consecutive patients undergoing CCTA was impossible. Finally, our study does not provide outcome data. Further study is warranted to determine whether these noninvasive functional parameters by using CCTA might have incremental prognostic value, acknowledging the limitations of CCTA and anatomic imaging.

Conclusions

Noninvasive Ffr derived from typically acquired CCTA images (FFR_{CT}) provides better diagnostic...
performance for detecting and excluding coronary artery lesions that cause ischemia compared to gradient of intraluminal radiological attenuation across lesion (TAG) or visual stenosis grade on CCTA.

REFERENCES


Key Words: cardiac computed tomography • diagnosis • fractional flow reserve • ischemia.