Technical development has enabled expanded and reliable use of coronary computed tomographic angiography (CCTA) for obstructive coronary artery disease (CAD) detection.\(^1,2\) Potentially, CCTA can be applied to a wider patient population when compared with catheter angiography (CAG), a long-standing reference standard for a diagnosis of CAD. The appropriateness of CCTA is determined based on patient clinical scenario and pre-test probability of CAD. The ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 Appropriate Use Criteria for Cardiac CT (AUC2010)\(^3\) is among the most widely used guidelines, classifying 93 different clinical scenarios into Appropriate, Inappropriate, and Uncertain indications for a CCTA. Prior stress imaging or CAG results are incorporated into the AUC2010 decision algorithm; periodic repeat CCTAs are defined as Inappropriate for asymptomatic patients or those with stable symptoms regardless of the results of prior stress imaging or CAG. For those with new/worsening symptoms, the guideline considers CCTA as Appropriate only if the prior stress imaging study was normal. Prior CCTA results, however, are not incorporated into this guideline.

**Background**—ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 Appropriate Use Criteria for Cardiac Computed Tomography (AUC2010) does not incorporate prior coronary computed tomographic angiography (CCTA) results in the appropriateness of a CCTA examination. The purpose of this study was to explore the criteria for forgoing repeat CCTA among patients with clinical scenarios suggesting CCTA as appropriate after prior CCTA excluding coronary artery disease.

**Methods and Results**—Among patients from a single center (February 2006 to April 2013) who underwent appropriate CCTA based on AUC2010, consecutive 555 CCTAs, which had a prior CCTA excluding significant stenosis (>50% stenosis in diameter), were selected. The median time difference between the studies was 34.2 (Q1–Q3, 22.9–50.1) months. Significant stenosis was detected at the time of repeat scan (by CCTA or subsequent catheter angiography) in 13.3% (74 of 555). A multivariable logistic model (C-statistic, 0.74; bootstrapped overfitting bias, 0.8%) identified 3 predictors of significant stenosis: time difference between the studies >3 years (adjusted odds ratio, 2.1; 95% confidence interval, 1.2–3.5), diabetes mellitus (odds ratio, 2.4; 95% confidence interval, 1.4–4.3), and 26% to 50% stenosis on the initial CCTA (odds ratio, 5.6; 95% confidence interval, 3.2–9.6). When these 3 factors were all absent (corresponding to 31.9% of the population), the probability of significant stenosis was 4.5% (95% confidence interval, 2.7–7.4%), whereas 17.1% of patients had significant stenosis among those with at least 1 positive variable. When coronary arteries were completely normal at the initial scan, the prevalence of significant stenosis was only 1.8% irrespective of other factors, and no patient underwent revascularization.

**Conclusions**—Nondiabetic patients with a prior CCTA <3 years showing no or ≤25% stenosis had a <5% prevalence of significant stenosis. The value of repeat CCTA in this group is likely small, especially when the prior CCTA demonstrated normal coronaries, even if the clinical scenario considered a CCTA appropriate. (Circ Cardiovasc Imaging. 2014;7:788-795.)

**Key Words:** coronary artery disease ■ coronary vessels ■ multidetector computed tomography ■ risk factors

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explore the criteria for forgoing repeat coronary CCTA among patients with clinical scenarios suggesting CCTA as appropriate after prior CCTA excluding significant stenosis.

**Methods**

**Population**

This retrospective Health Insurance Portability and Accountability Act-compliant study was approved by the human subjects review board at the institution. For patients who provided informed consent, clinical data were prospectively collected and recorded at the time of CT acquisition for research purposes. CCTA findings were also added to the database after a systemic review of the images, as detailed below. Among all scans during the period of 7 years (February 2006 to April 2013), a retrospective review of the database identified a total of 625 CCTA studies that met the following inclusion criteria:

1. A prior CCTA of the same patient performed at the same institution during the study period identified no significant stenosis;
2. The patient had no known history of CAD or infection/inflammatory condition (e.g., aortitis or Kawasaki disease) at the time of CT.

For these 625 repeat CCTAs, the appropriateness of indication was determined by reviewing the recorded clinical data; history, reasons for CT provided by the referring physicians, symptoms, prior ECG or stress test results, and pre-test probability when available.

The indication for repeat CCTA was then classified into Appropriate (n=555), Inappropriate (n=16), and Uncertain (n=54) based on the AUC2010; all 555 Appropriate repeat CCTA studies formed the current study cohort.

**Imaging Acquisition**

Scanning was performed using either a 64-detector row CT (Aquilion 64; Toshiba Medical Systems Corporation) or a 320-detector row CT (Aquilion ONE V4-51; Toshiba Medical Systems Corporation). Based on the CCTA findings and clinical assessment, 73 patients underwent CAG <2 weeks after the repeat CCTA. Details of CT acquisition, image postprocessing, and CAG technique are described elsewhere.4,5

**Stenosis Interpretation**

Coronary stenosis was evaluated by a consensus reading of 2 cardiovascular imagers (team 1) who were unaware of the clinical information. The CCTA and CAG images were interpreted separately and without knowledge of the other examination. For CCTA, thin-section (0.25–0.3 mm) images were reformatted to planes appropriate for interpretation, and stenosis was graded using images orthogonal to the coronary center line, based on the American Heart Association 16-segment model.4 For CAG, all projections were reviewed.

For both CCTA and CAG, the stenosis was classified into none (0%), 1% to 25%, 26% to 50%, 51% to 75%, 76% to 99%, and 100% of the luminal diameter. As noted above, positive for significant stenosis was defined when at least 1 segment had stenosis with >50% in diameter. For CCTA interpretation, the study was considered indeterminate when the evidence for significant stenosis was not definitive because of calcification or motion artifact.

**Clinical Data Collection**

An attending cardiologist with >10 years of experience in CCTA met all patients in the CT preparation room and directly took a clinical history, risk factors, symptoms, prior ECG or stress tests, and pre-test probability when available.

Blood pressure was measured on the CT couch in the supine position. The lipid profile, blood sugar, and hemoglobin A1c <3 months of CCTA were also obtained from the electronic medical records. The Duke Clinical Score14 pre-test probability of obstructive CAD was calculated when all necessary information was available. These clinical data were prospectively recorded in a research database at the time of CCTA.

For each patient in the study cohort, a retrospective review of the database was performed to collect relevant information. Risk factor definitions are as follows: hypertension—blood pressure >140/90 mm Hg or the use of antihypertensive medications; diabetes mellitus—fasting blood sugar >126 mg/dL, postprandial blood sugar >200 mg/dL, hemoglobin A1c >6.5%, or the use of medications; hyperlipidemia—total cholesterol >220 mg/dL, low-density lipoprotein cholesterol >140 mg/dL, fasting triglycerides >150 mg/dL, high-density cholesterol <40 mg/dL, or the use of lipid-lowering medications; current smoking—patients who had smoked during the past 1 year from the time of CCTA acquisition; history of cerebral infarction—with a history of hospitalization for cerebral infarction or those who showed hemiplegia because of cerebral infarction at the time of CCTA acquisition; typical angina9—chest pain/discomfort that meets all 3 of the following criteria: (1) substernal chest pain, (2) provoked by exertion or emotional stress, and (3) relieved by rest or nitroglycerin; atypical angina9—chest pain/discomfort with 2 characteristics of typical angina; nonanginal chest pain9—chest pain/discomfort that meets either 1 or none of the typical angina characteristics.

Because the AUC2010 does not consider CCTA appropriate for asymptomatic patients or patients with stable symptoms, the cohort included only patients with new/worsening symptoms.

**Statistical Methods**

**Prediction of Significant Stenosis**

Patients with significant stenosis at the time of repeat CCTA were identified from CAG when available and from CCTA for those patients for whom CAG was not performed. Indeterminate CCTA studies were considered negative for stenosis in the main analysis. Baseline characteristics were compared between those with and without significant stenosis, using an unpaired t test for normally distributed continuous variables, Fischer exact test for categorical variables, and Wilcoxon rank-sum test for non-normally distributed variables.

A multivariable logistic regression model was created to predict significant stenosis at the time of repeat CCTA by including age, sex, and all variables that showed a P value <0.1 in the univariate analysis. The final model included only those variables with a P value <0.05 in the initial multivariable model to build a parsimonious model that has small number of variables with meaningful predictability for straightforward clinical implementation. Model fit of the final model was assessed by Hosmer–Lemeshow test and Pearson goodness-of-fit test, and C-statistic was calculated as the discriminatory power of the model. The bootstrap method was used for internal validation of the prediction model (1000 resamples); the percent difference between the apparent C-statistic (ie, computed from the main model) and the bootstrapped C-statistic was calculated as an indicator of overfitting.

Because some patients received ≥2 repeat CCTAs, generalized estimating equations were used to account for intrapatient correlation and obtain robust standard errors.10

**Inter-/Intraobserver Variability in Stenosis Evaluation**

A total of 56 CCTAs were selected from the cohort to evaluate inter-/intraobserver variability in the assessment of stenosis and the effect of the presence of each predictor on the variability. For this subset, we selected patients whose overall prevalence of each of the factors was 50% to compare variability between those with and without predictors. Otherwise samples were selected randomly based on the medical record number. A separate team including 2 cardiovascular imagers (team 2) that was blinded to the main results assessed the coronary stenosis and repeated the assessment after 1 week. Inter-/intraobserver variability was evaluated by the k statistic and the Kruskal–Wallis test compared the percent agreement rates between those with and without significant predictors.

**Test Characteristics**

Using CAG as a reference standard (n=73), we calculated sensitivity, specificity, positive predictive value, negative predictive value, and accuracy (% of true positive plus true negative) of CCTA for the detection of significant stenosis.

**Sensitivity Analysis**

Indeterminate CCTA studies were considered positive for significant stenosis, and the prevalence of significant stenosis and test characteristics
of the CCTA were reanalyzed. All statistical analyses were performed on STATA version 11.2 (Stata Corp, College Station, TX).

Results

Population

A total of 555 repeat CCTA studies were analyzed from 492 patients; 48, 6, and 1 patient, respectively, received 2, 3, and 4 repeat studies. For patients with ≥2 repeat scans, each repeat scan was compared with the initial scan. The median time difference between the first and repeat study was 34.2 months (Q1–Q3, 22.9–50.1 months).

Detection of Significant Stenosis

Among the 555 repeat CCTA studies, at least 1 significantly stenotic segment was detected by CCTA for 68 cases (12.3%). Thirty-three cases (5.9%) were categorized as indeterminate. The CAG (performed in 49 patients with significant stenosis on CCTA plus in 24 patients with an indeterminate CCTA) detected at least 1 significant stenosis in 55 patients; 54 of them received percutaneous coronary intervention subsequently. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the CCTA were 76.4%, 83.3%, 93.3%, 53.6%, and 78.1%, respectively. The final number of cases with significant stenosis was 74 (13.3%; 55 confirmed by CAG plus 19 detected by CCTA without performing CAG).

Prediction of Significant Stenosis

Tables 1 and 2 summarize the clinical and imaging characteristics for those with (n=74) versus without (n=481) significant stenosis. Status of diabetes mellitus at the time of repeat CCTA and the maximum stenosis detected on prior CCTA was significantly different between the groups. For the prediction model below, information on previous stenosis was included as binary variable (0–25% or 26–50%) for simplicity.

The initial and final multivariable logistic models are presented in Table 3. The final model included presence of diabetes mellitus at the time of repeat CCTA and the maximum stenosis detected on prior CCTA (adjusted odds ratio, 2.42; 95% confidence interval, 1.35–4.34), >3 years of time difference between the scans (odds ratio, 2.06; 95% confidence interval, 1.22–3.48), and having at least 1 segment with 26% to 50% stenosis on prior CCTA images (odds ratio, 5.57; 95% confidence interval, 3.24–9.58). The model had good discrimination (C-statistic, 0.74) with the Hosmer–Lemeshow χ² statistic of 1.94 (P value for lack of fit=0.75) and Pearson χ² of 3.29 (P value for lack of fit=0.51). The bootstrapped C-statistics was 0.73, and thus the overfitting bias was 0.8%.

Among the patients with all these factors absent (corresponding to 31.9% of the population), the probability of having significant stenosis was 4.5% (95% confidence interval, 2.7–7.4%; Table 4; Figure 1), whereas significant stenosis was detected in 17.1% of patients with at least 1 positive factor among the 3 (Figures 2 and 3). The observed prevalence of CAG-confirmed stenosis and the prevalence of patients undergoing percutaneous coronary intervention were 3.4% among the patients with all 3 factors being negative (Table 4). Among patients who had 0% stenosis (ie, normal coronary arteries) based on the initial CCTA scan (n=165; median time interval, 41.9 (24.5–56.3) mo), >3 y since prior CCTA, % 44.1% 55.4% 0.068 BMI, kg/m² 23.4±2.6 23.6±3.1 0.59 BMI difference between scans, kg/m² −0.21±1.22 −0.10±1.19 0.47 Type of chest pain, %

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Type of chest pain, %

Typical chest pain 12.2 6.4 0.099 Atypical chest pain 58.1 68.8 Nonanginal symptom 29.7 24.7

Family history of CAD, %

30.6 (72) 27.2 (464) 0.55 Diabetes mellitus, † %

Known 28.4 15.2 0.029 Newly diagnosed 2.7 1.9 Controlled 0.0 1.7 Never 68.9 81.3 Dyslipidemia, † %

Known 71.6 61.5 0.33 Newly diagnosed 8.1 9.2 Controlled 5.4 5.4 Never 27.0 34.4 Smoking, † %

Known 13.5 14.7 0.13 Newly started 0.0 1.0 Stopped 8.1 2.7 Never 73.4 81.5 History of cerebral infarction, † %

Known 5.4 5.0 0.75 Newly diagnosed 0.0 1.5 Never 94.6 93.6 Chronic kidney disease, † %

Never 94.6 93.6

Pretest probability from Duke Clinical Score* (no. of patients with available data) 59.9±5.8 (65) 55.2±26.3 (373) 0.18

BMI indicates body mass index; CAD, coronary artery disease; and CCTA, coronary computed tomographic angiography.

*At the time of repeat CCTA study.

†Known: observed at the time of both prior and repeat CCTA studies; newly diagnosed/started: observed only at the time of repeat CCTA; controlled/stopped: observed only at the time of prior CCTA; never: not observed at the time of both prior or repeat CCTA.
36.9 months), only 1.8% (n=3) developed a significant stenosis irrespective of other factors, and none of these patients underwent percutaneous coronary intervention.

**Inter-/Intraobserver Variability**

Overall inter-/intraobserver agreements were good (κ=0.704–0.765). The inter-/intraobserver variability between the groups with and without the predictive factors was nonsignificant (Table 5).

**Sensitivity Analysis**

When classifying indeterminate CCTA studies into positive for significant stenosis, the sensitivity, positive predictive value, and accuracy of CCTA were 100%, 78.1%, and 78.1%, respectively. The specificity was 0%, and the negative predictive value was not able to be calculated because all CCTAs undergoing CAG were positive for stenosis under this definition.

The total number of examinations with significant stenosis increased to 79, but all additional cases had at least 1 positive variable identified in the final model. Therefore, the observed prevalence of patients having significant stenosis among those with all factors being negative was the same as that from the main analysis (4.5%).

**Discussion**

Nondiabetic patients with a prior CCTA <3 years showing no or ≤25% stenosis had <5% prevalence of significant stenosis at the time of repeat CCTA. Among patients with normal coronary arteries on the initial scan, the overall prevalence of significant stenosis was only 1.8%, irrespective of other factors. Moreover, no patient in this group underwent revascularization. Because this was not a prospective study, our cohort is a selected population for whom clinicians had a clinical suspicion for the interval development of CAD, despite a prior negative CCTA. In addition, >50% stenosis in diameter is a conservative outcome; we acknowledge that adverse cardiac events are the ideal study outcome because not all lesions of this type may cause ischemia. The current data thus cannot discriminate those patients who should receive a repeat scan, but supports that while using this conservative outcome in a high-risk population, patients in the identified subgroup have little chance to have diseased coronary vessels. One would expect the prevalence of significant stenosis needing treatment to be much lower if similar criteria were applied to a general population with indications for repeat CCTA.

Assessment of the value of any repeat study is of high interest for screening and follow-up. Although recent technologies have reduced radiation dose and contrast usage for CCTA, a comprehensive risk–benefit assessment remains mandatory. Although there is a descriptive study reporting that 22 out of 23 patients without CAD on the initial CCTA had no stenosis on the subsequent scan (median interval=27.3 months), the current study is the initial report on the prediction of significant stenosis on a repeat scan after a prior nonsignificant CCTA. In the AUC2010, repeat CCTA is not recommended for patients without symptoms or with stable symptoms. We found that even among patients with new/worsening symptoms, the probability of significant stenosis on repeat CCTA is low in a subgroup of patients meeting specific criteria. We think that future expansion of scenarios by including prior CCTAs will improve extant guidelines, contribute to safe and

### Table 2. Imaging Characteristics on Prior CCTA

<table>
<thead>
<tr>
<th>Maximum stenosis, %</th>
<th>Significant Stenosis Detected (n=74)</th>
<th>No Significant Stenosis Detected (n=481)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>4.1</td>
<td>33.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1–25%</td>
<td>40.5</td>
<td>46.8</td>
<td></td>
</tr>
<tr>
<td>26–50%</td>
<td>55.4</td>
<td>19.5</td>
<td></td>
</tr>
<tr>
<td>No. of 26–50% stenotic segments, %</td>
<td>0 44.6</td>
<td>80.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>1 32.4</td>
<td>16.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 12.2</td>
<td>2.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 6.8</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 2.7</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 1.4</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Presence of risky plaque,* %</td>
<td>12.2</td>
<td>6.0</td>
<td>0.078</td>
</tr>
</tbody>
</table>

CCTA indicates coronary computed tomographic angiography.

*Risky plaques defined as those having a necrotic core (<30 Hounsfield Unit) and positive remodeling index (>1.1).

### Table 3. Multivariable Logistic Regression Models for Prediction of Significant Stenosis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Initial Model</th>
<th>Final Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>P Value</td>
</tr>
<tr>
<td>Age*</td>
<td>1.01</td>
<td>0.45</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.17</td>
<td>0.57</td>
</tr>
<tr>
<td>≥1 26–50% stenosis on a prior CCTA</td>
<td>5.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus*</td>
<td>2.50</td>
<td>0.002</td>
</tr>
<tr>
<td>Time difference &gt;3 y</td>
<td>1.97</td>
<td>0.013</td>
</tr>
<tr>
<td>Hypertension*</td>
<td>1.76</td>
<td>0.068</td>
</tr>
<tr>
<td>Typical chest pain*</td>
<td>1.95</td>
<td>0.10</td>
</tr>
<tr>
<td>Risky plaque*</td>
<td>1.62</td>
<td>0.30</td>
</tr>
</tbody>
</table>

CCTA indicates coronary computed tomographic angiography; CI, confidence interval; and OR, odds ratio.

*At the time of the repeat CCTA study.
appropriate care of patients, and will lead to efficient use of resources in patient management.

Our final prediction model includes only 3 significant predictors because our aim was to include the smallest number of variables with meaningful predictability so that the model can be simple enough to be used in the clinical setting. Diabetes mellitus is a strong risk factor for obstructive CAD and accelerates progression of atherosclerosis. The current data highlight the benefit to evaluate diabetic status whenever a repeat CCTA is considered for patients with new/worsening symptoms. Previously reported risk factors of rapid stenosis progression (male sex, smoking status, and younger age) are not significant predictors in the current study, most likely because of the difference in populations. A lesion with between 26% and 50% coronary stenosis on prior CCTA images was the strongest predictor in the current study. Although lesion-by-lesion analysis was beyond the scope of this study, we hypothesize that the significant lesions on repeat study represent progression from nonsignificant ones as opposed to de novo lesions, as shown in the figures. A normal initial scan was associated with low prevalence of >50% stenosis at the repeat scan. In conjunction with previous literature showing that patients with nonobstructive lesion had higher event rates than those with normal CCTA, our data may support that lesions with mild to moderate stenosis can become more important clinically.

The time interval between CCTA studies is intuitive as a predictor of new stenosis, consistent with the previous CAG studies. We identified a 3-year cutoff based on the data distribution, but more data may be needed to identify the most appropriate and clinically relevant cutoff; the safe interval could be >3 years in a general population with indications for repeat CCTA, given the conservative definition of outcome in this study and a selection bias among those patients referred for the study. Given the fact that no patient with 0% stenosis at the initial scan received percutaneous coronary intervention during the study period, and based on the previous study reporting 100% cumulative cardiac event–free survival for patients with normal coronary arteries, this subgroup could have >5 years of safe interval and should be differentiated from others.

The AUC incorporates either a prior or contemporary coronary artery calcium score into the decision algorithm. Although we acknowledge that the calcium score is associated with the risk of future cardiovascular events, our model did not include calcium scoring at the time of prior CCTA because these data were not acquired for some patients. We also did not include calcium scoring at the time of repeat CCTA study because (1) our goal was to detect the subpopulation with low probability of significant stenosis in whom CT could be avoided altogether, and (2) the specificity of calcium scoring

### Table 4. Probability and Observed Prevalence of Significant Stenosis

<table>
<thead>
<tr>
<th>Diabetes Mellitus*</th>
<th>Interval &gt;3 y</th>
<th>26–50% Stenosis on Prior CCTA</th>
<th>% of Population</th>
<th>Calculated Probability (95% CI)</th>
<th>Overall Stenosis†</th>
<th>CAG-Confirmed Stenosis</th>
<th>Percutaneous Coronary Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>1.8%</td>
<td>55.8% (39.5–70.9)</td>
<td>70%</td>
<td>50%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>–</td>
<td>4.0%</td>
<td>38.1% (25.4–52.6)</td>
<td>36.4%</td>
<td>31.8%</td>
<td>31.8%</td>
<td></td>
</tr>
<tr>
<td>–</td>
<td>+</td>
<td>7.7%</td>
<td>34.4% (24.2–46.2)</td>
<td>34.9%</td>
<td>20.9%</td>
<td>20.9%</td>
<td></td>
</tr>
<tr>
<td>–</td>
<td>–</td>
<td>10.8%</td>
<td>20.4% (13.6–29.4)</td>
<td>18.3%</td>
<td>13.3%</td>
<td>10.0%</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>–</td>
<td>5.4%</td>
<td>18.8% (11.3–29.8)</td>
<td>10.0%</td>
<td>10.0%</td>
<td>10.0%</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>–</td>
<td>7.7%</td>
<td>10.2% (5.8–17.3)</td>
<td>14.0%</td>
<td>9.3%</td>
<td>9.3%</td>
<td></td>
</tr>
<tr>
<td>–</td>
<td>+</td>
<td>30.6%</td>
<td>8.8% (5.8–13.0)</td>
<td>9.4%</td>
<td>5.9%</td>
<td>5.9%</td>
<td></td>
</tr>
<tr>
<td>–</td>
<td>–</td>
<td>31.9%</td>
<td>4.5% (2.7–7.4)</td>
<td>4.5%</td>
<td>3.4%</td>
<td>3.4%</td>
<td></td>
</tr>
</tbody>
</table>

CAG indicates catheter angiography; CCTA, coronary computed tomographic angiography; and CI, confidence interval.

*At the time of the repeat CCTA.

†Significant stenosis detected by CAG if available and by CCTA if CAG was not performed.

**Figure 1.** Multiplanar reformatted coronary computed tomographic angiography images of the left anterior descending artery from a nondiabetic 72-year-old man performed in December 2009 (A) and in May 2011 (B) when the patient had substernal chest pain at night that was relieved by nitroglycerin. The 90% stenosis was detected in the proximal segment in May 2011 and was revascularized.
to diagnose obstructive CAD is low, with a high false-positive rate, when applied to low-risk populations.26

Detection of hemodynamically significant coronary stenosis or vulnerable plaque would have served as better study outcomes. However, at present, hemodynamic significance is clinically measured by fractional flow reserve on CAG and is often not performed routinely. Recent advances in computational fluid dynamics enable calculation of coronary flow on CCTA images.27,28 These are promising metrics but are still experimental. Plaque component analysis based on the CT number is becoming popular, but it still needs further validation or improvement to be reliably used as an outcome measure.29

The strength of this article is that we have a large clinical population that underwent repeat CCTA after a prior CCTA excluding significant stenosis. This is partly because of the high availability of CT devices in Japan with 97.3 scanners per million individuals, 3 times the ratio in the United States.30 A similar sized study population may not be obtained in a country where CT is less available, nor would the population from those countries be as representative of those with appropriate indication as ours. An ideal setting for the current study would be a prospective cohort of patients with appropriate indication all undergoing repeat CCTA. Because a study of this type is ethically difficult to justify, a study using the current database is likely to be the next best option.

There are limitations to this study. First, this is a single-center study with single ethnicity and lacks external validation. Ethnicity can influence the probability of significant stenosis.31

Specifically, the prevalence of CAD is low in Japan.32,33 Moreover, with 74 events, the study only has modest precision and statistical power. We think that identified predictors are reasonable and recommend an external validation as the next step. Second, we did not include the details of medical treatment and follow-up after the prior CCTA. These data are not applied in the current guidelines, and it was assumed that patients were managed with best practice standards. Although the current database is from a specialized cardiac institution with sufficient board-certified cardiologists, future studies

| Table 5. Inter-/Intraobserver Agreements in the Assessment of Coronary Stenosis on CCTA |
|-------------------------------------|-------|-------|-------|-------|
| Overall                            | 0.704 | 85.7% | 0.732 | 87.5% | 0.765 | 89.3% | 0.95 |
| Diabetes mellitus                   | 0.655 | 82.1% | 0.728 | 85.7% | 0.780 | 89.3% | 0.69 |
| Time interval >3 y                  | 0.752 | 89.3% | 0.718 | 89.3% | 0.739 | 89.3% | 0.51 |
| 26–50% stenosis on prior CCTA       | 0.646 | 78.6% | 0.786 | 85.7% | 0.698 | 82.1% | 0.23 |

CCTA indicates coronary computed tomographic angiography.
*Values from Kruskal–Wallis test.
should evaluate the effects of these preventive treatments during the CCTA interval. Third, we acknowledge that the luminal stenosis is not the only factor to be considered as outcome, as described above. Flow-limiting lesions with low fractional flow reserve or the collection of major adverse cardiac events would be the ideal outcome. These data were not available and represent a limitation to the current study.

Conclusions
Non-diabetic patients for whom a prior CCTA <3 years showed no or ≤25% coronary stenosis had low prevalence of obstructive CAD, even if the clinical scenario considered a CCTA examination appropriate. Patients with completely normal coronary arteries at the initial scan had only 1.8% prevalence of significant stenosis irrespective of other factors. After further validation, these findings may contribute to expanding the clinical guideline scenarios, resulting in improvement of appropriate patient care and efficient use of resources.

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Disclosures
Dr. Rybicki has a research agreement with Toshiba Medical Systems Corporation that is unrelated to this project. The other authors report no conflicts.

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**CLINICAL PERSPECTIVE**

Coronary computed tomographic angiography (CCTA) examines coronary arteries to detect obstructive coronary artery disease (CAD). Although CCTA is less invasive than catheter angiography, a long-standing gold standard for CAD diagnosis, it still has radiation exposure and uses iodinated contrast medium. Therefore, CCTA should be performed only when the clinical scenario considers CCTA appropriate, that is, CAD is suspected. However, we currently do not have evidence on what to do with patients who had a prior CCTA excluding the CAD diagnosis, but have developed new or worsening symptoms. Should these patients undergo CCTA again to search newly developed CAD? Our study identified a criterion to guide us for making this decision; for patients without diabetes mellitus who have no lesion or $\leq$25% stenosis on a prior CCTA performed less than 3 years ago, the probability of detecting new CAD is low, suggesting that CCTA is not necessary. Patients for whom the CCTA was normal on the initial scan had a 0 rate of revascularization during the study period. Our results can be used to limit the target for repeat CCTA to those who can most benefit from the examination and improve patient safety as well as medical cost containment.
Repeat Coronary Computed Tomographic Angiography in Patients With a Prior Scan Excluding Significant Stenosis
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