Multislice Computed Tomography in the Exclusion of Coronary Artery Disease in Patients With Presurgical Valve Disease

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Background—Multislice computed tomography (MSCT) has shown high negative predictive value in ruling out obstructive coronary artery disease. Preliminary studies in patients with valvular heart disease (VHD) have demonstrated the potential of MSCT angiography (CTA) in such patients, precluding need for invasive angiography (XA). However, larger prospectively designed studies, including patients with atrial fibrillation and incorporating dose reduction algorithms, are needed.

Methods and Results—To evaluate the clinical utility of 64-slice CT in the preoperative assessment in patients with VHD, we prospectively studied 452 consecutive patients undergoing routine cardiac catheterization for eligibility. Two hundred thirty-seven patients underwent both MSCT and XA. Segment-based, vessel-based, and patient-based agreement between CTA and XA was estimated assuming that “nonevaluable” segments were positive for significant coronary stenosis. In a patient-based analysis, sensitivity, specificity, positive predictive value, and negative predictive values of CTA were 95%, 89%, 66%, and 99%, respectively; in vessel-based analysis, 90%, 92%, 48%, and 99%, respectively; and in segment-based analysis, 89%, 97%, 38%, and 100%, respectively. No significant differences were found between patients with or without atrial fibrillation. A CAC value of 390 was the best cutoff for the identification of patients with positive or inconclusive CTA (which would not be exempted from XA in the clinical setting).

Conclusions—In the preoperative assessment of patients with predominant VHD, the diagnostic accuracy of 64-slice CTA for ruling out the presence of significant coronary artery disease is very good even when including patients with irregular heart rhythm. Using this approach, CAC quantification before CTA can be successfully used to identify patients who should be referred directly to XA, sparing unnecessary exposure to radiation.

Key Words: angiography • coronary disease • tomography • valves • calcium score

Current guidelines for the management of valvular heart disease (VHD) recommend preoperative coronary angiography for the detection of concomitant obstructive coronary artery disease (CAD). In a substantial proportion of these patients, especially those who are young and without significant risk factors, the probability of concomitant significant CAD is small. The invasive nature of the procedures, attendant complications, and patient discomfort raise the question of other noninvasive modalities that may provide this information.2,3

Clinical Perspective on p 313

Multislice computed tomography (MSCT) has shown high negative predictive value (NPV) in ruling out obstructive CAD compared with x-ray angiography (XA). Preliminary studies with 16-,6–8 40-,9 and 64-slice CT (64SCT),10,11 in patients with predominant VHD have demonstrated the potential of such an approach, precluding need for invasive XA. However, studies published with 64SCT, despite demonstrating better sensitivity and specificity when compared with the previous-generation scanners, fail to represent the actual VHD population as patients with atrial fibrillation (AF)—a very prevalent condition in this group—were excluded. Furthermore, the only 64SCT study including different valve pathologies reported a high radiation exposure, because no tube current modulation techniques were applied. Larger prospectively designed studies including patients with AF and the use of dose reduction algorithms are needed to demonstrate true utility in routine clinical practice.12–14

We conducted a prospective study to evaluate the clinical utility of 64SCT in the preoperative assessment of CAD in patients with a predominant diagnosis of VHD.
Methods

Population
During an 18-month period (June 2006 to December 2007) we prospectively screened 452 consecutive patients with VHD undergoing a routine cardiac catheterization for preoperative assessment of CAD. Thirty-nine patients were excluded because of known CAD, 28 because of limited patient/hospital time availability to perform both examinations before surgery, 21 because of hemodynamic clinical instability, 19 because of renal insufficiency, 11 because of previous allergic reaction to iodinated contrast media, 9 because of heart rate >85 in the immediate pre-MSCT evaluation despite maximal therapy, and 3 because of scanner breakdown. Eighty-six patients refused to provide written informed consent. The final population consisted of 237 individuals, who were clinically stable at the time of the evaluation and had no history of CAD.

Patient Preparation
MSCT scans and XA were performed on the same day in 88% of patients and in 100% of patients within 2 weeks of each other. The first examination performed was XA in 90% of the cases. Patients undergoing XA and MSCT scans during the same day received 5 to 20 mg of intravenous metoprolol 10 minutes before the scan if baseline heart rate was >65 bpm. Patients undergoing MSCT on a different day than XA received 50 mg or 100 mg of oral metoprolol 1 hour before the MSCT scan if baseline heart rate was >65 bpm. An additional dose of 5 to 10 mg of intravenous metoprolol was administered 10 minutes before the MSCT scan if heart rate remained >65 bpm. All patients received 0.5 mg of sublingual nitroglycerin 5 minutes before the scan. B-Blocker doses were either reduced (atenolol 50 mg PO or 2.5 to 7.5 mg IV) or not given (if heart rate <70 or systolic blood pressure <105 mm Hg) in patients with aortic stenosis and in patients with significant left ventricular systolic dysfunction and concomitant Class III/IV heart failure. Thirty-four (14%) patients received 5 mg of oral diazepam 1 hour before the scan.

Scan Protocol
All scans were performed using a 64SCT scanner (Somatom Sensation 64, Siemens Medical Solutions, Forchheim, Germany). All patients underwent a low-dose scan (collimation 24×1.2 mm; gantry rotation time, 330 ms; pitch, 0.2; tube voltage, 120 kV; tube current, 190 mA) to assess coronary artery calcification (CAC). After that scan, a MSCT coronary angiography (CTA) acquisition (collimation, 64×0.6 mm; tube current, 850 mA) was performed. Tube current modulation was used with ECG pulsing for decreasing radiation dose. In 31 (13%) patients with very irregular heart rhythms (predominantly AF), tube current modulation was not used. In 9 (4%) patients, with body weight <65 kg, tube voltage was reduced to 100 kV. Depending on the scan time, a bolus of 80 to 100 mL of contrast (Ultravist, Iopromide 370 mg/mL, Bayer Schering Pharma AG, Berlin, Germany) was injected at 5 mL/min via a power injector, followed by a 40 mL saline “chaser,” using either the previously placed 5F femoral vein catheter (for XA) or a dedicated antecubital vein 18-gauge access catheter. A bolus-tracking technique was used, with a region of interest placed into the ascending aorta, set to detect a predefined threshold of 150 HU.

Image reconstruction of the CAC acquisition was performed using an effective slice thickness of 3 mm. For CTA, a multiphase set of 10 retrospective reconstructions of the R-R interval, ranging from 10% to 100% of the R-R interval plus an additional 65% phase, was reconstructed and sent to a postprocessing workstation (Aquarius WorkStation, Tera Recon Inc, San Mateo, Calif). If necessary, additional phases were reconstructed.

Mean radiation exposure was calculated by the method proposed by the European Working Group for Guidelines on Quality Criteria in CT. The effective radiation dose was calculated by the product of the chest coefficient (0.017) and the dose-length product (DLP) obtained during each scan.15

MSCT Analysis
CAC was reported as the mean Agatston scores and was calculated using a detection threshold of 130 HU and semiautomated software (Syngo Calcium Scoring, Siemens Medical Solutions) as described previously.16 For CTA analysis, sets of reconstructed images were evaluated on a dedicated workstation by 2 experienced cardiologists, unaware of the XA results. Axial-source images, multplanar reformations, and thin-slab maximum intensity projections (5 mm) were used for detection of stenoses >50% using the 17-segment modified American Heart Association (AHA) classification.3 Interobserver disagreements were resolved by consensus in a joint session. Segments considered “nonevaluable” owing to significant calcification or artifact were assumed as positive for the study purpose and thus all segments were used for analysis in an “intention-to-diagnose” manner.

X-Ray Coronary Angiography
XA was performed according to standard techniques by experienced cardiologists. Vascular access was obtained through a femoral approach with Seldinger technique using a 6F or 7F catheter. In some patients, femoral venous access with a 5F catheter was also obtained for hemodynamic assessment. Two experienced cardiologists, unaware of the CTA results, analyzed all coronary segments for stenoses >50% using the procedures described for CTA. Segments distal to an occluded vessel were excluded from analysis. All other segments were included for the estimation of agreement with CTA.

Statistical Analysis
The diagnostic performance of CTA for the detection of significant CAD was evaluated against XA as the reference standard. Agreement between CTA and XA was estimated at 3 levels: segment-based, vessel-based, and patient-based. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were estimated for CTA as a test and XA used as a gold standard indicating the true disease status. Confidence intervals were calculated on the basis of binomial distribution. “Nonevaluable” coronary segments in CTA were coded as being positive for a significant coronary stenosis. Segments “nonevaluable” in XA were excluded from the analysis regardless of their result in CTA. Intermodality agreements between CTA and XA were expressed as k values. Separate analyses were carried out by CAC categories, by presence of AF, and by valve pathologic. A receiver-operator curve (ROC) analysis was performed to assess the ability of CAC to predict positive or inconclusive CTA (in whom XA would not be exempted). The optimal threshold for CAC was defined at the highest Youden index (sensitivity+specificity−1). The same approach was used to assess the ability of CAC to predict significant CAD by XA.

All data are described as means and standard deviations for continuous variables and as percentages for categorical variables. Comparisons between patient characteristics in groups with positive/inconclusive CTA studies and those with negative examinations were performed using t tests or Fisher exact tests as appropriate.

CAC and CTA were also compared as predictors of CAD defined by XA using generalized linear models with a logit link (logistic regression). The Akaike information criterion (AIC) was used as goodness-of-fit criterion for the prediction comparison. A probability value <0.05 was considered significant. All analysis used SPSS analysis software (Release 16, SPSS Inc, Chicago, Ill).

Results
A total of 237 patients were enrolled in the study. The demographic characteristics are presented in Table 1. XA excluded significant stenosis in 82% (193 subjects). Mean heart rate during CTA was 67±9 bpm (range, 44 to 106 bpm). Intravenous β-blocker (7.7±4.5 mg) was used in 93 patients (39%), whereas oral β-blocker was administered in 10 (4%). Mean total radiation exposure was calculated at 12.5±2.5
mSv (2.7±0.5 mSv for CAC score; 9.8±2.3 mSv for CTA). Patients with AF were exposed to a higher effective radiation dose compared with those without this rhythm (11.1±3.0 versus 9.6±2.2 mSv, for CTA, P<0.02) on account of tube current modulation not being used in 44% of these patients, compared with only 9% in those without this disorder.

The mean Agatston calcium score was 443±835 (median, 835; range, 0 to 6617). The ability of the CAC alone to predict the necessity of XA (due to a positive or inconclusive CTA) was assessed by plotting an ROC curve (Figure 1). The ROC curve had an area under the curve of 0.92 (95% CI, 0.87 to 0.97). A threshold value of 390 was found at the highest Youden index. At this threshold, sensitivity was 84% and specificity, 92%. This cutoff value for CAC reflects the best compromise between (1) including the largest proportion of patients in which CTA alone could correctly exclude CAD and (2) including the lowest proportion of positive/inconclusive CTA cases (neither of which would exempt cardiac catheterization).

The area under the curve for the prediction of CAD (as assessed by XA) by CAC ROC analysis was 0.87 (95% CI, 0.81 to 0.94). A cutoff value of 338 was observed for the best Youden index. At this threshold, sensitivity was 84% and specificity, 92%. This cutoff value for CAC reflects the best compromise between (1) including the largest proportion of patients in which CTA alone could correctly exclude CAD and (2) including the lowest proportion of positive/inconclusive CTA cases (neither of which would exempt cardiac catheterization).

Analysis of MSCT images excluded the presence of CAD in 173 patients (73%). One hundred seventy-one of these did not have significant CAD by XA (true-negatives), but 2 patients had significant luminal stenosis (1 in mid left anterior descending artery and 1 in the first diagonal) that was not identified by CTA (false-negatives). In 64 patients (27%), CTA suggested the presence of significant CAD, or at least, could not exclude it owing to calcium or motion artifact. Significant CAD was confirmed in 42 of these cases (66%). (Figure 2) In a patient-based analysis, sensitivity, specificity, PPV, and NPV were 95%, 89%, 66%, and 99%, respectively (Table 2). Patient-based analysis of CTA in predicting significant CAD according to CAC are presented in Table 3.

When comparing the prediction of CAD between CTA and CAC, the regression model considering CTA as predictor was superior, with a much better AIC (AIC=108) compared with the model considering CAC as predictor of CAD (AIC=162). In a model considering both measurements, CTA and CAC as covariates, the prediction of CAD was not improved (AIC=109) compared with the model considering only CTA as covariate.

### Vessel-Based Analysis

For vessel-based analysis, each coronary segment was assigned to 1 of the 4 “main vessels” (right coronary artery, left main, left anterior descending artery, and circumflex artery). A total of 948 vessels (237 patients ×4) were used for this analysis. Results are presented in Table 4.

### Segment-Based Analysis

Of a total of 4029 segments (237 patients ×17 AHA segments), only 3862 segments were available for comparison owing to nondominance or occlusion involving 167 (4%) segments. Of these, there were 3774 (98%) without significant stenosis and 88 (2.3%) with stenosis >50%. The most common cause for inability to assess lumen was heavy vascular calcification in 122 segments and the inclusion of these segments in our analysis drove the observed PPV. Only

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**Table 1.** Patient Demographics: Characteristics of Patients With Positive Versus Negative CTA

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total</th>
<th>Positive</th>
<th>Negative</th>
<th>Signif. Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>237</td>
<td>64</td>
<td>173</td>
<td>...</td>
</tr>
<tr>
<td>Male sex</td>
<td>114 (48%)</td>
<td>38 (59%)</td>
<td>26 (44%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Age, y</td>
<td>67±10 (39–87)</td>
<td>73±8</td>
<td>65±10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27±4 (17–39)</td>
<td>27±4</td>
<td>27±4</td>
<td>...</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>32 (14%)</td>
<td>6 (9%)</td>
<td>26 (15%)</td>
<td>NS</td>
</tr>
<tr>
<td>Paced rhythm</td>
<td>2 (0.8%)</td>
<td>1 (2%)</td>
<td>1 (0.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>151 (64%)</td>
<td>49 (77%)</td>
<td>102 (59%)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>102 (43%)</td>
<td>31 (48%)</td>
<td>71 (41%)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>40 (17%)</td>
<td>16 (25%)</td>
<td>24 (14%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Positive smoking history</td>
<td>36 (15%)</td>
<td>15 (23%)</td>
<td>21 (12%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>30 (13%)</td>
<td>6 (9%)</td>
<td>24 (14%)</td>
<td>NS</td>
</tr>
<tr>
<td>Angina</td>
<td>62 (26%)</td>
<td>31 (48%)</td>
<td>31 (18%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aortic valve stenosis</td>
<td>161 (68%)</td>
<td>55 (86%)</td>
<td>106 (61%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mitral valve regurgitation</td>
<td>41 (17%)</td>
<td>9 (14%)</td>
<td>32 (18%)</td>
<td>NS</td>
</tr>
<tr>
<td>Aortic valve regurgitation</td>
<td>33 (14%)</td>
<td>5 (8%)</td>
<td>28 (16%)</td>
<td>NS</td>
</tr>
<tr>
<td>Mitral stenosis</td>
<td>27 (11%)</td>
<td>3 (5%)</td>
<td>24 (14%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Agatston calcium score</td>
<td>444±199</td>
<td>1314±1204</td>
<td>122±199</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1-Vessel CAD</td>
<td>27 (11%)</td>
<td>25 (39%)</td>
<td>2 (0.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2-Vessel CAD</td>
<td>9 (4%)</td>
<td>9 (14%)</td>
<td>0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>3-Vessel CAD</td>
<td>8 (3%)</td>
<td>8 (13%)</td>
<td>0</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Values are n (%), unless otherwise indicated.
2 of the reported false-positive segments occurred in noncalcified segments. In both these segments, XA confirmed the presence of a plaque but no evidence of a significant luminal stenosis. In 52 segments (35 patients) “stair-step artifact” made interpretation difficult; 23 segments had suboptimal contrast opacification and 2 were subject to “streak” artifact in the right coronary artery secondary to pacemaker. Similar to Mangath et al.,7 we also found that isolated “step,” “motion,” or “blurring” artifacts (all more common in patients with AF), despite being diagnostically challenging, did not significantly limit vessel evaluation and segments affected by them could ultimately be assessable by means of “toggling” through the multiphase images. Similarly, the “streak” artifact caused by the presence of the pacemaker lead in the right chambers only affected some phases of the reconstructed set and had no impact on CTA accuracy.

There were only 10 (0.3%) false-negative segments (8 patients). The majority (n=7) of these false-negative segments were caused by apparently nonsignificant (“borderline”) calcified plaques (Figure 3), 2 were explained by poor lumen contrast, and 1 was caused by motion artifact in the phases with full-output radiation dose and not perceived in phases with lower output tube radiation. Rhythm disturbances appeared to have a limited impact in the occurrence of false-negatives (0.23% in non-AF versus 0.42% in AF-patients), mainly because the segments poorly visualized tend to be classified as positives. This way, in the subgroup of patients with AF, the NPV is still around 100% in segment-based analysis and 96% (versus 99%) in patient-based analysis (Table 2).

Two of these false-negative segments had a significant impact in terms of per-patient analysis, as they would classify that patient as a false-negative. In the other 6 patients, though, the impact of the false-negative segments would have been obscured, as these patients would have been referred for XA due to detection of other positive segments.

Characteristics of Patients With Positive CTA

Characteristics of patients with positive CTA are depicted in Table 1. Positive CTA patients were usually older, more often...
male, and with more risk factors. As expected, there was also a higher prevalence of patients with angina and aortic stenosis and a higher mean CAC in this group. There were no significant differences between the groups with regard to body mass index, symptoms, and presence of AF.

Discussion

Guidelines for the management of VHD recommend preoperative cardiac catheterization for the detection of CAD in all male patients age 35 or older, in all postmenopausal women, and in premenopausal women with any risk factors for CAD. The recently published European Guidelines state that “in expert centers, MSCT can be useful to exclude CAD in patients who are at low risk of atherosclerosis.” Although it seems reasonable to replace XA with MSCT in this clinical context, this approach has not been fully validated.

In this prospective study, we report the predictive accuracy of preoperative CTA in the diagnosis of CAD in patients predominantly with VHD. The main finding of our investigation is that CTA can effectively rule out significant CAD in the vast majority of patients with VHD, including those with AF. Furthermore, quantification of CAC before CTA can effectively allow further discrimination, with a score of 390 representing the cutoff value beyond which patients would benefit more from a direct referral for XA (since CTA ability to exclude CAD is very low in this subgroup). An additional contribution of this study is the implementation of tube current modulation in the majority of patients, including those with AF. The mean radiation dose used is lower than reported in similar previous studies that excluded irregular rhythm and aortic stenosis. Without cardiac catheterization after CTA should take into account the overall quality of the study and the extent of artifact.

Predictive Accuracy of CTA

The accuracy of MSCT has been shown in multiple clinical scenarios. The high sensitivity and NPV of MSCT are strengths that have argued for its use in patients with VHD, in whom unnecessary XA and associated risks should be avoided. However, this must be tempered by the radiation exposure associated with the technique, particularly in patients at risk (younger patients and female patients). Unlike previous small studies, our investigation targeted a large number of consecutive patients without consideration of underlying rhythm, etiology of VHD, or coronary risk factors, to truly capture the spectrum of patients referred for XA in the preoperative context. Compared with previously reported studies of CTA in VHD, our patient population was by far the oldest (and with higher CAC). This may reflect our effort to minimize exclusions, and, together with the a priori analysis strategy of not excluding coronary segments and interpreting unevaluable segments as “positive” for CAD, partially explain the relatively low PPV found. The NPV of CTA was uniformly high regardless of patient-based, vessel-based, or segment-based interpretations.

In contrast to previous 64SCT studies published in preoperative patients with VHD—which did not have any false-negatives on the patient-based analysis—we found 2 false-negative tests (1 in a patient with AF and 1 in a sinus rhythm examination). The total number of false-negative segments (0.3%) is, however, in line with data previously published (0.2% to 0.4%). If the presence of positive segments in CTA was used in this population as the only test to decide whether cardiac catheterization was necessary, 2 patients with false-negative results on CTA would have undergone surgery without the correct diagnosis of concomitant single-vessel disease. These findings must be tempered by the clinical context and clearly emphasize that the decision to proceed without cardiac catheterization after CTA should take into account the overall quality of the study and the extent of artifact.

Table 2. Patient-Based Analysis of CTA in Predicting Significant CAD

<table>
<thead>
<tr>
<th>CAD</th>
<th>n</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>Sensit. (%)</th>
<th>Specif. (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accu. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>19</td>
<td>237</td>
<td>42</td>
<td>171</td>
<td>22</td>
<td>2</td>
<td>0.72</td>
<td>95 (84–99)</td>
<td>89 (83–93)</td>
<td>66 (51–75)</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>22</td>
<td>161</td>
<td>35</td>
<td>106</td>
<td>20</td>
<td>0</td>
<td>0.70</td>
<td>100 (92–100)</td>
<td>84 (77–90)</td>
<td>64 (50–76)</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>15</td>
<td>33</td>
<td>4</td>
<td>27</td>
<td>1</td>
<td>1</td>
<td>0.76</td>
<td>80 (28–99)</td>
<td>96 (82–100)</td>
<td>80 (28–99)</td>
</tr>
<tr>
<td>Mitral stenosis</td>
<td>11</td>
<td>27</td>
<td>2</td>
<td>23</td>
<td>1</td>
<td>1</td>
<td>0.63</td>
<td>67 (9–99)</td>
<td>96 (79–100)</td>
<td>67 (9–99)</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>15</td>
<td>41</td>
<td>6</td>
<td>32</td>
<td>3</td>
<td>0</td>
<td>0.76</td>
<td>100 (61–100)</td>
<td>91 (77–98)</td>
<td>67 (30–93)</td>
</tr>
<tr>
<td>AF</td>
<td>16</td>
<td>32</td>
<td>4</td>
<td>25</td>
<td>2</td>
<td>1</td>
<td>0.67</td>
<td>80 (28–99)</td>
<td>93 (76–99)</td>
<td>67 (22–96)</td>
</tr>
<tr>
<td>No AF</td>
<td>19</td>
<td>205</td>
<td>38</td>
<td>146</td>
<td>20</td>
<td>1</td>
<td>0.72</td>
<td>97 (87–100)</td>
<td>88 (82–92)</td>
<td>66 (52–76)</td>
</tr>
</tbody>
</table>

TP, True-positive; TN, true-negative; FP, false-positive; FN, false-negative; κ, kappa value; Sensit., sensitivity; Specif., specificity; Accu., accuracy.

Table 3. Patient-Based Analysis of CTA in Predicting Significant CAD According to Calcium Score

<table>
<thead>
<tr>
<th>CAD</th>
<th>n</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>Sensit. (%)</th>
<th>Specif. (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accu. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>19</td>
<td>237</td>
<td>42</td>
<td>171</td>
<td>22</td>
<td>2</td>
<td>0.72</td>
<td>95 (84–99)</td>
<td>89 (83–93)</td>
<td>66 (51–75)</td>
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<tr>
<td>CAC ≤10</td>
<td>3</td>
<td>71</td>
<td>2</td>
<td>68</td>
<td>1</td>
<td>0</td>
<td>0.79</td>
<td>100 (22–100)</td>
<td>99 (92–100)</td>
<td>67 (9–99)</td>
</tr>
<tr>
<td>CAC 11–400</td>
<td>8</td>
<td>100</td>
<td>6</td>
<td>90</td>
<td>2</td>
<td>2</td>
<td>0.73</td>
<td>75 (35–97)</td>
<td>98 (92–100)</td>
<td>75 (35–97)</td>
</tr>
<tr>
<td>CAC 401–1000</td>
<td>30</td>
<td>33</td>
<td>10</td>
<td>12</td>
<td>11</td>
<td>0</td>
<td>0.40</td>
<td>100 (74–100)</td>
<td>52 (31–73)</td>
<td>48 (26–10)</td>
</tr>
<tr>
<td>CAC &gt;1000</td>
<td>73</td>
<td>33</td>
<td>24</td>
<td>1</td>
<td>8</td>
<td>0</td>
<td>0.15</td>
<td>100 (88–100)</td>
<td>11 (0.3–48)</td>
<td>75 (57–89)</td>
</tr>
</tbody>
</table>

TP, True-positive; TN, true-negative; FP, false-positive; FN, false-negative; κ, kappa value; Sensit., sensitivity; Specif., specificity; Accu., accuracy. CAC values are Agatston score.
Should Preoperative Patients With VHD and AF Be Excluded From MSCT?

Patients with AF represent a significant proportion of preoperative patients with VHD. They represented around 14% of our study population. Despite the slightly lower sensitivity and NPV found (with a higher specificity and PPV, though), overall diagnostic accuracy of MSCT and intermodality agreement remained very good in these patients, and no significant differences were detected between those with and those without AF. The higher incidence of “step” and motion artifacts in patients with AF implies, however, longer postprocessing and “time-consuming” detailed segment analysis and comes at the cost of higher radiation exposure (as tube current modulation was used less often). Multiphase reconstructions and the ability to rapidly interchange or navigate between different phases of the R-R cycle while maintaining the same orientation and vessel projection is of particular importance in this group of patients. The availability of software that permits this type of analysis is an important advance in CTA and allows its use in most patients with irregular rhythms.

Can We Predict Which Patients With VHD Will Need XA?

Calcium Score

High calcium burden in the coronary arteries decreases visualization of the lumen and complicates CTA assessment. Similar to previous studies, the higher the CAC, the lower was the intermodality agreement in our study (Table 3).6,10 In patients with high CAC, XA should still remain the primary presurgical test to rule out coronary lesions requiring revascularization. In prior work in patients with aortic stenosis, Gilard et al6 suggested the use of a CAC cutoff of 1000 to identify patients who should avoid continuing to CTA, as XA would most certainly be necessary. In our study, we found a lower threshold value.390 This finding is consistent with previous studies that report a trend for lower CTA accuracy for CAC above 400. Since the value of 400 represents an important cutoff validated by prior large studies in other populations, we suggest that patients with VHD and a CAC >400 should be directed to XA rather than CTA.22,23 In fact, in our sample, a cutoff value of 400 has the same specificity and only a minimally reduced sensitivity (83% instead of 84%) when compared with the 390 threshold.

Pretest Probability

As expected, older patients, male patients, patients with more coronary risk factors, patients with angina, and patients with the diagnosis of aortic stenosis were more likely to have a higher CAC and to have a positive CTA evaluation. Thus, elderly patients, particularly those with any 1 or more of these factors, may benefit from direct referral to XA to avoid an excessive number of duplicate examinations and the associated radiation and contrast-medium exposure.

Stated differently, by being deliberate in our patient selection and choosing only those with low to intermediate probability of CAD, to eventually undergo MSCT, we would still reduce the need for XA in approximately 70% of the patients without having a significant number of patients who would be submitted to both examinations. The advantages of this approach in terms of safety, patient comfort, time, and costs must be tempered with radiation exposure. In the present study, we clearly identified a group of high pretest probability patients to whom preoperative assessment of CAD with CTA should not be applied because

### Table 4. Vessel-Based and Segment-Based Analyses

<table>
<thead>
<tr>
<th>CAD, %</th>
<th>n</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>Sensit. (%)</th>
<th>Specif. (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accu. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessel-based</td>
<td>8</td>
<td>948</td>
<td>64</td>
<td>808</td>
<td>69</td>
<td>7</td>
<td>0.59</td>
<td>90 (81–96)</td>
<td>92 (90–94)</td>
<td>48 (39–57)</td>
</tr>
<tr>
<td>RCA</td>
<td>8</td>
<td>237</td>
<td>17</td>
<td>198</td>
<td>20</td>
<td>2</td>
<td>0.56</td>
<td>89 (67–99)</td>
<td>91 (86–94)</td>
<td>46 (23–51)</td>
</tr>
<tr>
<td>LM</td>
<td>1</td>
<td>237</td>
<td>2</td>
<td>230</td>
<td>5</td>
<td>0</td>
<td>0.44</td>
<td>100 (22–100)</td>
<td>98 (95–99)</td>
<td>29 (4–71)</td>
</tr>
<tr>
<td>LAD</td>
<td>13</td>
<td>237</td>
<td>28</td>
<td>180</td>
<td>27</td>
<td>2</td>
<td>0.59</td>
<td>93 (78–99)</td>
<td>87 (82–91)</td>
<td>51 (37–65)</td>
</tr>
<tr>
<td>Cx</td>
<td>8</td>
<td>237</td>
<td>17</td>
<td>200</td>
<td>17</td>
<td>3</td>
<td>0.59</td>
<td>85 (62–97)</td>
<td>92 (88–95)</td>
<td>50 (35–71)</td>
</tr>
<tr>
<td>Segment-based</td>
<td>2</td>
<td>3862</td>
<td>78</td>
<td>3647</td>
<td>127</td>
<td>10</td>
<td>0.52</td>
<td>89 (80–94)</td>
<td>97 (96–97)</td>
<td>38 (31–45)</td>
</tr>
</tbody>
</table>

TP, True-positive; TN, true-negative; FP, false-positive; FN, false-negative; κ, kappa value; Sensit., sensitivity; Specif., specificity; Accu., accuracy; RCA, right coronary artery; LM, left main coronary artery; LAD, left anterior descending coronary artery; Cx, circumflex artery.

Figure 3. Cases illustrating false-positive and false-negative findings. A, Calcified plaques in the proximal and mid right coronary artery and noncalcified plaque in the distal right coronary artery are seen, suggesting a stenosis >50% in CTA. B, Corresponding view on XA does not confirm significant stenoses. C and D, Significant stenosis involving the origin of the first diagonal seen on XA (D) that was not correctly identified in CTA (C), mainly due to the presence of a calcified plaque (interpreted as <50%) and poor lumen opacification.
its ability to exempt cardiac catheterization would be small. However, identification of patients to whom the noninvasive approach would be clearly beneficial is not easy. European guidelines state that MSCT can be useful to exclude CAD in patients with VHD who are at low risk of atherosclerosis. However, some authors argue that those patients are represented mostly by young people and women, who are simultaneously at higher risk of having complications associated with radiation exposure. Future advances in MSCT may overcome this limitation because new hardware and acquisition protocols promise substantial reduction in radiation exposure (to levels similar to XA).

Study Limitations
We acknowledge that this study has multiple limitations. Only patients scheduled for elective valve surgery (no emergent cases) without known CAD were included. Patients with previous coronary bypass surgery or stents were excluded. Patients with heart rate >85 bpm despite maximal therapy were also not studied. This study was conducted in a single center with experience in MSCT and as such these results may not be representative of all sites. The low prevalence of CAD found (compared with Northern European and American VHD populations) may also influence results. However, other studies conducted in VHD European populations found similar prevalence of disease (18% to 20%).

Given the rapid evolution of scanner hardware, the diagnostic accuracy of recently introduced scanners with higher temporal resolution might be even better. The higher temporal resolution achieved will probably represent a very important advance in patients with rhythm disturbances and will most certainly decrease the gap between patients with AF and those without AF, even at higher heart rates.24,25

Conclusions
In the preoperative VHD population studied, the diagnostic accuracy of 64SCT for ruling out the presence of significant CAD was very good, even in patients with AF. CTA may serve as a gatekeeper to XA in patients scheduled for elective valve surgery, irrespective of rhythm, particularly in patients with low to intermediate pretest probability of CAD. Using this approach, CAC quantification before CTA can be successfully used to identify patients who should be referred directly to XA, sparing unnecessary exposure to radiation.

As any other imaging technique, despite its high NPV, MSCT is not free of false-negatives, and this factor should be taken into consideration when evaluating preoperative patients, especially when borderline calcified lesions are detected.

Disclosures
None.

References

**CLINICAL PERSPECTIVE**

Current guidelines for the management of valvular heart disease recommend preoperative coronary angiography for the detection of concomitant coronary artery disease (CAD) in all male patients age 35 or older, all postmenopausal women, and in premenopausal women with any risk factors for CAD. These patients are usually submitted to coronary angiography by means of cardiac catheterization. This study sought to evaluate the potential role for multislice computed tomography (MSCT) to replace cardiac catheterization as first-line examination in this clinical context. The main finding of this investigation is that MSCT coronary angiography (CTA) can effectively rule out significant CAD in the vast majority of patients with valve disease, including those with atrial fibrillation. Furthermore, assessment of pretest probability and quantification of coronary artery calcification (CAC) before CTA can effectively allow further discrimination. Based on the study findings, the authors propose a protocol in which patients scheduled for elective valve surgery with low to intermediate probability of CAD would undergo CAC assessment before CTA. Patients with a calcium score <400 would then be submitted to CTA, whereas patients with a high probability of CAD and patients with a CAC >400 would be referred directly for invasive coronary angiography. With this approach, cardiac catheterization could be avoided in approximately 70% of the patients, without a significant number of patients undergoing both examinations (sparking unnecessary exposure to radiation).
Multislice Computed Tomography in the Exclusion of Coronary Artery Disease in Patients With Presurgical Valve Disease
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