Multislice computed tomography in the exclusion of coronary artery disease in pre-surgical valve disease patients

Nuno Bettencourt, MD¹, João Rocha¹, Mónica Carvalho¹, Daniel Leite¹, Andre Michael Toschke MD², Bruno Melica MD¹, Lino Santos MD¹, Alberto Rodrigues MD¹, Manuel Gonçalves MD¹, Pedro Braga MD¹, Madalena Teixeira MD¹, Lino Simões MD¹, Sanjay Rajagopalan MD³, Vasco Gama MD¹

¹ Cardiology Department - Centro Hospitalar de Gaia/Espinho, Portugal
² Kings College London
³ Ohio State University – Columbus, Ohio, USA


Corresponding author:
Nuno Bettencourt
Rua D. Luís de Ataíde, 66
porto, 4150-471 Portugal
Tel: +351934258281
Email: bettencourt.n@gmail.com
ABSTRACT

Background: Multislice computed tomography (MSCT) has shown high negative predictive value in ruling out obstructive coronary artery disease (CAD). 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 (AF) and incorporating dose reduction algorithms, are needed.

Methods and Results: To evaluate the clinical utility of 64-slice-CT in the pre-operative assessment in patients with VHD, we prospectively studied 452 consecutive patients undergoing a routine cardiac catheterization for eligibility. 237 patients underwent both MSCT and XA. Segment-based, vessel-based and patient-based agreement between CTA and XA was estimated assuming that “non-evaluable” segments were positive for a significant coronary stenosis. In a patient-based analysis, sensitivity, specificity, positive predictive value and negative predictive value of CTA were 95%, 89%, 66% and 99%, respectively. In vessel based analysis were 90%, 92%, 48%, and 99% while in segment-based analysis were 89%, 97%, 38% and 100%, respectively. No significant differences were found between patients with or without AF. A CAC value of 390 was found to be the best cut-off for the identification of patients with positive or inconclusive CTA (which would not be exempted from XA in the clinical setting).

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

Keywords: angiography; coronary disease; tomography; valves; calcium score.
INTRODUCTION

Current guidelines for the management of valvular heart disease (VHD) recommend pre-operative coronary angiography for the detection of concomitant obstructive coronary artery disease (CAD).\(^1,2\) 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, raises the question of other non-invasive modalities that may provide this information.\(^2,3\)

Multislice computed tomography (MSCT) has shown high negative predictive value (NPV) in ruling out obstructive coronary artery disease (CAD) compared to x-ray angiography (XA).\(^4,5\) 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 to 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, as 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 pre-operative 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 pre-operative assessment of CAD. Thirty-nine patients were excluded due to known CAD, 28 due to limited patient/hospital time availability to perform both exams before surgery, 21 due to hemodynamic/clinical instability, 19 due to renal insufficiency, 11 due to previous allergic reaction to iodinated contrast media, 9 due to heart rate higher than 85 in the immediate pre-MSCT evaluation despite maximal therapy and 3 due to scanner breakdown. Eighty-six (86) 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 prior 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 exam performed was XA in 90% of the cases. Patients undergoing XA and MSCT scans during the same day, received 5-20 mg of IV metoprolol 10 minutes before the scan, if baseline heart rate was >65 beats/minute. Patients undergoing MSCT on a different day than XA received 50 mg or 100 mg of oral metoprolol 1 hour prior to the MSCT scan, if baseline heart rate exceeded 65 beats/minute. An additional dose of 5-10 mg of IV metoprolol was administered 10 minutes before the MSCT scan, if heart rate remained >65 beats/minute. All patients received 0.5 mg of sublingual nitro-glycerine 5 minutes prior to scan. Beta-blocker doses were either reduced (atenolol 50 mg PO or 2.5-7.5 mg IV) or not given (if heart rate <70 or systolic blood pressure <105 mmHg) 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 (Somaton Sensation 64, Siemens Medical Solutions, Forchheim, Germany). All patients underwent a low dose scan (collimation 24x1.2 mm; gantry rotation time 330 ms; pitch 0.2; tube voltage 120 kV; tube current 190 mAs) to assess coronary artery calcification (CAC). Following that scan, a CTA acquisition (collimation 64x0.6 mm; tube current 850 mAs) was performed. Tube current modulation with electrocardiographic pulsing for decreasing radiation dose was used in most patients, with full tube current applied at 60-65% of the RR interval. 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 cc/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 multi-phase set of 10 retrospective reconstructions of the RR interval, ranging from 10 to 100% of the RR interval plus an additional 65% phase was reconstructed and sent to a post-processing workstation (Aquarius® WorkStation, Tera Recon Inc, San Mateo, California, USA). 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.\textsuperscript{15}

**MSCT analysis**

CAC was reported as the mean Agatston scores and was calculated using a detection threshold of 130 HU and semi-automated software (Syngo Calcium Scoring, Siemens Medical Solutions) as described previously.\textsuperscript{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, multiplanar reformations and thin-slab maximum intensity projections (5 mm) were used for detection of stenoses >50% using the 17-segment modified AHA classification.\textsuperscript{17} Inter-observer disagreements were resolved by consensus in a joint session. Segments considered “non-evaluable” owing to significant calcification or artefact were assumed as positive for the study purpose and thus all segments were used for analysis in an “intent-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 6 or 7 Fr catheter. In some patients femoral venous access with 5 Fr 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), NPV and overall accuracy were estimated for
CTA as a test and XA as a gold standard indicating the true disease status. Confidence intervals were calculated based on the binominal distribution. "Non-evaluable" coronary segments in CTA were coded as being positive for a significant coronary stenosis. Segments “non-evaluable” in XA were excluded from the analysis regardless of their result in CTA. Inter-modality agreements between CTA and XA were expressed as kappa values. Separate analyses were carried out by CAC categories, by presence of AF and by valve pathology.

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 exams were performed using t-tests or Fisher’s exact tests as appropriate.

CAC and CTA were also compared as predictors of CAD defined by XA using generalised 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 p value <0.05 was considered significant.

All analysis used SPSS analysis software (Release 16, SPSS Inc, Chicago, Illinois).
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 beats/min (range 44-106 beats/min). Intravenous beta-blockade (7.7±4.5 mg) was used in 93 patients (39%) while oral beta-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 to those without this rhythm (11.1±3.0 vs. 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 105, range 0-6617. 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 0.87–0.97). A threshold value of 390 was found at the highest Youden index. At this threshold sensitivity was 84% and specificity 92%. This cut-off 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 0.81–0.94). A cut-off value of 338 was observed for the best prediction of significant CAD at the highest Youden index.

Analysis of MSCT images excluded the presence of CAD in 173 patients (73%). 171 of these did not have significant CAD by XA (true-negatives) but 2 patients had significant luminal stenosis (one in mid Left anterior descending artery and one in the first diagonal), that were 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 artefact. 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 to 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 to the model considering only CTA as covariate.

**Vessel Based Analysis**

For vessel-based analysis, each coronary segment was assigned to one of the 4 “main vessels” (Right coronary artery, Left main, Left anterior descending artery and Circumflex artery). A total of 948 vessels (237 patients x 4) were used for this analysis. Results are presented in table 4.

**Segment Based Analysis**

Of a total of 4029 segments (237 patients x 17 AHA segments), only 3862 segments were available for comparison owing to non-dominance 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 2 of the reported false-positive segments occurred in non-calcified 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 artefact” made
interpretation difficult; 23 segments suffered suboptimal contrast opacification and 2 were subject to “streak” artefact in the RCA secondary to pacemaker. Similar to Mangath et al, we also found that isolated “step”, “motion” or “blurring” artefacts (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" artefact 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 (eight patients). The majority (n=7) of those false-negative segments were due to apparently non-significant (“borderline”) calcified plaques (figure 3), two were explained by poor lumen-contrast and one due to motion artefact in the phases with full-output radiation dose and not perceived in phases with lower output tube radiation. Rhythm disturbances seemed to have a limited impact in the occurrence of false-negatives (0.23% in non-AF vs 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% (vs 99%) in patient-based analysis (Table 2).

Two of those 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 six 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 regards
to body mass index, symptoms and presence of AF.
DISCUSSION

Guidelines for the management of VHD recommend pre-operative cardiac catheterization for the detection of CAD in all male patients aged 35 or more, all post-menopausal women and in premenopausal women with any risk factors for CAD.1, 2 The recently published European Guidelines2 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 pre-operative CTA in the diagnosis of CAD in patients with predominantly 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 prior to CTA can effectively allow further discrimination, with a score of 390 representing the cut-off 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 patients10 and is in line with doses currently used in the clinical setting.12,18-20

Predictive accuracy of CTA

Accuracy of MSCT has been shown in multiple clinical scenarios.4,5 The high sensitivity and NPV of MSCT are strengths that have argued for its use in patients with VHD, where unnecessary XA and associated risks could be avoided. However, this has to be tempered by the radiation exposure associated with the technique, particularly in patients at risk (younger patients and females).21 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 pre-operative context. Compared to 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 pre-operative VHD patients – which did not have any false-negative on the patient-based analysis – we found 2 false-negative tests (one in a patient with AF and another in a sinus-rhythm exam). The total number of false-negative segments (0.3%) is, however, in line with data previously published (0.2-0.4%). 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 obviously need to be tempered by the clinical context and clearly emphasises that the decision to proceed without cardiac catheterization after CTA should take in account overall quality of study and the extent of artefact.

Should preoperative VHD patients with AF be excluded from MSCT?

Patients with AF represent a significant proportion of pre-operative 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 without AF. The higher incidence of “step” and motion artefacts in AF patients, implies, however, longer post-processing 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 inter-change or navigate between different phases of the RR 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 utilization 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). In patients with high CAC, XA should still remain the primary pre-surgical test to rule out coronary lesions requiring revascularization. In prior work in patients with aortic stenosis, Gilard et al suggested the use of a CAC cut-off 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 cut-off 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. In fact, in our sample, a cut-off value of 400 has the same specificity, and only a minimally reduced sensitivity (83% instead of 84%) when compared to the 390 threshold.

**Pre-test probability.** As expected, older patients, males, patients with more coronary risk factors, patients with angina and patients with the diagnosis of aortic stenosis were both more likely to have a higher CAC and to have a positive CTA evaluation. Thus elderly patients, particularly those with any one or more of these factors may benefit from direct referral to XA, in order 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 about 70% of the patients, without having a significant number of patients that would be submitted to both exams.

The advantages of this approach in terms of safety, patient comfort, time and costs need to be tempered with radiation exposure. In the present study, we clearly identified a group of high pre-test probability patients to whom pre-operative assessment of CAD with CTA should not be applied since its ability to exempt cardiac catheterization would be small. However, identification of patients to whom the non-invasive approach would be clearly beneficial is not easy. European guidelines state that MSCT can be useful to exclude CAD in VHD patients who are at low risk of atherosclerosis. However, some authors argue that those patients are majorly represented by young people and females, which are simultaneously at higher risk of having complications associated to radiation exposure. Future advances in MSCT may overcome this limitation since 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 by-pass surgery or stents were excluded. Patients with heart rate >85 beats/minute despite maximal therapy were also not studied. This study was conducted in a single centre with experience in MSCT and as such these results may not be representative of all sites. The low prevalence of CAD found (compared to Northern European and American VHD populations) may also influence results. However, other
studies, conducted in VHD European populations found similar prevalence of disease (18%-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 AF and non-AF patients, even at higher heart rates.24,25
CONCLUSIONS

In the pre-operative 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, irrespectively of rhythm, particularly in patients with low-to-intermediate pre-test probability of CAD. Using this approach, CAC quantification prior to 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


14. Roberts WT, Bax JJ, Davies LC. Cardiac CT and CT coronary angiography: technology and application. *Heart.* 2008; 94:781-792.


**Table 1.** Patient demographics. Characteristics of patients with positive vs negative CTA

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Positive</th>
<th>Negative</th>
<th>Signif. level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (n)</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 (yrs)</td>
<td>67±10 (39-87)</td>
<td>73±8</td>
<td>65±10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (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 (66%)</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±835</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.
### Table 2. Patient-Based Analysis of CTA in predicting significant CAD

<table>
<thead>
<tr>
<th></th>
<th>CAD (%)</th>
<th>n</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>k</th>
<th>Sensit. (%)</th>
<th>Specif. (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accu. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient-based</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ao Stenosis</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>
<td>99 (96-100)</td>
<td>90 (85-93)</td>
</tr>
<tr>
<td>Ao Regurg</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>
<td>96 (82-100)</td>
<td>94 (80-99)</td>
</tr>
<tr>
<td>Mit 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>
<td>96 (79-100)</td>
<td>93 (76-99)</td>
</tr>
<tr>
<td>Mit Regurg</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>
<td>100 (91-100)</td>
<td>93 (80-98)</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>
<td>96 (80-99)</td>
<td>91 (75-98)</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 (52-78)</td>
<td>99 (96-100)</td>
<td>90 (85-94)</td>
</tr>
</tbody>
</table>

Accu.=Accuracy; Ao=Aortic valve; AF=Atrial fibrilation; CAD=Coronary artery disease; FN=False-negative; FP=False-positive; k=Kappa value; Mit=Mitral valve; PPV=Positive predictive value; NPV=Negative predictive value; Regurg=Regurgitation; Sensit.=Sensitivity; Specif.=Specificity; TN=True-negative; TP=True-positive.
Table 3. Patient-Based Analysis of CTA in predicting significant CAD, according to calcium score

<table>
<thead>
<tr>
<th></th>
<th>CAD (%)</th>
<th>n</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>k</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>
<td>99 (96-100)</td>
<td>90 (85-93)</td>
</tr>
<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>
<td>100 (96-100)</td>
<td>99 (92-100)</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>
<td>98 (92-100)</td>
<td>96 (90-99)</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>
<td>100 (78-100)</td>
<td>67 (51-84)</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>
<td>100 (5-100)</td>
<td>76 (58-89)</td>
</tr>
</tbody>
</table>

Accu.=Accuracy; CAC=Coronary artery calcification (Agatston Score); CAD=Coronary artery disease; FN=False-negative; FP=False-positive; k=Kappa value; PPV=Positive predictive value; NPV=Negative predictive value; Sensit.=Sensitivity; Specif.=Specificity; TN=True-negative; TP=True-positive.
Table 4. Vessel-Based and Segment-based analyses

<table>
<thead>
<tr>
<th></th>
<th>CAD (%)</th>
<th>n</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>k</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></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCA</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>
<td>99 (98-100)</td>
<td>92 (90-94)</td>
</tr>
<tr>
<td>LM</td>
<td>1</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>
<td>99 (96-100)</td>
<td>91 (86-94)</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>
<td>99 (96-100)</td>
<td>88 (83-92)</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>
<td>99 (96-100)</td>
<td>92 (87-95)</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>
<td>100 (99-100)</td>
<td>96 (96-97)</td>
</tr>
</tbody>
</table>

Accu.=Accuracy; CAD=Coronary artery disease; Cx=circumflex artery; FN=False-negative; FP=False-positive; k=Kappa value; LAD=Left anterior descending coronary artery; LM=Left main coronary artery; PPV=Positive predictive value; NPV=Negative predictive value; RCA=Right coronary artery; Sensit.=Sensitivity; Specif.=Specificity; TN=True-negative; TP=True-positive.
FIGURE LEGENDS.

**Figure 1.** Receiver-operating characteristics (ROC) curve. CAC as predictor of the necessity of an invasive angiogram (due to a positive or inconclusive CTA). Area under the curve (AUC) = 0.92 (0.87-0.97). The optimal threshold value of CAC estimated at the highest Youden index was 390.

**Figure 2.** Cases illustrating true-positive and true negative-findings.
A. RCA occlusion correctly identified in CTA. B. Corresponding view on XA. C and D. CTA and XA images of a patient with a normal coronary angiogram.

**Figure 3.** Cases illustrating false-positive and false-negative findings.
A. Calcified plaques in proximal and mid RCA and non-calcified plaque in distal RCA are seen suggesting a stenosis >50% in CTA. B. The 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.
$\text{CAC} = 390$
Figure 2a. True-positive

Figure 2b. True-negative
Figure 3a. False-positive

Figure 3b. False-negative
Multislice computed tomography in the exclusion of coronary artery disease in pre-surgical valve disease patients

Nuno Bettencourt, João Rocha, Mónica Carvalho, Daniel Leite, Andre Michael Toschke, Bruno Melica, Lino Santos, Alberto Rodrigues, Manuel Gonçalves, Pedro Braga, Madalena Teixeira, Lino Simões, Sanjay Rajagopalan and Vasco Gama

_Circ Cardiovasc Imaging_. published online April 6, 2009;
_Circulation: Cardiovascular Imaging_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circimaging.ahajournals.org/content/early/2009/04/06/CIRCIMAGING.108.827717

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation: Cardiovascular Imaging_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation: Cardiovascular Imaging_ is online at:
http://circimaging.ahajournals.org/subscriptions/