Cardiac multislice spiral computed tomography as an alternative to coronary angiography in the preoperative assessment of coronary artery disease before aortic valve surgery: A management outcome study

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Summary
Background. — Conventional coronary angiography (CA) is still recommended before valvular surgery. Preliminary studies suggest that multislice spiral computed tomography coronary angiography (MSCT-CA) can be used to rule out coronary artery disease (CAD).

Abbreviations: ASE, Agatston score equivalent; CAD, coronary artery disease; CA, coronary angiography;
CI, confidence interval; CT, computed tomography; MSCT-CA, multislice spiral computed tomography coronary angiography.

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Background

In all forms of valvular heart disease, significant associated CAD worsens the perioperative prognosis. CA is still recommended in the preoperative assessment of patients with valvular heart disease (Grade 1 American College of Cardiology/American Heart Association guidelines 1998 and 1999; Grade 1 European Society of Cardiology 2007 [1–3]), although no large-scale clinical trial has assessed the contribution of this invasive investigation. We published a preliminary study [4] that suggested that MSCT-CA might serve as an alternative to invasive coronary angiography in patients scheduled for aortic valve replacement. MSCT-CA was compared with conventional CA. In patients with a calcium score of < 1000, the sensitivity of the MSCT-CA in detecting significant stenosis was 100% and its specificity was 80%. The positive and negative predictive values were 55 and 100%, respectively. The objective of the present study was to assess prospectively the perioperative myocardial ischaemic outcome of patients undergoing valve surgery, after ruling out significant CAD solely on the basis of a normal MSCT-CA result.

Methods

This was a single-centre, prospective, diagnostic, management outcome study. The institutional review board approved the study and all patients provided written informed consent.

From 1st July 2005 to 30th June 2008, all consecutive patients aged 18 years and over who were referred to our...
cardiology department for CA in the preoperative assessment of aortic valve disease (stenosis or regurgitation) were considered for inclusion. Exclusion criteria were: irregular heart rate; iodinated contrast agent contraindication; renal insufficiency; and already rejected for valve surgery for non-CAD reasons.

Our main objective was to validate prospectively the ruling out of significant CAD on the basis of a normal or subnormal MSCT-CA result.

We assumed that patients with a normal or subnormal coronary artery network have a perioperative risk of an ischaemic cardiac event of approximately 1% [5]; in a preliminary study [4], we detected “normal” patients with a negative predictive value of 100% compared with CA; in the same study, we found that CA could have been avoided in 35/55 cases.

Therefore, 110 patients with a normal MSCT-CA were needed, given the hypothesis that none or one of them (approximately 1%) would present with a cardiac ischaemic event during the perioperative period, allowing us to obtain an upper limit of the 95% confidence interval (CI) of <5% for the risk of an ischaemic event (Euro Heart Survey) [5]. In accordance with our previous data to obtain 110 patients with a calcium score <1000 and a normal or subnormal MSCT-CA we planned to include 205 patients.

Except for MSCT-CA and (possibly) CA, clinicians in charge of the patient were allowed to perform any other preoperative evaluation. They made the decision to schedule surgery or reject the patients. Patients not operated on within 6 months after the initial evaluation (including preoperative MSCT-CA) were excluded from the analysis.

**MSCT protocol and image reconstruction**

The MSCT data sets were acquired using a 16-slice MSCT (Philips Mx8000 IDT 16, Eindhoven, The Netherlands). Briefly, a native scan without contrast medium was performed to determine total coronary calcium. A calcified lesion was defined as an area of >3 connected pixels, >130 Hounsfield units, and was expressed as ASE. On the basis of previously published data [4], we determined that in this particular population, contrast medium injection was useless when the ASE was >1000.

Next, a volume data set was acquired (16 × 0.75 mm cross-section; gantry rotation time, 420 ms; table feed, 2.8 mm per rotation), covering the distance from the carina to the diaphragmatic side of the heart. The entire heart was scanned during a single breath-hold; 80–120 mL of contrast agent (Iomeron 350, Bracco SA, Milano, Italy) was injected continuously at a rate of 4 mL/s. Automated detection of peak enhancement in the aortic root was used to time the scan.

Cross-sectional images were reconstructed with a slice thickness of 0.8 mm at 0.4 mm intervals with retrospective gating. A scoring method analogous to the Agatston score [6] was used to quantify coronary calcium.

All data sets were analysed independently by two physicians experienced in MSCT, using multiplanar reformations, three-dimensional reconstructions by the “volume rendering” technique and “comprehensive cardiac” software. They were asked to give a consensus on the presence of significant CAD on a per patient basis. Image quality was classified as “good” (no or only minor motion artefacts), “moderate” (substantial motion artefacts), or “bad” (significant motion artefacts and/or low signal-to-noise ratio and no luminal assessment of significant stenosis possible in at least one vessel). In addition, the observers were asked to state their recommendations for patient management (i.e., CA indicated or not).

CA was performed when recommended on the same day after MSCT if the ASE was >1000, and 2 days later if the MSCT was of bad quality or if significant CAD was suspected. Angiograms were evaluated by an independent observer, blinded to the MSCT-CA results, using quantitative CA (Numeric System, DX-DLX, General Electric Medical Systems, Buc, France) as the gold standard of stenosis detection. Lesions with a ≥50% diameter reduction counted as significant stenosis.

**Follow-up**

All patients were followed for 30 days after aortic valve surgery. Perioperative myocardial infarction was defined as a significant elevation (≥20 ng/mL) of plasma troponin Ic during the first 24 hours after surgery and no other clear explanation. During the postsurgery period, myocardial infarction was defined by the association of chest pain, new onset Q waves and troponin Ic elevation (≥0.2 ng/mL above the last measurement) [7,8]. The outcome events were judged by an adjudication committee, comprising three independent experts who were blinded to the tests performed before surgery. In cases of death or suspected myocardial infarction within the 30-day period, the patient chart was reviewed, and death and troponin elevation were judged as being related or unrelated to a coronary artery ischaemic event. Unrelated events were due to obvious perioperative causes, such as a drawback in myocardial protection (isolated troponin Ic elevation with no Q waves and no wall-motion abnormality).

**Statistical analysis**

General characteristics, CAD risk factors and clinical signs were expressed as means and standard deviations for continuous variables and as percentages for qualitative variables. The rates of myocardial infarction and death during follow-up in patients undergoing aortic valve surgery with no prior CA on the basis of a normal MSCT-CA were assessed with their respective 95% CIs. All analyses used SPSS analysis software, version 12.0 (SPSS Inc., Chicago, IL, USA).

**Results**

The patient flowchart is presented in Fig. 1. From 1 July 2005 to 30 June 2008, 215 patients were considered for inclusion in the study. As specified previously, we excluded a posteriori 16 patients from the analysis, as they did not undergo surgery within a period of 6 months after initial preoperative evaluation.

The patients’ general characteristics were as follows: 118 men (59%); mean age, 69 ± 12 years; mean heart rate, 68 ± 9 beats per minute; previous oral treatment with beta-
blockers, \( n = 40 \) (20%); and intravenous beta-blockers before injection, \( n = 28 \) (14%). Of the 199 patients included, 63 (31.66%) with an ASE > 1000 did not undergo CT opacification and underwent CA on the same day. Of the 136 patients with an ASE < 1000 and who underwent MSCT-CA, CA was also performed 2 days after MSCT-CA in 12 patients (6.0%) because of the bad quality of the MSCT and in 18 patients (9.0%) because of abnormalities in the coronary artery network detected by MSCT-CA. The remaining 106 patients (78% of patients with an ASE < 1000) had a normal MSCT-CA (good quality, \( n = 85 \); intermediate quality, \( n = 21 \)) and underwent aortic valve surgery without prior CA. The baseline characteristics of these patients are summarized in Table 1. Of these 106 patients, six underwent a Ross’s intervention, three underwent a Tyrone David’s intervention and seven a Bentall’s procedure. Finally, 49 biological and 48 mechanical prostheses were implanted.

The calcium score was 0 for 42 patients, 38 of whom had a normal injected MSCT. In four cases, quality was poor and CA was performed and was normal in all cases. Finally, 93 patients underwent CA, which was considered normal (no significant stenosis) in 39 cases and abnormal in 54 cases. Only 33 of these 54 patients benefited from a coronary revascularization; the others had distal severe lesions.

One patient died during surgery (a 77-year-old woman who died after a perioperative right ventricular injury that was impossible to repair; 0.94%, 95% CI 0.17—5.15).

Follow-up

The mean postsurgery troponin I concentration was 9.17 ± 26.3 ng/mL.

Of the 199 patients finally included and analysed, seven had a suspected acute myocardial infarction after surgery. The adjudication committee reviewed all of these patients’ charts, blinded to the results of the preoperative CAD assessment: three had a normal preoperative MSCT-CA, one had a normal CA and three had an abnormal CA (in these cases surgical revascularization was associated with the valve replacement). Of the three patients with a normal MSCT-CA, only one was considered to have had a perioperative myocardial infarction, whereas two patients had a drawback in myocardial protection during aortic cross-clamping time. These two patients had elevated troponin I concentration without Q waves on the electrocardiogram and no wall-motion abnormality on the echocardiogram (the calcium score was 0 for one of them). In both cases, the myocardial protection problem was noted in the surgery report. The patient who had a myocardial infarction had a mild stenosis on the first diagonal artery that had been reported on the MSCT-CAD but had been considered to be non-significant on a small artery. The postoperative CA confirmed the occlusion of the diagonal artery at the level of the stenosis. No percutaneous intervention was performed.

Of the 106 patients, none suffered from an ischaemic event during the 30-day follow-up period but two patients...
died: one had a haemorrhagic stroke on day 1, the other died on day 12 from septic shock. Thus, the final 30-day myocardial infarction rate was 1/106 (0.94%, 95% CI 0.17—5.15) and the 30-day death rate was 3/106 (2.8%, 95% CI 1.0—8.0).

Considering only those patients who underwent CA, 39/39 (100%) patients with a normal test underwent surgery with no ischaemic event, but one had a significant increase in troponin blood concentration due to a lack of myocardial protection. Three patients with significant CAD had a myocardial infarction (3/54: 5.6%, 95% CI 1.9—15.1).

Considering patients with an ASE > 1000 (who all underwent CA), the final 30-day myocardial infarction rate was 2/63 (3.2%, 95% CI 0.9—10.9). These two patients benefited from combined surgery with coronary artery revascularization.

Discussion

In this prospective management outcome study, a normal or subnormal MSCT-CA allowed us to avoid CA in 106/199 (53%) patients referred to our centre for the preoperative evaluation of CAD before aortic valve surgery. One patient experienced a perioperative myocardial infarction. This rate (0.94%, 95%CI 0.17—5.15) is concordant with data published previously on perioperative ischaemic events in European patients with previous normal or subnormal coronary angiography [5].

Cardiac MSCT is a rapidly evolving technique that allows noninvasive depiction of the epicardial coronary circulation. A huge amount of literature is being published on this technique. Most evaluations compare CT with the gold standard coronary angiography on a per segment or a per patient analysis. As the technique has improved, data using 4-section CT [9], 16-section CT, 64-section CT [10], and now dual-source CT [11] have become available, emphasizing the good negative predictive value of the test. Most of these data were acquired by trained teams in single-centre studies. This is one limitation of our study: it was done in a single centre with trained physicians doing a double analysis of each CT.

Data from multicentre studies are rare and possibly less optimistic [12]. Nevertheless, in clinical practice, the most important factor is no longer the comparison with the reference test but the clinical outcome follow-up in various clinical indications. Gilard et al. [13] suggested that it was safe to use a normal or subnormal MSCT to rule out significant CAD in patients with atypical chest pain or discordant stress tests; this allowed them to be managed less invasively, by reducing the number who required CA. The risks of subsequent death (0%), new referral for CA (3.5%) or coronary events (0.7%) compared favourably with those after normal CA, which were 0.4%, 4.3%, and 0.6%, respectively.

Another study published by Gilard et al. [4] evaluated the ability of MSCT-CA to rule out significant CAD in 55 patients scheduled for CA in the preoperative evaluation of CAD before aortic valve replacement. For all patients, MSCT-CA findings were compared with CA as the gold standard. The sensitivity of the MSCT-based strategy in detecting significant stenosis was 100%. The results of this initial study on a small number of patients suggested that MSCT-CA might serve as an alternative to CA in the preoperative evaluation of CAD in patients with aortic valve stenosis. Laissy et al. [14] and Reant et al. [15], in a per segment analysis, showed that MSCT-CA had a 93% and 99% negative predictive value, respectively, compared with CA, for ruling out significant CAD in comparable populations. The next step in the validation of MSCT-CA in this particular indication (in order to avoid performing CA in cases of normal or subnormal MSCT-CA and to rule out significant CAD on the sole basis of a normal or subnormal MSCT-CA), was to perform a management outcome study—that is, a study in which clinical decision is based on this test alone.

In the Euro Heart Survey on Valvular Heart Disease [5], CA was performed in 84.9% of operated patients. Reasons advocated for not performing CA were: absence of cardiovascular risk factor (31.3%); acute endocarditis; poor haemodynamic conditions; no catheterization facility available; and absence of evidence of ischaemia. Perioperative myocardial infarction was rare (1%) in the population with no associated coronary artery revascularization but was not zero. Most acute coronary syndromes occur by rupture or erosion of 'high-risk plaques' that are not significantly stenotic in more than two-thirds of cases; thus, it will never be possible to detect 100% of high risk patients using pure anatomical imaging tests. Molecular imaging might help soon in these indications.

There are many advantages to performing CT instead of CA in the preoperative evaluation of patients with severe aortic valve disease. The cost of CT is probably much less than CA in all countries and local complications are rare.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± Standard Deviation</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>68.4 ± 12</td>
</tr>
<tr>
<td>Men</td>
<td>55.0</td>
</tr>
<tr>
<td>Creatinine clearance (mL/min/m²)</td>
<td>74.3 ± 16</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
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<tr>
<td>Body mass index</td>
<td>25.6 ± 4.2</td>
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<tr>
<td>Smokers</td>
<td>37.7</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>45.7</td>
</tr>
<tr>
<td>Diabetes</td>
<td>11.0</td>
</tr>
<tr>
<td>Family history of coronary artery disease</td>
<td>11.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>49.7</td>
</tr>
<tr>
<td>Severe aortic stenosis (n = 89)</td>
<td></td>
</tr>
<tr>
<td>Valve area (cm²)</td>
<td>0.64 ± 0.15</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>54.8 ± 14</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>64 ± 13</td>
</tr>
<tr>
<td>Annuloaortic ectasia (n = 6)</td>
<td></td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>58 ± 11</td>
</tr>
<tr>
<td>Major aortic regurgitation (n = 11)</td>
<td></td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>63 ± 12</td>
</tr>
<tr>
<td>Multislice spiral computed tomography</td>
<td></td>
</tr>
<tr>
<td>Dose length product (mGy/cm)</td>
<td>672 ± 100</td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation or %. LVEF: left ventricular ejection fraction.
There is no necessity for hospitalization so all the pre-operative assessment can be performed in the outpatient setting. Cost and radiation exposure of calcium scoring are low and only patients with a poor quality or abnormal MSCT-CA (30/199 in our study; 15.1%) need undergo both MSCT-CA and CA. Cardiac multidetector CT is a rapidly evolving technique that needs strong clinical evaluation to support its worldwide use. Many studies validate its high negative predictive value compared with CA findings. The primary reason for performing CAD assessment before valve surgery is to avoid perioperative ischaemic events. Obviously, long-term follow-up was not performed in this study and patients were not randomized, so it was not possible to compare long-term occurrence of ischaemic events after a normal CA or a normal MSCT. This kind of randomized comparison might be the next and final step to provide sufficient data to justify MSCT being incorporated into future guidelines.

Conclusion

In this prospective study, we showed that it was as safe to perform aortic valve surgery after a normal or subnormal MSCT-CA as after a normal or subnormal CA. This approach could avoid the need for CA in more than 50% of cases and it might be integrated soon into the guidelines on the management of severe aortic valve disease.

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Conflict of interest statement

None.

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References