Institutional report - Coronary

Coronary artery disease in patients with cardiac tumors: preoperative assessment by computed tomography coronary angiography

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Abstract

We studied the diagnostic accuracy of computed tomography coronary angiography (CTCA) for the diagnosis of significant coronary artery disease (CAD) compared to conventional coronary angiography (CCA) in patients with primary cardiac tumors. Thirty-eight consecutive patients with primary cardiac tumors (27 females, 11 males; mean age 56 ± 6 years, range 32–86 years) underwent dual-source CTCA and CCA. Significant stenosis was defined as diameter reduction >50%. CCA served as the standard of reference. The prevalence of significant CAD in the study population was 8% (3/38 patients). Five of 544 segments (0.9%) in 1/38 patients (2.6%) was considered of non-diagnostic image quality on CTCA because of motion artifacts. In a segment-based analysis taking not-evaluative segments as false-positive, sensitivity, specificity, positive and negative predictive value of CT was 100%, 99%, 70%, and 100%, respectively. Preoperative CCA could have been avoided in 95% (36/38) of the patients and CCA would have confirmed the CTCA diagnosis in 5% (2/38) of the patients. Our results indicate that CTCA provides a high diagnostic performance for diagnosing significant CAD in patients with primary cardiac tumors. CTCA may thus be used as a filter test prior to surgery.

Keywords: Primary cardiac tumors; Coronary artery disease; Computed tomography; Conventional coronary angiography

1. Introduction

Primary cardiac tumors represent a relatively rare entity with a reported prevalence of only about 0.02% in the general population [1]. Nevertheless, they may cause significant morbidity and mortality if not treated appropriately. Surgical resection is the method of choice for most primary cardiac tumors [2]. Significant coronary artery disease (CAD) worsens the perioperative morbidity of patients undergoing cardiac surgery [2]. Nevertheless, recommendations for the preoperative evaluation of CAD with conventional coronary angiography (CCA) in these patients prior to surgery are not uniform. The common practice on whether or not to perform CCA usually depends on the age and risk factors of the individual patient [3–6].

Computed tomography coronary angiography (CTCA) has emerged over the past decade as a non-invasive alternative to CCA for imaging the coronary arteries. Besides the target population of CTCA, i.e. patients with a low- to intermediate risk of CAD and having an inconclusive stress test [7], a potential gatekeeper function of CTCA as a filter test has been proposed [8]. For example in patients with valvular disease prior to non-coronary cardiac surgery, CTCA has shown excellent performance characteristics as a gatekeeper for CCA [9].

In this study, we evaluated the diagnostic performance of CTCA to detect or rule-out significant CAD in patients prior to elective surgery for primary cardiac tumors in order to explore the role of CTCA as a gatekeeper to CCA.

2. Materials and methods

2.1. Study population

The Institutional Committee on Human Research has approved the study, and written informed consent was obtained prior to patient inclusion. Between July 2006 and September 2009, 38 consecutive patients with primary cardiac tumors were referred for CCA prior to cardiac surgery for the diagnosis or exclusion of CAD. Exclusion criteria were previous allergic reactions to iodinated contrast media, denial of informed consent, renal insufficiency (serum creatinine level > 150 mmol/l), and pregnancy. The final study population comprised 38 patients (27 females, 11 males; mean age 56 ± 6.8 years, range 32–86 years) who

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all underwent CTCA in our institution. Patient demographics are shown in Table 1. CCA and CTCA were performed within 14±9 days (range 1–30 days). Surgery was performed within 30±17 days (range 1–56 days) after CCA and CTCA.

2.2. CT-scan protocol

All patients were scanned on a dual-source CT-scanner (Somatom Definition, Siemens Healthcare, Forchheim, Germany) with detector collimation 2×32×0.6 mm, slice acquisition 2×64×0.6 mm using a z-flying focal spot, gantry rotation time 330 ms, pitch 0.2–0.5 depending on the heart rate, tube current time product 330 mAs per rotation, and tube potential 120 kV. An initial non-enhanced scan was performed for calcium scoring with the following scan parameters: detector collimation 2×32×0.6 mm, slice acquisition 2×64×0.6 mm using a z-flying focal spot, gantry rotation time 330 ms, tube current time product 80 mAs per rotation, and tube potential 120 kV.

Then, all patients received a single dose of 2.5 mg isosorbide dinitrate sublingually per rotation, and tube potential 120 kV. A try rotation time 330 ms, tube current time product 80 mAs

Table 1

Demographic data and types of primary cardiac tumors

| Patients | 38 |
| Gender | 56±6 |
| Female | 27 |
| Male | 11 |
| Primary cardiac tumor | | |
| Myxoma | 23 |
| Left atrial | 22 |
| Right atrial | 1 |
| Fibroelastoma aortic valve | 6 |
| Sarcoma | 4 |
| Pulmonary artery | 2 |
| Left ventricle | 1 |
| Right ventricle | 1 |
| Hemangioma | 2 |
| Tricuspid valve | 1 |
| Epicardium | 1 |
| Paraganglioma left atrium | 1 |
| Sinus histiozytosis right atrium | 1 |
| Cusheus calcification mitral valve annulus | 1 |
| Risk factors for coronary artery disease | | |
| Hypertension (%) | 36 |
| Smoker (%) | 32 |
| Hypercholesterolemia (%) | 20 |
| Diabetes (%) | 8 |

S.D., standard deviation.

Calcium Scoring, Siemens) by an experienced observer who was not involved in CTCA data readout.

For analysis of CTCA data, coronary arteries were segmented according to a scheme proposed by the American Heart Association [10]: the right coronary artery (RCA) was defined to include segments 1–4, the left main (LM) and left anterior descending artery (LAD) to include segments 5–10, and the left circumflex artery (LCX) to include segments 11–15. The intermedial artery was designated as segment 16, if present. All segments with a diameter of at least 1 mm at their origin were included. Segments distal to an occluded vessel were excluded from the analysis because of potential reduced opacification of the coronary artery segments distal to the stenosis. Vessel diameter measurements were made using electronic calipers.

All CTCA images were evaluated by two independent and experienced observers using axial-source images and multiplanar reformations (MPR) on a per-segment basis.

First, both readers judged the image quality of all coronary segments as being diagnostic or not. In segments with non-diagnostic image quality, the reasons for impairment were selected using the following list: motion artifacts, insufficient contrast attenuation, severe calcium deposits in the vessel walls, and image noise. Calcium deposits in the wall of the coronary vessels may cause reduced image quality due to ‘blooming artifacts’ which can limit the visualization of the vessel lumen. This may lead to an overestimation of the stenosis that tends to result in false-positive (FP) ratings potentially reducing the specificity of CTCA.

When one of the two observers classified a vessel segment as being non-diagnostic, the segment was rated as being non-diagnostic independent of an opposite rating of the other reader.

Second, both observers assessed all coronary segments for the presence of significant stenoses. Significant stenosis was defined as luminal diameter narrowing exceeding 50%. Vessel diameters were measured on reconstructions perpendicularly oriented to the vessel centerline using electronic calipers. For any disagreement in stenosis assessment, consensus agreement was appended.

2.4. Conventional coronary angiography

CCA was performed according to standard techniques in multiple projections. The angiograms were evaluated by one experienced observer who was blinded to the findings from CTCA by using computerized quantitative coronary angiography analysis software (Xcelera, Philips Medical Systems, The Netherlands). Each vessel segment was scored as being significantly stenosed, defined as a diameter reduction exceeding 50%, or not. Coronary artery analysis was performed in all vessels with a luminal diameter of at least 1 mm, excluding those vessels distal to complete occlusions.

2.5. Statistical analysis

All statistical analyses were performed by using commercially available software (SPSS, release 17.0, Chicago, IL, USA). Continuous variables were expressed as means±stan-
Table 2
Diagnostic performance of CTCA for the diagnosis of significant (>50%) coronary artery stenoses in patients with primary cardiac tumors

<table>
<thead>
<tr>
<th>Segment</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segment-based</td>
<td>9</td>
<td>346</td>
<td>3</td>
<td>0</td>
<td>100 (59–100)</td>
<td>99 (98–100)</td>
<td>70 (35–93)</td>
<td>100 (99–100)</td>
</tr>
<tr>
<td>Vessel-based</td>
<td>3</td>
<td>70</td>
<td>2</td>
<td>0</td>
<td>100 (48–100)</td>
<td>99 (95–100)</td>
<td>83 (36–100)</td>
<td>100 (97–100)</td>
</tr>
<tr>
<td>Patient-based</td>
<td>2</td>
<td>22</td>
<td>1</td>
<td>0</td>
<td>100 (29–100)</td>
<td>90 (90–100)</td>
<td>100 (29–100)</td>
<td>100 (90–100)</td>
</tr>
</tbody>
</table>

The analyses were performed including all segments: segments of non-diagnostic image quality were rated as positive for stenosis.

CTCA, computed tomography coronary angiography; TP, true-positive; TN, true-negative; FP, false-positive; FN, false-negative; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

standard deviations, and categorical variables as frequencies and percentages.

Inter-observer agreements regarding the diagnosis of significant stenoses were evaluated using κ statistics: κ values of 0.00–0.20 were considered to indicate poor agreement; κ values of 0.21–0.40 fair agreement; κ values of 0.41–0.60 moderate agreement; κ values of 0.61–0.80 high agreement; and κ values of 0.81–1.00 excellent agreement.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated from χ²-tests of contingency, and the 95% confidence intervals (CIs) were calculated from binomial expression on a per-segment, per-vessel, and per-patient basis. Per-segment, per-vessel (i.e. at least one stenosis identified in the artery), and per-patient (i.e. at least one stenosis identified in the patient) analyses were performed for all segments. Segments of non-diagnostic image quality were rated as positive.

CCA was taken as the standard of reference. A P<0.05 was considered significant for all tests.

3. Results

The average CTCA scan duration was 12.7±1.4 s (range 10.3–16.4 s), the average scan range was 138.1±11.8 mm (range 91.0–167.0 mm), and the average heart rate during scanning was 67.3±11.8 bpm (range 54–96 bpm). None of the patients was on baseline beta-blocker medication at the time of CT.

3.1. Conventional coronary angiography

CCA identified seven coronary segments with significant stenoses in 3/38 patients (8%). Two-vessel disease was found in two patients (67%, segments 9, 10, 12, and 13; 2 and 6, respectively) and single-vessel disease in one (33%, segment 7) of the three patients. Significant coronary artery stenoses were excluded in 35/38 patients (92%).

3.2. Computed tomography coronary angiography

Of the 608 theoretically possible coronary artery segments, 544 (90%) were evaluated with CTCA. Forty-one segments (6%) were missing because of anatomical variants and 23 segments (36%) had a diameter <1 mm at their origin.

Calcium scoring scans revealed calcified vessel wall deposits in 11 patients (29%). Two of these 11 patients (18%) had significant coronary stenoses (as determined by CCA), whereas nine patients (82%) had calcifications not causing significant stenoses. The Agatston score of all 38 patients was 126±335 (range 0–1511). The mean Agatston score in the patients with significant stenoses was 1049±595 (range 412–1511), being significantly (P<0.001) higher than that in the patients without significant stenoses (43±107, range 0–453).

Five hundred and thirty-nine of 544 segments (99.1%) in 37 of the 38 patients (97%) were rated as being of diagnostic image quality. All segments with non-diagnostic image quality were present in the one patient (segment 2, 6, 11, 335).
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Fig. 2. A 62-year-old female patient with a cardiac myxoma in the left atrium prior to cardiac surgery. (a) Axial contrast-enhanced CT image in the 4-chamber view shows the left atrial myxoma (arrows) prolapsing through the mitral valve into left ventricle. LV, left ventricle; RV, right ventricle; LA, left atrium. Curved multiplanar reformations of CTCA demonstrate diagnostic image quality of the right coronary artery (b), left anterior descending artery (c), and circumflex artery (d) without significant stenoses. Note the myxoma (arrows) in the left atrium (LA).

Fig. 3. A 56-year-old male patient with a cardiac myxoma in the left atrium. (a) Axial contrast-enhanced CT image in the 4-chamber view shows the left atrial myxoma (black arrows) prolapsing through the mitral valve into left ventricle during the cardiac cycle. Curved multiplanar reformations of CTCA demonstrate significant stenosis of the left anterior descending artery (white arrow) (b). Circumflex artery (c) and right coronary artery have no obstructive coronary artery disease (d).

13, 14) with significant stenosis (segment 2 and 6). Non-diagnostic image quality was caused by motion artifacts. Insufficient contrast attenuation, severe vessel wall calcifications, or image noise were not found to be the cause of non-diagnostic image quality in any segment of the 37 remaining patients.

3.3. Diagnostic performance

Inter-observer agreement for the detection of significant coronary stenosis at CTCA was $k=0.84$, indicating an excellent agreement between the two observers.

CTCA correctly [true-positive (TP)] classified seven of significantly obstructed segments (100%). Three FP and no false-negative (FN) ratings occurred on a per-segment basis. FP ratings (including the one segment with non-diagnostic image quality) occurred in side-branches ($n=2$; segment 11, 12) and distal segments ($n=1$; segment 8).

In a per-segment analysis including all segments, the sensitivity, specificity, PPV, and NPV were 100%, 99%, 70%, and 100% (Table 2).

In a per-vessel analysis including all segments, CTCA correctly (TP) classified five of five significantly obstructed vessels (100%). One FP and no FN ratings occurred on a per-vessel basis. The sensitivity, specificity, PPV, and NPV were 100%, 99%, 83%, and 100% (Table 2).

In a per-patient analysis including all segments, CTCA correctly (TP) classified three of three patients (100%) having at least one significant coronary artery stenosis. One FP and no FN ratings occurred on a per-patient basis. The sensitivity, specificity, PPV, and NPV were 100%, 100%, 100%, and 100% (Table 2).

Preoperative CCA could have been avoided in 95% (36/38) of the patients (Figs. 1 and 2), CCA would have been
performed to confirm the CT diagnosis in 5% (2/38) (Fig. 3).

4. Discussion

The symptoms produced by cardiac tumors are often non-specific and may simulate a wide variety of other diseases including myocardial ischemia [11]. Therefore, preoperative CCA is often performed in patients with primary cardiac tumors for ruling-out concomitant CAD [5]. In our population, the prevalence of significant CAD was 8%. According to the Bayesian theorem, the prevalence of disease affects the diagnostic performance of a test. When the prevalence decreases, the PPV will decrease and the NPV will increase and when the prevalence increases the PPV will increase and the NPV will decrease. In both cases, the sensitivity and specificity remains relatively unaffected [12]. Therefore, the low prevalence of significant CAD in our patients with primary cardiac tumors is also reflected in the high NPV that indicates a benefit of non-invasive coronary imaging with CT with regard to the number of avoidable conventional angiograms.

In this study, CCA depicted in patients with primary cardiac tumors 99.1% of all coronary segments with diagnostic quality. Only five side-branches had to be excluded from analysis due to motion artifacts. None of the coronary segments had to be excluded from analysis because of severe vessel wall calcifications. This is most probably explained by the relatively low cardiovascular risk profile, low prevalence of CAD, and the relatively low Agatston score, which can be indicative for significant coronary artery stenosis if high. Additionally no FN ratings occurred on a per-segment basis that seems to be related to the relatively low number of patients; however, FN ratings are generally marginal in comparison to FP ratings as evidence in larger study populations [13]. On a per-segment basis, the PPV of dual-source CT coronary angiography was slightly decreased in comparison with the per-patient analysis owing to FP ratings that is still a problem of CTA [13].

The diagnostic performance of CTA for the assessment of significant CAD in patients undergoing elective surgery for primary cardiac tumors proved to be excellent in our study. Similar results have been reported in the literature in stable, symptomatic patients having a low- to intermediate pre-test probability of CAD. Although the reported sensitivities and specificities of CTA vary from 73–99% to 90–97%, the NPV was invariably high ranging from 96–100% [14]. This leads to the widely accepted conclusion that a normal CTA reliably rules-out significant CAD, also in regard of the mid-term follow-up [13]. Our data indicate that these performance characteristics of CTA hold true also in patients with primary cardiac tumors undergoing elective surgery for tumor removal. On an intent-to-diagnose basis while taking not-evaluable coronary segments into account, the accuracy of CTA was 100% on a per-patient basis. Regarding the preoperative imaging work-up of patients with primary cardiac tumors, CCA could have been avoided in 95% of our patients when performing CTA instead.

An additional important issue of CTA is the concomitant visualization of the tumors and their relationship to the surrounding tissue with the same, cross-sectional imaging data that might be important for planning surgery. Particularly, the large field-of-view of CT provides additive information about the mediastinum and lungs [15].

In conclusion, CTA has an excellent diagnostic performance for the diagnosis or exclusion of significant CAD in patients undergoing elective surgery for primary cardiac tumors. Our preliminary results strengthen the role of CTA as a non-invasive gatekeeper in patients undergoing cardiac, non-crownary surgery.

References

