Routine use of coronary computed tomography as initial diagnostic test for angina pectoris

Utilité du scanner coronaire comme examen initial de l’angor stable

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Summary

Background. — Coronary computed tomography (CCT) detects coronary obstruction with high sensitivity and might be useful for diagnosis of angina pectoris.

Aim. — In this pilot study, we sought to prospectively evaluate the performance of CCT as initial work up and determine the significance of this strategy according to the pretest likelihood of having coronary artery disease (CAD).

Methods. — One hundred and eighty patients with chest discomfort and suspected angina were prospectively referred for CCT with a 64-slice CT scan. Invasive coronary angiography (ICA) was performed on the basis of CCT findings (stenosis >50%). Patients were classified into tertiles according to estimated pretest probability of obstructive CAD using the Duke Clinical Score (low, intermediate and high). Strategy failure was defined as unnecessary ICA or major adverse cardiac event (MACE) within 6 months in patients without significant stenosis by CCT.

Results. — Pretest probability for CAD was 53±29%. Significant stenosis was detected by CCT in 51 patients; 47 (26%) underwent ICA. Sixteen strategy failures were reported: 15 patients (10%) were referred for ICA that did not confirm significant coronary stenosis and one MACE occurred in a patient without significant stenosis by CCT. Strategy failures were 8% in low-probability, 1.7% in intermediate-probability and 15% in high-probability patients (P=0.03).

KEYWORDS
Angina;
Coronary disease;
Diagnosis;
Tomography

Abbreviations: CAD, coronary artery disease; CCT, coronary computed tomography; CI, confidence interval; ECG, electrocardiogram; ICA, invasive coronary angiography; MACE, major adverse cardiac event.

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Background

Current guiding principles for angina pectoris recommend functional testing in order to establish the presence of myocardial ischaemia [1]. Coronary angiograms confirm obstructive coronary artery disease (CAD) and are performed on the basis of initial functional tests, especially stress echo and nuclear imaging. Coronary computed tomography (CCT) is a rapidly developing technique that allows reliable evaluation of the coronary arteries compared with invasive coronary angiography (ICA) [2—4]. CCT has shown high sensitivity for detecting obstructive coronary disease in a non-invasive manner and subsequently has been introduced for diagnosis of angina pectoris [5,6]. Although CCT does not evaluate the functional impact of CAD, its overall performance (availability and reliability) appears promising and might play a role in angina diagnosis. The adequate value of CCT as initial work up for chronic angina has not been established. From retrospective analysis, CCT usefulness appears to be dependent on the pretest probability of having CAD and might be most advantageous in subsets of patients, especially those with an intermediate risk [7]. In this pilot study, we prospectively included patients with suspected angina (non-acute coronary syndrome), evaluated the performance of CCT as initial work up, and determined the impact of such a strategy on further investigations and clinical events according to the pretest likelihood of having CAD.

Conclusions. — CCT as an initial step for angina diagnosis is most effective in patients with an intermediate probability of CAD. In patients with low or high likelihood, it is associated with a high rate of unnecessary ICA but not with adverse events.

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Résumé

État des lieux. — Le coroscanner détecte les obstructions coronaires avec une grande sensibilité et pourrait être utile au diagnostic le l’angor stable.

Objectifs. — Dans cette étude pilote, nous avons prospectivement évalué la performance du coroscanner comme examen initial et déterminé la pertinence de cette stratégie en fonction de la probabilité de la maladie coronaire.

Méthodes. — Cent quatre-vingt patients avec douleur thoracique suspecte d’angor ont été évalués par coroscanner multicoupes. Une coronarographie n’était indiquée que sur la base du coroscanner (sténose > 50 %). Les patients ont été classés en fonction de leur probabilité initiale de maladie coronaire en utilisant le score de Duke (faible, intermédiaire, élevé). Un échec de la stratégie était défini comme réaliser une coronarographie blanche (absence de sténose significative) ou la présence d’un événement cardiaque à six mois chez les patients à coroscanner normal.

Résultats. — La probabilité initiale de maladie coronaire était de 53 ± 29 %. Une sténose significative a été détectée par scanner chez 51 patients et 47 (26 %) ont été coronarographiés. Quinze patients (10 %) ont eu une coronarographie blanche et un patient est décédé alors qu’il n’avait pas de sténose au coroscanner. Les échecs de la stratégie étaient de 8, 1,7 et 17 % dans les groupes respectifs de probabilité de maladie coronaire faible, intermédiaire et élevée (p = 0,015).

Conclusions. — Le coroscanner comme étape initiale du diagnostic de l’angor stable est plus pertinent chez les patients à risque intermédiaire de maladie coronaire. Chez les autres patients, une telle stratégie est associée à un taux élevé de coronarographie blanche.

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angiography was performed within 1 month after CT and was based on CT findings (suspected stenosis > 50%). The protocol was reviewed and accepted by the ethics committee of our Cardiology Board.

Scan protocol

All patients with a heart rate greater than 70 beats/min received intravenous beta-blockers (atenolol 5–15 mg) before CT examination; target heart rate was less than 60 beats/min. All scans were performed with a 64-slice CT scanner (Lightspeed VCT; GE Healthcare, Chalfont St. Giles, UK) that features a gantry rotation time of 350 ms, a temporal resolution of 175 ms and a spatial resolution of 0.54 mm². Tube voltage was 120 kV (100 kV for patients weighing < 70 kg) and X-ray tube current was modulated on the ECG (250–650 mA). CT was acquired in a breath-hold and was ECG gated. Rotation speed and pitch were adjusted to the acquisition protocols and to the heart rate. Calcium scoring was not performed. A bolus of contrast media (Ioxaglate 320 mg I/mL, Guerbet) was infused into an antecubital vein with the use of a dual-barrel injector (70 cc of contrast medium at 5 cc/s washed out by 30 cc of isotonic solution at 3.5 cc/s). CT data were analysed by the use of an offline Advantage Workstation (GE Healthcare) using prior interactive interpretation of axial images followed by (curved) multiplanar reconstruction. Phases from 0–90%, every 10%, were systematically reconstructed to allow for imaging of coronary arteries. Segments were scored as positive for significant CAD if there was a greater or equal to 50% diameter reduction of the lumen (in a vessel with a reference diameter greater or equal to 2 mm) by visual assessment.

Three experienced observers (> 500 CT coronary angiograms) who were blinded to previous medical history and symptoms participated in the study (one interpreter per patient). Optimal quality CT scan was defined as lumen visual assessment available in all coronary arteries greater than 2 mm in diameter. For patients with non-optimal quality CT (including heavy calcification without lumen assessment), ICA was suggested.

Angiographic analysis

Baseline quantitative angiography was performed using the contrast-filled injection catheter for image calibration. Cine angiographic stenosis was defined as stenosis greater than 50%. Quantitative coronary angiographic analysis was performed using the Integris H5000C software (Philips, Amsterdam, The Netherlands). Myocardial revascularization was recommended on the basis of current guidelines on the management of stable angina, in view of symptoms, functional tests, medical history and ICA findings [1].

Outcome

Clinical follow-up was performed at 6 months by phone call and/or physician visit. A major cardiac event was defined as death (all-cause mortality), Q-wave and non-Q-wave myocardial infarction (total creatinine kinase elevation greater or equal to three times normal and/or new pathological Q-waves in greater or equal to two contiguous leads) or ICA. Strategy failure was defined as either performing an ICA that showed no significant stenosis in a patient with suspected stenosis by CCT (unnecessary ICA) or a major adverse cardiac event (MACE) in a patient without suspected stenosis by CCT (false negative CCT).

Statistics

Continuous variables are expressed as means ± standard deviations. Categorical data are expressed as percentages. Chi² statistics and Fisher’s exact test were used to compare continuous variables and categorical values, respectively. A p value less than 0.05 was considered statistically significant. Statview 5.0 software (SAS Institute Inc., Cary, NC, USA) and the VASSAR web calculator (www.vassar.edu) were used to perform the analysis.

Results

Baseline characteristics of the population are presented in Table 1. Pretest probability of CAD was 53 ± 29%. According to tertiles, patients were classified as low probability (range 2–33%), intermediate probability (34–69%) and high probability (70–100%). Only 45 patients (25%) had a previous submaximal stress test; 135 had no previous test before CCT. CCT was defined as optimal in 163 patients (91%). Radiation dose was 1200 ± 355 mGy·cm (20.4 ± 6.0 mSv). No significant side effect besides nausea was reported and all patients were discharged immediately after CT. Reasons for non-optimal CT were heart rate greater than 80 beats/min despite atenolol (n = 8), heavy coronary calcifications (n = 5), extrasystoles during acquisition (n = 3) and high corpulence (n = 1). CT identified 51 patients with suspected coronary stenosis greater than 50% (Table 2). Four patients did not undergo ICA: two patients declined; and two patients were asymptomatic with a negative stress test after medical treatment initiation and were not referred for ICA in view of CT findings (one-vessel disease/distal left anterior descending in one patient; two-vessel disease/diagonal and obtuse marginal in one patient). ICA was performed in 47 patients, and significant stenosis (> 50%) was confirmed in 32 patients (Table 3). The rate of ICA without significant coronary stenosis was 83% in low-probability patients, 30% in high-probability patients and 9% in intermediate-probability patients (p = 0.007).

### Table 1 Baseline characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (n)</td>
<td>180</td>
</tr>
<tr>
<td>Mean age ± SD (years)</td>
<td>63 ± 11</td>
</tr>
<tr>
<td>Men (%)</td>
<td>56</td>
</tr>
<tr>
<td>Hypercholesterolaemia (%)</td>
<td>38</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>16</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>32</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>33</td>
</tr>
<tr>
<td>Typical angina (%)</td>
<td>34</td>
</tr>
</tbody>
</table>

SD: standard deviation.
Table 2  Results: imaging.

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 180)</th>
<th>Low probability (n = 60)</th>
<th>Intermediate probability (n = 60)</th>
<th>High probability (n = 60)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCT findings</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td><strong>CCT findings</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optimal imaging</td>
<td>163 (91)</td>
<td>57 (95)</td>
<td>54 (90)</td>
<td>52 (87)</td>
<td>NS</td>
</tr>
<tr>
<td>Atherosclerotic plaques</td>
<td>95 (53)</td>
<td>18 (30)</td>
<td>32 (53)</td>
<td>45 (75)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Calcified plaques</td>
<td>80 (44)</td>
<td>16 (27)</td>
<td>26 (43)</td>
<td>38 (63)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Number of diseased vessels</td>
<td>0.9 ± 1.1</td>
<td>0.5 ± 0.8</td>
<td>0.9 ± 1.1</td>
<td>1.5 ± 1.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Stenosis &gt; 50%</td>
<td>51 (28)</td>
<td>6 (10)</td>
<td>14 (23)</td>
<td>31 (52)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ICA findings</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stenosis &gt; 50%</td>
<td>32 (18)</td>
<td>1 (1.7)</td>
<td>10 (17)</td>
<td>21 (35)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

CCT: coronary computed tomography; ICA: invasive coronary angiography; NS: not significant. Data are number (%) or mean ± standard deviation.

Table 3  Coronary computed tomography and subsequent invasive procedures; impact of pre-test probability of coronary artery disease.

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 180)</th>
<th>Low probability (n = 60)</th>
<th>Intermediate probability (n = 60)</th>
<th>High probability (n = 60)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-test CAD risk (%)</td>
<td>53 ± 29</td>
<td>20 ± 9</td>
<td>52 ± 11</td>
<td>86 ± 9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Positive CCT</td>
<td>51 (28)</td>
<td>6 (10)</td>
<td>14 (23)</td>
<td>31 (52)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ICA</td>
<td>47 (26)</td>
<td>6 (10)</td>
<td>11 (18)</td>
<td>30 (50)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ICA without coronary stenosis &gt; 50%</td>
<td>15 (8)</td>
<td>5 (8)</td>
<td>1 (1.7)</td>
<td>9 (15)</td>
<td>0.03</td>
</tr>
<tr>
<td>Revascularization</td>
<td>29 (16)</td>
<td>1 (1.7)</td>
<td>10 (17)</td>
<td>18 (30)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

CAD: coronary artery disease; CCT: coronary computed tomography; ICA: invasive coronary angiography. Data are number (%) or mean ± standard deviation.

Rate of ICA without stenosis was 5/6 (83%) in low probability patients, 1/11 (9%) in intermediate probability patients and 9/30 (30%) in high probability patients (p = 0.007).

artery disease by ICA. Revascularization was performed in 29 patients, all by percutaneous coronary angioplasty, including 17 patients with typical angina pectoris and 12 patients with atypical chest pain and coronary stenosis greater than 70% by ICA. Ultimately, eight patients had a stress test (one ischaemia on nuclear test; seven tests were submaximal).

Six-month follow-up was available in 94% of patients with negative CCT (121/129). One patient with normal coronary arteries by CCT died of dilated cardiomyopathy diagnosed at time of initial clinical work up (left ventricle dilatation by CCT). No additional MACE was reported in patients without significant stenosis by CCT. Of note, one patient with recurrent chest pain and normal CCT was recently diagnosed with porphyria.

Strategy failure was observed in 16 patients (9%): unnecessary ICA (n = 15); MACE (n = 1). Strategy failures were 8.3% (n = 5) in low-probability patients, 1.7% (n = 1) in intermediate-probability patients and 15% (n = 9) in high-probability patients (p = 0.03). Overall, sensitivity was 0.97 (95% confidence interval [CI]: 0.82 to 1.0), specificity was 0.86 (95% CI: 0.79 to 0.91), the positive predictive value was 0.63 (95% CI: 0.48 to 0.75) and the negative predictive value was 0.99 (95% CI: 0.95 to 1.0).

Discussion

CCT has been compared with ICA for the detection of significant coronary artery lesions in several studies [9]. These...
studies demonstrated that significant coronary artery lesions can be identified with high sensitivity, especially since the introduction of newer imaging modalities (>64-detector tomography). Angina diagnosis is based on functional tests and coronary imaging is recommended once myocardial ischaemia is established. Given that CCT showed a very high negative predictive value for CAD, CCT in angina might be an alternative to a functional test for excluding significant coronary stenosis. CCT is already promising for acute chest pain, but has been poorly evaluated as an initial test for angina pectoris [10,11]. As the prevalence of a normal study decreases with age, severity of complaints and traditional risk factors, CCT may be more useful in patients with low-to-intermediate pretest likelihood of CAD [7,12]. However, referring those patients for CCT may induce a high false positive rate and numerous unnecessary invasive angiograms. This study provides prospective evaluation of CCT for angina diagnosis according to the pretest probability of CAD.

We defined strategy failure as a combined endpoint of unnecessary ICA in patients with suspected stenosis by CCT (false positive CCT) or MACE in patients without stenosis by CCT (false negative CCT). Confirming the high negative predictive value of CCT, we observed a MACE in only one patient with a normal CCT in our study. Patients with normal CCT did not experience cardiac ischaemic events and did not undergo ICA. Therefore, strategy failures were mostly driven by false positive CCTs.

The main finding of our study was that the use of CCT for angina diagnosis is associated with an acceptable rate of ‘blank angiogram’ (10%). CCT was most accurate in patients with an intermediate likelihood of CAD. Strategy failure CCT (requiring ICA with unconfirmed stenosis by angiography) was lower in this group than in high- or low-risk patients. In the intermediate-risk group, we observed significant coronary stenosis by angiogram in 17% of patients, 91% of whom had this confirmed. An unnecessary angiogram was performed in only 1/60 patients (1.7%). The present study confirms that a strategy that includes CCT as initial work up in suspected angina is relevant in patients with an estimated probability of CAD ranging from 35—70%.

Patients with a high likelihood of CAD are not considered to be good candidates for CCT, according to current recommendations [13,14]. In this group, one-third of patients positive for CCT did not show significant CAD ultimately; this can be explained by higher atherosclerotic burden and higher coronary calcium, which tend to overestimate the severity of atherosclerosis [15]. Calcifications and stenosis overestimation accounted for unnecessary angiograms in five patients (8% of the entire group; 16% of patients with high risk and positive CCT). Thus, this group showed the highest rates of non-optimal, non-conclusive CCT imaging and atherosclerotic plaque (13% and 75%, respectively). Therefore, the occurrence of a negative-normal CCT is low and the ability to rule out CAD is narrow in this subgroup of patients. However, we observed that 50% of patients had no significant coronary stenosis on the basis of CCT and did not require further testing. A strategy recommending CCT as an initial step in diagnosis would enable us to rule out CAD in half of the patients and to focus on the other half with additional testing. We estimate that this performance might be sufficient to justify further investigation comparing such a strategy with established work up (mainly by stress tests).

The pertinence of CCT when CAD probability is low remains unclear. CCT has not been evaluated in angina diagnosis prospectively, but studies have shown that CCT might reliably rule out acute coronary syndrome in the emergency setting in low-risk patients [16,17]. In our experience, we observed that CCT was accurate (optimal quality in 91%) and negative in 90% of low-risk patients. A large number of patients can be excluded from CAD by initial CCT imaging. However, this strategy led to a high number of unnecessary angiograms. The highest rate of strategy failure was, in fact, observed in this group (six additional invasive angiograms were needed to detect one patient with significant disease). In our view, three commentaries can be discussed. First, CCT specificity is not good enough to adequately identify patients when prevalence is very low (1/60). Second, positive CCT should be augmented by additional testing before referring for ICA. Third, the definition of positive CCT is inadequate. Thus, we used ‘50% diameter reduction of the lumen by visual assessment’ to determine significant stenosis by CCT. Even if this definition is widely accepted, it might be insufficient to quantify CAD obstruction in this subgroup of low-risk patients; new tools need to be developed to better evaluate lumen stenosis, including automated quantification [18,19].

Current guidelines and routine practice include a functional stress test to detect myocardial ischaemia as an initial step in angina diagnosis. Based on proven ischaemia, coronary imaging is performed. CCT as an initial test shortcuts this preliminary step and focuses on CAD imaging only. This strategy does ignore patients who experience true angina without coronary obstruction. Nevertheless, it enables significant coronary stenosis to be ruled out early and is not associated with adverse clinical events. As this strategy appears to be optimal in intermediate-risk patients, CCT should be compared with the functional test in this subset of patients.

Limitations

This study had several limitations. Definitions were very restrictive and all patients with inconclusive CCT were considered positive. As CCT quality is limited by heart rate and coronary calcification, adequate imaging is not available in all patients and might involve numerous additional invasive tests. We observed that image quality was acceptable in this study (only 9% of CCT images were non-optimal — among them significant stenosis by subsequent ICA) and that it impacted slightly on results. This suggests that at least patients with heavy coronary calcifications should be considered positive and justifies further ICA, as long as the rate of non-conclusive CCT remains less than 10%.

We defined strategy failure as CCT requiring ICA without confirmed significant coronary obstruction. This means that significant coronary stenosis by ICA classifies patients correctly as having significant CAD even in absence of myocardial ischaemia. Secondly, we observed in our study that some patients with positive CCT in secondary coronary vessels were not scheduled for ICA as they became asymptomatic with medication. This choice reflects the current belief that some patients with angina do not require revascularizations, especially those with distal or less severe vessel disease [20]. Ultimately, some patients might be
recommended for medical treatment on the basis of CCT findings only.

**Conflicts of interest statement**

None.

**References**


