Symposium: clinical Research

High-resolution computed tomography in patients with atypical ‘cardiac’ chest pain: a study investigating patients at 10-year cardiovascular risks defined by the Framingham and PROCAM scores

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Background and objective Atypical ‘cardiac’ chest pain (ACCP) is not usually caused by myocardial ischaemia. Current non-invasive investigations for these symptoms are not yet as accurate as invasive coronary angiography. The latest 64-row multi-detector computed tomography (MDCT) technology is non-invasive, has high specificity and negative predictive values for the detection of significant coronary disease. Our aim was to investigate if this modality can provide more information in the assessment of outpatients with ACCP in addition to established cardiovascular risk scores. Methods Seventy consecutive patients presenting to the outpatient clinic with ACCP underwent 64-row MDCT scan of the coronary arteries. They were categorized into low, medium or high risk groups based upon the Framingham and PROCAM scores. We defined a clinically abnormal MDCT scan as coronary stenosis ≥50% or calcium score >40 Agatston. Results Fifty-three (75.7%) patients did not have clinically abnormal scans. Framingham score classified 43 patients as low-risk while PROCAM classified 59 patients as low-risk. MDCT scans were abnormal for 18.6% and 22.0% of the respective low-risk group of patients. For patients with medium-to-high risk, 33.3% and 36.4% of Framingham and PROCAM patient groups respectively had abnormal MDCT scans. Conclusion MDCT adds valuable information in the assessment of patients with ACCP by identifying a significant proportion of patients categorized as low-risk to have underlying significant coronary stenosis and coronary calcification by established cardiovascular risk scores. (J Geriatr Cardiol 2006; 3(1):17–21)

Key Words multi-detector computed tomography: atypical ‘cardiac’ chest pain; coronary artery disease; risk stratification

Introduction

Atypical ‘cardiac’ chest pain (ACCP) is defined as a cluster of symptoms that include pain, pressure or discomfort in the chest, neck, back or arms that is not clearly exertional or not otherwise consistent with pain or discomfort from myocardial ischaemia.¹ Earlier publications defined this as ‘non-specific’ or ‘nonanginal’ chest pain.²,³ While many patients with ACCP do not have significant myocardial ischaemia, up to 22% of patients, in fact, have been found to have genuine acute ischaemia.⁴ In light of this, the management of patients presenting with ACCP in the cardiology outpatient setting varies from centre to centre. While many physicians prefer the non-invasive investigations as first line to detect or exclude the presence of significant coronary artery disease, some proceed directly to the ‘gold standard’ investigation of invasive conventional coronary angiography (CCA).⁵,8 Such non-invasive investigations, which include exercise stress testing, thallium scanning, single-photon-emission computed tomography, dobutamine stress echocardiography and electron-beam computed tomography, have reported variable sensitivity and specificity scores of up to 90%.⁹‑¹³

The recent development and availability of 64-row multi-detector computed tomography (MDCT), superseding previous generation 16-row technology, has begun to show promise as a non-invasive method in detecting coronary artery stenosis.¹⁴,²¹ More recently, Mollet et al, in their study of 52
patients. 6 of whom had atypical pain, reported a high accuracy in detecting coronary stenoses in a variety of patient groups. Results from our own centre, in a study of 261 patients divided by clinical presentation, have shown similar trends. In particular, there are reportedly very high specificity and negative predictive values for this imaging modality. Despite this, there has been relative lack of MDCT data on patients with different clinical presentations. We have reported the influence of clinical presentation upon accuracy of coronary stenosis detection by 64-row MDCT. The aim of this study was to investigate whether MDCT can provide more information on patients with ACCP, in addition to established cardiovascular risk algorithms such as the Framingham and PROCAM risk assessment scores.

**Methods**

**Study population**

We analysed data retrospectively from 70 consecutive patients with ACCP who presented to the Cardiac Clinic between August and November 2005, and underwent a MDCT scan of their coronary arteries. Exclusion criteria were any known history of congenital or valvular heart disease, inability to perform an adequate breath hold for 15 sec, presence of atrial fibrillation or other tachyarrhythmias, resting heart rate of >75 bpm after preprocedural medications, documented renal insufficiency (serum creatinine of >140 μmol/L) and known allergy to iodine contrast media. All patients had written informed consent as to having an MDCT scan as the investigation of choice for ACCP, and were aware that their results may be used for future research analysis. Our scan protocol and interpretation of coronary vessel stenoses are detailed in our previous study.

**Data collection**

From the clinical notes, data consisting of the patient’s age, presence of diabetes, treated hypertension, significant family history of coronary artery disease, history of smoking and fasting lipid profile (FLP) were collected. Significant family history is defined as angina, myocardial infarction or sudden death without obvious cause before the age of 60 in a 1st degree blood relative. History of smoking was detailed to both Framingham and PROCAM criteria, i.e. actively smoked in the last 1 month and 1 year, respectively. FLP was defined as the routine venous sample obtained within two weeks prior to the MDCT scan analysed at a centralised laboratory.

We obtained MDCT results from each patient’s clinical notes. We defined ‘no significant stenoses’ as <50% stenosis indicated in the MDCT report. An ‘abnormal result’ constituted any MDCT report that indicated any stenosis =50% or the presence of significant calcification that made interpretation of any coronary artery segment difficult. We chose 50% stenosis as significant as we felt any degree of stenosis at or above this level to be physiologically significant and flow-limiting, thereby most likely causing ACCP. Significant calcification was defined as an Agatston Score >400, a level above which patients are thought to be at higher risk for coronary events.

**Statistical analysis**

All collected data was transferred into a Microsoft Office Excel 2003 spreadsheet, and analysed with SPSS 12 for Windows. Data was transcribed onto the Framingham and PROCAM risk calculators on the universal access website www.chd-taskforce.com. The subsequent score was categorized to low, medium and high risk groups, indicating a 10-year cardiovascular event risk of <10%, 10-20% and >20% respectively. We then analysed these groups individually for the presence or absence of significant coronary stenosis as identified on each patient’s MDCT scan. When the age or FPL parameters exceeded limits as indicated by the Framingham or PROCAM, we chose to use the upper or lower limit of the variable concerned, so that the respective risk calculator could generate an actual percentage score. All patients were followed up after the MDCT scan by a cardiologist, regardless of the results, so as to discuss the subsequent management plan.

**Results**

The baseline patient characteristics is summarized in Table 1. MDCT scan was considered clinically abnormal in 17 of 70 patients (24.3%). All patients categorized as ‘low risk’ by either risk assessment score had coronary calcification of less than 20 Agatston Score.

**Analysis with Framingham scores**

There were 43 patients categorized as ‘low risk’, among whom 35 (81.4%) were found to have no significant stenosis or calcification while 8 (18.6%) patients had clinically abnormal scans. Of the 15 patients categorized as ‘medium risk’, 12 (80%) had no significant stenosis or calcification. In 12 patients categorized as ‘high risk’, 6 (50%) had no significant stenosis or calcification on MDCT scan. When ‘medium risk’ and ‘high risk’ patient groups were combined, 18 out of 27 patients (66.7%) had no significant stenosis or calcification while 9 (33.3%) patients had clinically-abnormal scans (Table 2).

**Analysis with PROCAM scores**

There were 59 patients categorized as ‘low risk’. Of these, 46 (78.0%) were found to have no significant stenosis or calcification while 13 (22%) had clinically abnormal scans. Of the 6 patients categorized as ‘medium risk’,3 (50%) had no significant stenosis or calcification. Of the remaining 5 categorized ‘high risk’, 4 (80%) had no significant stenosis or calcification. When we combined ‘medium risk’ and ‘high risk’ patient groups, 7 of the 11 patients (63%) had no significant stenosis or calcification while 4 (36.3%) patients had clinically-abnormal scans (Table 2).

A clinically-abnormal MDCT scan (‘Abnormal’ MDCT) is defined as the presence of stenosis=50% or significant coronary calcification of >400 Agatston score. A clinically-normal MDCT scan (‘Normal’ scan) is defined as absence of lesions >50% stenosis and calcium score <400 Agatston score. Patients with ‘Significant stenosis and calcification’ denotes a
Table 1. Baseline characteristics of patients (mean±SD)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yr)</td>
<td>54.2±9.20</td>
</tr>
<tr>
<td>Male/Female</td>
<td>40/30</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10 (14.3%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>35 (50%)</td>
</tr>
<tr>
<td>Smoked within the last 1 month</td>
<td>11 (15.7%)</td>
</tr>
<tr>
<td>Significant family history for cardiovascular disease of IHD</td>
<td>7 (10%)</td>
</tr>
<tr>
<td>Mean systolic BP (mmHg)</td>
<td>136.9±17.80</td>
</tr>
<tr>
<td>Mean total cholesterol (mmol/L)</td>
<td>5.21±1.13</td>
</tr>
<tr>
<td>Mean LDL-cholesterol (mmol/L)</td>
<td>3.07±1.10</td>
</tr>
<tr>
<td>Mean HDL-cholesterol (mmol/L)</td>
<td>1.43±0.39</td>
</tr>
<tr>
<td>Mean triglycerides (mmol/L)</td>
<td>1.61±0.93</td>
</tr>
</tbody>
</table>

Table 2. MDCT results for 70 patients with different risk levels

<table>
<thead>
<tr>
<th>Risk level</th>
<th>Number of patients</th>
<th>Normal scan (n,%)</th>
<th>Abnormal scan (n,%)</th>
<th>Significant stenosis and calcification (n,%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Framingham ‘Low risk’</td>
<td>43</td>
<td>35 (81.4%)</td>
<td>8 (18.6%)</td>
<td>4 (9.3%)</td>
</tr>
<tr>
<td>PROCAM ‘Low risk’</td>
<td>59</td>
<td>46 (78.0%)</td>
<td>13 (22.0%)</td>
<td>2 (3.4%)</td>
</tr>
<tr>
<td>Framingham ‘Medium-high risk’</td>
<td>27</td>
<td>18 (66.7%)</td>
<td>9 (33.3%)</td>
<td>4 (14.8%)</td>
</tr>
<tr>
<td>PROCAM ‘Medium-high risk’</td>
<td>11</td>
<td>7 (63.6%)</td>
<td>4 (36.4%)</td>
<td>3 (27.3%)</td>
</tr>
</tbody>
</table>

subgroup of patients in whom the MDCT scan was abnormal with significant stenosis >50% and calcium score >400 Agatston score.

Discussion

Cardiovascular risk scores such as the Framingham and the PROCAM algorithms can identify patients at risk of cardiac events.\textsuperscript{24,25} The Framingham and PROCAM algorithms were applied in our study since both are widely used in our clinical practice, although we are aware that they predominantly studied Caucasian populations.

‘Hard’ end points, such as acute coronary event or cardiovascular death in a 10-year period, are used in established risk algorithms, incorporating recognized cardiovascular risk factors. However, these risk assessment methods are based upon co-morbid diseases and lifestyles may not be sensitive enough to predict all future events or specific enough to exclude patients with low-likelihood of developing coronary disease. The same widely-used established cardiovascular risk scores also do not seem to be applicable worldwide. For example, the Framingham algorithm has been found to underestimate the presence of cardiovascular disease in Northern Hemisphere patients or overestimate it in Chinese populations.\textsuperscript{30-32} Therefore, attempts have been made to determine other indicators of cardiovascular risk, such as the presence of metabolic syndrome.\textsuperscript{33} The use of imaging modalities for risk stratification is not new. SPECT imaging and stress echocardiography have been used\textsuperscript{10,12,13} while coronary calcium score by electron-beam CT (EBCT) has provided an-
other non-invasive method of better risk-stratifying patients. 

Until the advent of MDCT, it was not ethically possible to accurately risk stratify patients by degree of coronary stenosis, especially those with ACCP, as the hazards of radiation exposure and contrast-related complications associated with conventional angiography far outweighed its benefits. 

With non-invasive MDCT, we can now visualise coronary arteries and assess the degree of any coronary stenosis directly. As our centre is now obtaining accurate rates of coronary disease detection by MDCT comparable to established centres, we are confident of our scan results obtained for this group of patients with ACCP. 

Our results suggest that, 76% of patients presenting to our cardiac clinic with ACCP did not have significant coronary stenosis that could cause these symptoms. This is consistent with previous reports using coronary angiography. 

Furthermore, as our results have shown, MDCT can identify sizeable subgroups of patients in both the ‘low risk’ as well as ‘medium-to-high’ risk groups who already harbour significant underlying coronary atherosclerosis. In the medium-to-high risk group for example, using either the Framingham or PROCAM algorithms, one-third of patients had abnormal MDCT scans while two-thirds did not have clinically abnormal scans. MDCT for this group of patients has improved the specificity in excluding significant disease.

Even more importantly, our results have shown that 20% of the ‘low risk’ patients have significant coronary disease or significant coronary calcification who would otherwise have been treated less aggressively based upon conventional risk stratification. MDCT has thus helped us to improve the sensitivity of detecting coronary disease. In addition, given the improved resolution of the 64-row MDCT, we were able to identify a group of patients with coronary stenosis <50% who we then managed more aggressively. We acknowledge that whether a clinically abnormal MDCT scan result puts the patients at much higher risk of acute coronary events in the next year or 10 years is not known. Large cohort studies will be required to investigate this issue. The significance of less severe stenosis (30–40% luminal narrowing) is also unclear although many physicians now accept that such lesions are more prone to rupture and subsequent acute thrombosis.

The identification of significant calcification (Agatston Score >400) in 14.8% and 27.3% patients, categorized by Framingham and PROCAM algorithms respectively, in the combined ‘Medium’ and ‘High Risk’ groups, is also significant. Herzog, et al performed MDCT on patients with ACCP and found that the sensitivity and specificity of the investigation in identifying significant coronary stenosis was increased when both MDCT analysis of the coronary vessel and calcium scoring were combined. 

Finally, even though the radiation doses of MDCT is approximately 3 to 4 times that of CCA, improved techniques can potentially reduce this to comparable levels. Invasive diagnostic CCA on the other hand still carries a small but significant risk of morbidity and mortality.

Study limitations
The major limitation of this paper is the patient number. However patient recruitment is consecutive from a single outpatient clinic and to date, this series represents one of the larger series of patients with ACCP who underwent MDCT.

Conclusion
In patients with ACCP, MDCT can add valuable information to existing Framingham and PROCAM cardiovascular risk stratification models. Further studies, involving larger patient numbers, will be required to investigate these findings. It is possible that MDCT can be used as an effective screening tool for cardiovascular disease in conjunction with established risk algorithms.

Acknowledgments
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References