Prognostic value of coronary multidetector CT angiography in patients with an intermediate probability of significant coronary heart disease

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ABSTRACT. The aim of this study was to determine the prognostic value of coronary multidetector CT angiography (MDCTA) in patients with an intermediate pre-test probability of significant coronary artery disease (CAD). Patients who underwent 64-slice coronary MDCTA and met the selection criteria were identified and assessed for intermediate pre-test probability. Coronary MDCTA scans were preceded by calcium scoring, whereas all MDCTA scans were interrogated for the presence of plaque composition and the distribution and degree of stenosis. Significant stenosis was classified as being >50% of the luminal diameter. All patients were followed up for the occurrence of (i) cardiac death, (ii) non-fatal myocardial infarction, (iii) unstable angina requiring hospital admission and (iv) revascularisation. 138 patients were included (follow-up of 19.9 months); of these, 8 had a cardiac event (all revascularisations) and all had a positive coronary MDCTA. Patients with normal coronary arteries or non-significant stenosis suffered no cardiac events during follow-up. There were significant differences between the two groups regarding the presence of significant stenosis ($p<0.001$), the presence of plaque ($p=0.011$) and a calcium score >10 ($p=0.003$); 36.4% of patients with significant stenosis underwent revascularisation. In conclusion, this is the first UK study to investigate survival data in a population of intermediate-risk patients with no prior history of CAD who were investigated with coronary MDCTA. Coronary MDCTA can confidently rule out significant CAD in the intermediate-risk population and guide risk factor modification in patients with demonstrated coronary atheroma.

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The aim of this study was to evaluate patients with an intermediate pre-test probability of significant coronary artery disease (CAD) using multidetector CT angiography (MDCTA) and to follow them up for cardiac events. The risk factor profile was determined for all patients. In our institution, patients at high risk of significant CAD are frequently referred directly for invasive catheter angiography (ICA); those at low risk do not require imaging. Intermediate-probability patients, however, who represent a large proportion of patients seen in the outpatient setting, need further testing, and risk is determined by clinical review and risk factor assessment [1, 2]. Exercise testing, stress echocardiography and myocardial perfusion with single positron emission CT (SPECT) studies are all well-established non-invasive methods for the investigation of this group. However, the sensitivity and specificity for significant CAD are less than ideal. Meta-analysis of the literature pertaining to these non-invasive methods quotes exercise testing as having a sensitivity and specificity of 68% and 77%, respectively [3], stress echocardiography a sensitivity

and specificity of 85% and 77%, respectively, and myocardial perfusion a sensitivity and specificity of 87% and 64%, respectively [4] (the definition of significant CAD varies within these meta-analyses and includes angiographic definitions of both 50% and 75% luminal narrowing being deemed significant). Often, these patients undergo ICA to rule out CAD as a result of an abnormal SPECT or stress echo, thus lengthening the patient journey and resulting in further irradiation. The development of MDCTA has provided an alternative algorithm for the investigation of this patient group. Studies that have compared MDCTA with ICA as the gold standard have shown the sensitivity to be between 93% and 99% and specificity to be between 95 and 98%, with a negative predictive value of 99–100% [5–8], all of whose values are superior to those of the other non-invasive modalities mentioned above. The prognostic outcomes backing up these data have until recently been lacking. However, recent prognostic studies looking at all-cause mortality [9] and cardiac events [10] reinforce the use of coronary MDCTA as a non-invasive diagnostic modality and also indicate that MDCTA data improve the prognostic assessment over baseline clinical risk factor assessment.

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Methods and materials

The study population consisted of those patients who were identified retrospectively from the radiology database as having seen a cardiologist for clinical assessment and undergone coronary artery calcium scoring and coronary MDCTA with a 64-detector row scanner in our institution between November 2005 and December 2007. A retrospective search of the cardiology database allowed clinical details pertaining to the presentation of the patient and their CAD risk factors to be acquired: (i) diabetes mellitus; (ii) hypercholesterolaemia; (iii) hypertension; (iv) obesity; (v) positive family history; and (vi) smoking.

Patients were included only if they had presented to the cardiology outpatient department or rapid-access chest pain clinic with atypical chest pain and were deemed by the cardiologist to have an intermediate pre-test probability of CAD. Intermediate-risk patients have traditionally been defined as those individuals with a 15–75% risk of CAD. For men, this included those with atypical pain who were >30 years old, and for women those with atypical pain who were >50 years old [1]. This largely represents populations identified as having intermediate risk of significant CAD; however, further history (including risk factor assessment) and examination allows for a more accurate and individual assessment [2]. These patients were referred for MDCTA. Clinical follow-up was acquired from the cardiology database.

The study was categorised as an audit and registered with the audit department.

Coronary MDCTA acquisition

All scans were performed using a GE VCT 64-slice CT scanner (GE Systems, Waukesha, WI, USA). Heart rates were optimised using 5–35 mg of intravenous metoprolol to try to obtain a heart rate of <60 beats per minute (bpm) if tolerated. A MDCT calcium score triggered prospectively was performed before coronary MDCTA: collimation 2.5×16 mm, gantry rotation 0.35 ms, tube voltage 120 kV and tube current 80 mA. The temporal window was set at 75% after the R-wave for electrocardiographically triggered prospective reconstruction.

MDCTA was carried out with the following parameters: collimation 64×0.625 mm, tube rotation 0.35 s and electrocardiogram (ECG)-modulated tube current 110–550 mA at 120 kV. Non-ionic contrast material was injected at 5–6.5 ml s⁻¹. The region of interest was placed over the ascending aorta and the scan triggered manually when aortic contrast was deemed appropriate. All scans were acquired with an inspiratory breath-hold of approximately 10–20 s to allow for heart rate stabilisation prior to scan acquisition. Aggressive dose modulation was utilised for all appropriate patients, with the maximal tube current centred at 75% of the R–R interval. Using retrospective segmental reconstruction algorithms, data from consecutive heart beats were used to generate images from various phases of the R–R interval depending on dose modulation. 75% was acquired as a default level, with phases from 45% to 95% being acquired in 10% increments if heart rate was

raised or ectopic beats frequently observed. Post-processing and interrogation were performed at a separate workstation; the reconstructed images were generated with a slice thickness of 0.5 mm and an increment of 0.35 mm and manipulated and interrogated using VCT cardiac IQ Express from GE systems, Waukesha, WI, USA).

Calcium scoring was carried out from MDCT scans, as described above, and calculated with calcium scoring software from GE Cardiac IQ Express.

Coronary MDCTA plaque distribution and assessment was carried out by cardiologist (G.M.H.) and a radiologist (C.A.R.) with a combined experience of 10 years in the interpretation of coronary MDCTA; for cases where there was disagreement, a consensus decision was reached. Plaque description was described by vessel plaque type and distribution. Significant stenosis was deemed as a plaque causing narrowing of >50% of the luminal diameter.

Patients free from both coronary plaque and calcium were deemed to be “normal”. Abnormal patients were those with any coronary plaque distribution of any severity.

Follow-up

This was conducted via the cardiology database and clinic letters. Clinical end points were the occurrence of (i) cardiac death, (ii) non-fatal infarction, (iii) unstable angina requiring hospitalisation and (iv) revascularisation.

Statistical analysis

Categorical baseline characteristics are expressed as numbers and percentages and were compared between the two groups with Fisher's exact test. Quantitative variables are presented as a median and range, and are compared using the Mann–Whitney test. Statistical analysis was carried out using SPSS software version 15 (SPSS Inc., Chicago, IL) and *p*-values <0.05 were considered statistically significant.

Results

A total of 138 patients were included in the study; all of these patients underwent diagnostic quality MDCTA examinations. Baseline characteristics are shown in Table 1. From these data, it was apparent that:

- In patients with normal coronary arteries (*n*=59), there were no cardiac events (*i.e.* revascularisations) in the follow-up period (average, 19.9 months; range, 13–28 months).
- In the presence of significant stenosis on MDCTA (*n*=22), eight patients underwent revascularisation (36.4%) during follow-up (average, 19.9 months; range, 13–28 months).
- In the presence of non-significant stenosis on MDCTA (*n*=57), no patient had a cardiac event (*i.e.* revascularisation) during follow-up (average, 19.9 months; range, 13–28 months).

Table 1. Patient demographics, risk factors and the number of patients with significant stenosis, a coronary artery plaque of any severity and a calcium score >10

Variable	All patients (n=138)	Revascularisation (n=8)	No revascularisation (n=130)	p-Value
Median age in years (range)	57 (22–82)	63 (47–78)	59 (22–82)	0.19 ^b
Mean follow-up in months (range)	19.9 (13–28)	21.5 (17–28)	19 (13–28)	0.12 ^b
Male gender	73 (52.9%)	7 (87.5%)	66 (50.8%)	0.07 ^a
Hypertension	65 (47.1%)	5 (62.5%)	60 (46.2%)	0.48 ^a
Hypercholesterolaemia	40 (28.9%)	5 (62.5%)	35 (26.9%)	0.045^a
Smoking history	43 (31%)	3 (37.5%)	40 (30.8%)	0.70 ^a
Diabetes mellitus	7 (5.1%)	0 (0%)	7 (5.4%)	1.0 ^a
Family history	37 (26.8%)	2 (25.0%)	35 (26.9%)	1.0 ^a
Obesity	12 (8.7%)	1 (12.5%)	11 (8.5%)	0.53 ^a
Significant stenosis (>50%)	22 (15.9%)	8 (100%)	14 (10.8%)	<0.001^a
Abnormal (i.e. any plaque)	79 (57.2%)	8 (100.0%)	71 (54.6%)	0.011^a
Calcium score (>10)	68 (49.3%)	8 (100%)	60 (46.2%)	0.003^a

Total numbers are shown in the second column. Numbers of patients in the “revascularisation” and “no revascularisation” groups are shown in the third and fourth columns. *p*-Values comparing the values in the “revascularisation” and “no revascularisation” groups are shown in the fifth column. Values in bold indicate statistically significant differences.

^aFisher's exact test.

^bMann-Whitney test.

Univariate analysis of the data comparing patients with and without events (revascularisation) is also shown in Table 1. There are no significant differences between the two groups with respect to the baseline risk factors except for the prevalence of hypercholesterolemia ($p=0.045$).

There are, however, significant differences between the two groups with regard to patients with significant stenosis ($p<0.001$), the presence of a plaque of any severity or distribution ($p=0.011$) and calcium score >10 ($p=0.003$).

Discussion

Patients with normal coronary arteries or non-significant stenosis suffered no cardiac events during follow-up (19.9 months). Calcium scoring and coronary MDCTA allowed for the detection, within the intermediate-risk population, of patients with severe CAD who required revascularisation ($n=8$). A total of 22 patients had significant CAD at MDCTA; all these patients underwent ICA. In 12 patients the MDCTA was in full agreement with the ICA, and in 10 patients MDCTA overestimated the severity of stenosis in one vessel or more. Not all patients with significant stenosis therefore required revascularisation. Even with severe stenosis seen on ICA, the decision to revascularise is dependent on a number of clinical factors not determined by the severity of stenosis alone.

Aside from the incidence of hypercholesterolaemia, these patients showed no significant difference in their risk factors from patients with intermediate risk and no cardiac events; this suggests that risk factor assessment alone does not allow for selection of patients in need of further invasive imaging and possibly revascularisation.

The shortcomings of this study include its retrospective nature, the small numbers of patients and the relatively short follow-up period. Data accuracy could

have been improved with follow-up in addition to the cardiology database and clinic letters, as patients may have attended other institutions for their coronary event. In addition, the small size of the event group rendered multivariate analysis impossible. Population size was limited by the strict inclusion criteria, in particular the exclusion of known CAD. However, this is the population (i.e. the intermediate pre-test probability patient) for which clinical decision making is difficult.

One of the criticisms of coronary MDCTA is its use for low-risk patients, the so-called “worried well”. However, our study population not only fulfils the recognised clinical criteria for intermediate risk but also, as can be seen from the risk factors, has recognised predispositions to CAD. As previously mentioned, exercise testing, stress echocardiography and myocardial perfusion with SPECT studies are all well-established non-invasive methods; however, their sensitivity and specificity are less than those of coronary MDCTA. This alternative accurate investigation can now be carried out with reduced radiation dose as a result of aggressive ECG dose modulation (an effective radiation dose for these studies was been estimated at between 10 mSv and 15 mSv). More recently, prospective gating, which is now routine clinical practice in the author's institution, has resulted in even more significant dose reductions [11]. The use of coronary MDCTA for these patients is ever more acceptable.

Conclusions

Coronary MDCTA can confidently rule out significant CAD in the intermediate-risk population and guide risk factor modification.

In our institution, as a result of the encouraging prognostic data and lower radiation burden, coronary MDCTA is firmly established in the algorithm for the investigation of intermediate probability chest pain.

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