Coronary artery status assessed with coronary computed tomography angiography

Five-year prognosis in patients with normal coronary arteries

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Summary

Objectives: The aim of this study was to assess the 5-year prognostic value of multidetector coronary computed tomography angiography (CCTA) in patients with normal coronary arteries.

Background: Use of CCTA is increasing in patients with suspected coronary artery disease. Although there is a large body of data supporting the prognostic role of CCTA for major adverse cardiac events in the long-term prognostic the role in patients with normal coronary arteries is still partially unknown.

Methods: Between April 2005 and March 2007, 506 consecutive patients (313 men) were studied with CCTA in order to detect the presence of coronary artery disease. Patients were classified as having strictly normal coronary arteries versus abnormal coronary arteries (plaques, calcified and obstructive coronary arteries). Patients with strictly normal coronary arteries were followed up for 5 years, for the occurrence of: (1) cardiac death, (2) nonfatal myocardial infarction, (3) unstable angina requiring hospitalisation, and (4) revascularisation.

Results: Two hundred patients (124 men, mean age 64 ± 27 years) were enrolled and subsequently followed up for exactly 5 years after the initial investigation. Pretest probability was 25 ± 15% in the total population and 13 ± 4% in the 200 studied patients. During this follow-up 2 patients (1%) died from noncardiac causes (1 sepsis and 1 chronic obstructive pulmonary disease), 1 patient underwent percutaneous atrial septal defect closure (0.5%) and 1 patient (0.5%) experienced nonfatal endocarditis. Acute coronary syndrome, myocardial infarction or stable angina pectoris did not occur during this follow-up. A total of 196 patients were free of adverse events (98%).

Conclusions: CCTA provides important prognostic information in patients with normal coronary arteries showing excellent long-term prognosis without coronary events.

Key words: cardiac computed tomography; normal coronary arteries; ischaemic heart disease; coronary stenosis

Ischaemic heart disease is the leading cause of mortality and morbidity [1]. There is a large body of data supporting the role of coronary computed tomography angiography (CCTA) [2–3], but its long-term prognostic role in patients with suspected coronary artery disease and strictly normal coronary arteries is still partly unknown, even if in the CONFIRM trial these patients are doing well in the long term [4]. It has recently been reported that coronary artery disease severity on CCTA is strongly correlated with the occurrence of major adverse cardiac events (MACE). Most of these studies are limited because of the short follow-up (no longer than 2 years) and the heterogeneity of the studied population. In addition, no long-term data are available on the value of CCTA in patients with suspected ischaemic heart disease and normal coronary arteries. Accordingly, the aim of the present study was to evaluate the long-term prognostic role of normal CCTA findings in a cohort of patients with suspected ischaemic heart disease.

Materials and methods

Patients and study protocol

The screened population consisted of consecutive patients who presented to our out-patient clinic for cardiac evaluation (exercise electrocardiogram, stress echocardiography or invasive coronary angiography) between April 2005 and March 2007 because of suspected coronary artery disease. Ischaemic heart disease was suspected on the basis of the patient history (new-onset chest pain), a high-risk profile, or abnormal or inconclusive stress test. In all patients, CCTA was performed in addition to the standard clinical workup in order to clarify the diagnosis of possible coronary disease. Some patients were excluded because they met at least one of the following exclusion criteria: unwillingness to participate or high probability of loss in follow-up, allergy to iodine contrast agents, known cardiovascular disease and coronary artery disease on CCTA. Thus, the analytical study population consisted of 200 patients with normal CCTA. Normal CCTA was defined as well visualised coronary arteries without any calcifications, narrowing or wall abnormalities (fig. 1). Patients with soft plaques were also excluded. The study was approved by our institutions' scientific and ethical committees, and all patients gave informed consent.

Figure 1: CCTA showing normal coronaries (left) in 3D reconstruction, normal LAD on the right.

A structured interview was conducted and a clinical history acquired. The following cardiac risk factors were assessed before CCTA: diabetes mellitus, hypercholesterolaemia, hypertension (blood pressure over 140/90 mm Hg or use of antihypertensive medications), positive family history of coronary artery disease, and current tobacco usage. Pretest probability of ischaemic heart disease was calculated based on the standard recommendations of the American Heart Association, and the Framingham cardiovascular disease (CVD) score was calculated [5–6].

Patient preparation, scan protocol and image reconstruction

Up to 20 mg of metoprolol was intravenously administered before CCTA in patients with heart rates >90 beats/min. In all patients, CCTA was performed using a 64-slice scanner Toshiba Acquilion (64 0.625-mm collimation, 330-ms gantry rotation time, VCT, Toshiba Medical Systems, Tokyo, Japan). Dose modulation was attained with "electrocardiographic gating" for a maximum gantry delivery between 40 and 80% during the R-R interval. Reconstructions were retrospective. A bolus of 80 ml of high concentration contrast (Iomeron 400 mg/ml, Bracco Imaging, Milan, Italy) was administered intravenously at 5 ml/s, followed by 50 ml of saline injected at the same infusion rate. The scan was initiated according to the bolus-tracking technique.

CCTA procedure

Two expert assessors unaware of the patients' clinical status evaluated all CCTA examinations. In the case of disagreement, a joint reading was performed and a consensus decision was reached. Coronary arteries were divided into 16 segments according to the American Heart Association classification [7]. Each segment was classified as interpretable or not. Patients were excluded when a proximal segment, mid-segment or more than three segments were uninterpretable. If a segment contained calcific plaques, the patients were excluded from the study. Coronary arteries were defined as normal provided no calcium was present along the complete artery. Reconstructions were performed at the time of the CCTA testing.

Follow-up

Follow-up, either clinic visit or telephone interview, was performed by two trained research nurses. A standardised questionnaire was used. Prognosis was measured as an endpoint of cardiac fatal event and nonfatal event. Patients were contacted by telephone and in the event of doubt their general practitioner was contacted. Finally, 42% of the patients had a clinical visit at time of follow-up. Patients were followed up for the occurrence of: (1) cardiac death, (2) nonfatal myocardial infarction, (3) unstable angina requiring hospitalisation, and (4) revascularisation. Follow-up was performed during the month following the end of the 5th year after the baseline CCTA. Patients were regularly followed up by their general practitioner and once a year by the research nurse in charge of the follow-up. In an unclear clinical situation the patient was evaluated by a cardiologist. At follow-up, deaths were reviewed and classified as cardiac (death caused by acute myocardial infarction, ventricular arrhythmia or refractory heart failure) or noncardiac. Myocardial infarction was defined as recommended by the European Heart Association [8]. The diagnosis of nonfatal myocardial infarction was based on the presence of typical chest pain, elevated cardiac enzymes, and typical ECG changes.

Statistical analysis

Statistical analysis was performed using SAS (SAS Institute Inc., Cary, North Carolina). Continuous variables are presented as mean ± standard deviation, and discrete variables as absolute numbers and percentages.

Results

Of the 506 patients prospectively screened, 306 were excluded because CCTA images showed clear coronary

artery disease or calcifications in 292 patients (95%) or were uninterpretable in 12 patients (4%). Two patients (1%) were excluded because of lack of consensus between the readers (table 1 and 2). Among these 306 patients, 146 (48%) had plaque with insignificant coronary stenosis and 160 (52%) showed significant coronary stenosis which was further confirmed by invasive coronarography. In the 200 patients with normal CCTA, the pretest probability of coronary disease at 10 years using the Framingham score was 20 ± 7% in the complete cohort of 506 patients. In the 306 patients with abnormal CCTA imaging this 10-year risk was 25 ± 15%, although in the 200 patients with normal coronary arteries it was 13 ± 4%. Demographic data are shown in table 1. Of the 200 remaining patients, follow-up was available for all (100%). Incidence of MACE during follow-up was 2% and two patients died (1%). Cause of death was chronic obstructive pneumopathy in one patient and sepsis in the other. Nonfatal endocarditis occurred in one patient (0.5%) and one patient underwent percutaneous closure of a septum secundum atrial septal defect. No patient experienced myocardial infarction or acute coronary syndrome, or developed chronic angina pectoris. The mean radiation exposure was 10 ± 4 mSv in our patients.

Table 1: Characteristics of the study population.

	Patients with normal coronary angiogram (200 pts)	Patients with abnormal coronary angiogram (306 pts)
Age (years)	64 ± 17	65 ± 11
Male	126 (63%)	240 (78%)
Diabetes	28 (14%)	68 (20%)
Smokers	72 (36%)	103 (34%)
Hypertension	88 (44%)	182 (60%)
Dyslipidaemia	102 (51%)	235 (77%)
Heredity	54 (27%)	92 (30%)
Dyspnoea	26 (13%)	36 (12%)
Atypical chest pain	110 (55%)	60 (19%)
Typical chest pain	32 (16%)	180 (59%)
Routine check-up	32 (16%)	30 (10%)
Framingham score	13 ± 4%	25 ± 15%

Table 2: Disposition of the patient population.

	506 patients screened
292 patients with coronary disease	
	214 patients
12 patients with uninterpretable CT	
	202 patients
2 patients refused to participate	
	200 patients included

Discussion

CCTA is considered a reliable method for ruling out coronary artery disease and detecting obstructive coronary stenosis [9–10]. However, data supporting the long-term prognostic value of CCTA, especially in patients with strictly normal coronary arteries, are limited. Prior studies have demonstrated a good predictive value of CCTA for mortality and morbidity from coronary artery disease [11–12]. Severity of coronary artery disease at CCTA has predictive value at 16 months, as recently shown [13], and this was also confirmed by the CONFIRM registry [4]. Our study had a longer follow-up in a very selected and completely homogeneous cohort of patients. We specifically demonstrated that patients without coronary artery stenosis had excellent long-term prognosis at 5 years with no occurrence of coronary events recorded. Pretest coronary artery disease probability was rather low at 25% in this group of patients. This is not surprising since all patients had normal coronary arteries.

The main message of our study is that patients with normal coronary arteries have a very favourable 5-year prognosis. Indeed none of our 200 patients experienced major adverse cardiac events during the follow-up period. In this group of patients, at relatively low risk, CCTA has a good prognostic value. In agreement with other studies with shorter follow-up of enrolled patients [14], our study confirmed that the absence of coronary artery disease at CCTA is associated with a high event-free survival rate for all cardiac events at 5 years. This is certainly owing to the absence of plaque at inclusion more than control of risk factors. We believe that this diagnostic modality can be safely used to exclude coronary artery disease in patients with suspected coronary artery disease and especially to reassure patients with intermediate results of stress tests, scintigraphy or stress echocardiography, without the need for an invasive coronary angiogram. A major concern of CCTA in comparison to stress echocardiography and stress test is radiation exposure. However, different approaches in the use of CCTA have been shown to reduce radiation exposure considerably [15, 16]. Our data also confirm the excellent survival of patients with a normal CCTA; as it has also been shown for patients with normal invasive coronarography [17–19]. However, at 7–10 years the survival rate is lower for patients with normal coronarography than for patients with normal CCTA. This reflects the difference between CCTA and invasive angiography in the assessment of normal coronary arteries, CCTA being probably more accurate to demonstrate “normal coronary arteries”. In these cited studies, some patients were

classified as having "normal coronary arteries", based on invasive coronarography; small plaques might have been present, but not diagnosed, with an impact on long-term prognosis. These patients would certainly not have been attributed to the "normal coronary arteries" group when evaluated by CCTA.

Radiation exposure could be a concern. However, it was a rather low dose in our cohort of patients and with modern CT machines the dose dramatically decreases from 4 to 6 times to a total dose of 1 to 2 mSv.

Some limitations must be considered. This was a single-centre study with a significant but limited number of patients. The cohort of patients as selected does not represent the daily practice of cardiologist since most of the patients have more typical symptoms than the ones included in this trial. However, our results show that in selected patients with normal coronary arteries CCTA is a very good diagnostic tool to exclude coronary artery disease and gives major information on long-term prognosis.

Conclusions

CCTA provides very helpful information in patients with unknown coronary artery disease and provides important prognostic information in patients with normal coronary arteries showing excellent long-term prognosis without coronary events. CCTA is useful in patients with a low pretest probability of ischaemic heart disease, atypical symptoms and in whom definitive exclusion of the disease is required.

Disclosure statement
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