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Research paper

Long term prognostic utility of coronary CT angiography in patients with no modifiable coronary artery disease risk factors: Results from the 5 year follow-up of the CONFIRM International Multicenter Registry

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ABSTRACT

Background: Coronary computed tomography angiography (coronary CTA) can prognosticate outcomes in patients without modifiable risk factors over medium term follow-up. This ability was driven by major adverse cardiovascular events (MACE).
Objective: Determine if coronary CTA could discriminate risk of mortality with longer term follow-up. In addition we sought to determine the long-term relationship to MACE.
Methods: From 12 centers, 1884 patients undergoing coronary CTA without prior coronary artery disease (CAD) or any modifiable CAD risk factors were identified. The presence of CAD was classified as none (0% stenosis), mild (1% to 49% stenosis) and obstructive (≥50% stenosis severity). The primary endpoint was all-cause mortality and the secondary endpoint was MACE. MACE was defined as the combination of death, nonfatal myocardial infarction, unstable angina, and late target vessel revascularization (>90 days).
Results: Mean age was 55.6 ± 14.5 years. At mean 5.6 ± 1.3 years follow-up, 145(7.7%) deaths occurred. All-cause mortality demonstrated a dose-response relationship to the severity and number of coronary vessels exhibiting CAD. Increased mortality was observed for >1 segment non-obstructive CAD (hazard ratio [HR]:1.73; 95% confidence interval [CI]: 1.07–2.79; p = 0.025), obstructive 1&2 vessel CAD (HR: 1.70; 95% CI: 1.08–2.71; p = 0.023) and 3-vessel or left main CAD (HR: 2.87; 95% CI: 1.57–5.23; p = 0.001). Both obstructive CAD (HR: 6.63; 95% CI: 3.91–11.26; p < 0.001) and non-obstructive CAD (HR: 2.20; 95% CI: 1.31–3.67; p = 0.003) predicted MACE with increased hazard associated with increasing CAD severity; 5.60% in no CAD, 13.24% in non-obstructive and 36.28% in obstructive CAD, p < 0.001 for trend.
Conclusions: In individuals being assessed for CAD with no modifiable risk factors, all-cause mortality in the long term (>5 years) was predicted by the presence of more than 1 segment of non-obstructive plaque, obstructive 1- or 2-vessel CAD and 3 vessel/left main CAD. Any CAD, whether non-obstructive or obstructive, predicted MACE over the same time period.

1. Introduction

Clinicians are frequently confronted with patients requiring assessment for chest pain or equivalent symptoms.[1] While cardiovascular risk factors provide some guidance,[2,3] there is no close association between traditional risk factors and the presence of atherosclerosis identified by coronary computed tomography angiography (coronary CTA).[4] The prognostic utility of coronary artery disease (CAD) detected by coronary CTA in those with no medically modifiable risk factors has been described for the medium term only. Over this time period (2.3 ± 1.2 years) the ability of coronary CTA to discriminate risk was largely driven by the combined endpoint of major adverse cardiovascular events (MACE) defined as death, nonfatal myocardial infarction, unstable angina, and late target vessel revascularization (>90 days).[4] However, CAD identified on coronary CTA did not confer an increased risk of mortality in the medium term. The primary purpose of this study was therefore to determine the long term (>5 year) prognostic utility of CAD detected in coronary CTA with regards to all-cause mortality in patients with no modifiable risk factors. To do so, we conducted a sub-analysis of the long-term Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter (CONFIRM) registry.

2. Method

2.1. Patient population

The rationale and methods of the CONFIRM registry have been described previously.[5] In the long term cohort of the CONFIRM registry, in which patients have a mean follow-up of 5.6 years, 12086 patients were prospectively enrolled between February 2003 and December 2009 across 12 sites in 6 countries within North America, Europe, and Asia. Enrolled sites collected clinical information on risk factors, clinical presentation and follow-up for all-cause mortality and MACE in addition to coronary CTA data(5). Institutional review board approval was obtained at each center.

2.2. Inclusion criteria

Inclusion criteria[1] age ≥ 18 years[2]; CAD evaluation by coronary CTA using a CT system with ≥64 detector rows[3]; clinically indication for CAD evaluation[4]; interpretable coronary CTA; and[5] prospective data collection for CAD risk factors. Clinical indications were defined as angina-equivalent symptoms including pain, tightness, and pressure, shortness of breath, pre-surgical evaluation, and structural indications (e.g., pulmonary vein mapping). In addition, individuals without chest pain syndrome could be assessed for CAD in the context of congenital heart disease, risk assessment of CAD in individuals who were considered to have severe vascular disease or had a concerning family history of vascular disease.

2.3. Chest pain categorization

Categorization of chest pain was based on the Diamond-Forrester criteria for angina pectoris.[6] At each site, symptom category was prospectively determined through either written survey or interview by a doctor or allied health professional.

2.4. Exclusion criteria

Exclusion criteria for our analysis were all patients with modifiable risk factors for coronary artery disease (n = 8501) and patients with known CAD (n = 1593) and those with missing data relating to modifiable risk factors (n = 73), stenosis assessment (n = 33) and age (n = 2). Modifiable coronary risk factors included diabetes mellitus, hypertension, dyslipidemia, and smoking. Standardized definitions for modifiable risk factors were used. Diabetes mellitus was defined as a fasting glucose level of 126 mg/dL