



The relationship between coronary artery calcium score and the long-term mortality among patients with minimal or absent coronary artery risk factors



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ARTICLE INFO

Article history:

Received 5 January 2015

Received in revised form 10 March 2015

Accepted 15 March 2015

Available online 16 March 2015

Keywords:

Coronary artery calcification

Long-term

Mortality risk

Low risk

Risk factor

ABSTRACT

Background: Coronary artery calcium (CAC) is strongly predictive of all-cause mortality in intermediate-risk groups, but this relationship is not well defined in very low-risk individuals. We investigated the relationship between CAC scoring and the long-term all-cause mortality among patients with ≤ 1 cardiovascular disease (CVD) risk factor.

Methods: We analyzed a retrospective cohort of 5584 asymptomatic patients with no known CVD (mean 56.6 ± 11.6 years, 69% men) and ≤ 1 risk factor who were physician referred for a CAC scan. Mortality was ascertained through linkage with the Social Security Death Index. We calculated the prevalence of CAC stratified by age and risk factors. We also examined the association between CAC and mortality using multivariable Cox Proportional hazards models.

Results: During a mean follow-up of 10.4 ± 3.1 years, 168 individuals (3.0%) died. Overall, 54.5% of patients had a CAC > 0 and 9.8% had CAC ≥ 400 . There was a greater risk of mortality with increasing CAC 1–99 (HR 1.9, 95% CI 1.2–3.1), 100–399 (HR 2.1, 95% CI 1.2–3.6) and ≥ 400 (HR 2.8, 95% CI 1.6–4.8) compared to CAC = 0 ($p < 0.0001$ for trend). Similar results were observed when the population was stratified by zero or one risk factor. Among patients < 45 years old, there was a 0.7% incidence of mortality compared to 8.1% for individuals ≥ 65 years old.

Conclusions: During long-term follow-up, an increasing CAC was significantly associated with a higher risk of all-cause mortality among patients with a very low CVD risk factor profile. CAC scanning may be a potentially useful tool for risk stratification among low CVD risk individuals who are ≥ 45 years old.

Published by Elsevier Ireland Ltd.

1. Introduction

Cardiovascular risk prediction began with the Framingham Risk Score (FRS) which is based on demographics, blood pressure, cholesterol, and anti-hypertensive medication use [1]. However, the FRS and the newer Atherosclerotic Cardiovascular Disease (ASCVD) Risk Prediction model [2] are heavily weighted by age and can inaccurately estimate the risk of CVD, especially in younger individuals and those at low risk of CVD.

Coronary artery calcium (CAC) is a marker of coronary artery disease and associated with other conditions in calcium deposits [3,4]. CAC is a robust predictor of CVD events [5,6] and all-cause mortality [7,8] for individuals with an intermediate CVD risk [1,9,10]. Current guidelines give a IIa recommendation for the use of CAC screening in individuals

at intermediate CVD risk, but the guidelines do not recommend CAC screening for low or low-intermediate risk groups due to the low absolute event rates in these groups [1,9,10]. However, a study by Taylor et al. demonstrated that 38% of sudden cardiac death occurred in individuals categorized as low risk by the FRS [11] and several previous analyses have demonstrated that individuals classified as low risk can have advanced sub-clinical atherosclerosis seen on CAC score [12,13]. The utility of CAC to risk stratify individuals who are defined as low risk using traditional CVD risk factors is not well defined and in this analysis we examine the relationship between CAC and all-cause mortality in asymptomatic individuals with 0 or 1 CVD risk factors.

2. Methods

2.1. Study population

Results from this analysis are derived from a cohort of 23,705 patients who had a physician referred CAC scan between 1998 and 2011. We excluded subjects aged < 20 years old, those with any chest

Abbreviations: CAC, coronary artery calcium; CVD, cardiovascular disease

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Table 1
Baseline characteristics.

	Overall (n = 5584)	No risk factors (n = 1533)	One risk factor (n = 4051)
Age	56.6 ± 11.6	55.9 ± 12.1	56.8 ± 11.4
Male gender (%)	69.3	71.7	68.4
Hypertension (%)	7.8	–	10.8
Diabetes (%)	1.7	–	2.3
Hyperlipidemia (%)	30.8	–	42.4
Current smoking (%)	2.7	–	3.8
Family history of CVD (%)	29.6	–	40.8
Race/ethnicity (%)			
Caucasian	77.9	74.3	79.2
Hispanic/Latino	8.8	10.7	8.0
African-American	3.8	4.0	3.7
Asian	8.9	10.5	8.4
Others	0.6	0.5	0.7
Coronary artery calcium score (Mean±SD; 25th, 75th percentile)	121.6 ± 293.5 (0; 75)	96.9 ± 264.3 (0;42)	131.0 ± 303.3 (0;87)

Abbreviations: CVD—cardiovascular disease.

pain, a history of known CVD (prior coronary revascularization or myocardial infarction), or follow-up of ≤365 days. The remaining 5584 patients who were asymptomatic, without known CVD, and had zero or one traditional CVD risk factor were included in this analysis. Patient demographics and CVD risk factors were self-reported by questionnaire [7]. Hypertension was defined by a history of high blood pressure or use of antihypertensive medication. Hypercholesterolemia was defined as use of cholesterol lowering medication or a history of a high total cholesterol, high low-density lipoprotein cholesterol, low high-density lipoprotein cholesterol, and/or high triglycerides. Diabetes mellitus was defined as the use of oral glucose lowering medications or insulin. A family history of CVD was defined as a parent or sibling with a

history of fatal or nonfatal myocardial infarction and/or coronary revascularization. Current smoking was defined as any cigarette smoking at the time of scanning. This study was approved by the Institutional Review Board of Harbor UCLA Medical Center.

2.2. Non-contrast CT image acquisition protocol

All patients underwent non-contrast electron beam computed tomography (EBCT) with an Imatron C-150XL Ultrafast computed tomography scanner (GE-Imatron, South San Francisco, California) or 64-slices multi detector CT (MDCT) (Lightspeed VCT, General Electric Healthcare Technologies, Milwaukee, WI) at Harbor UCLA Medical

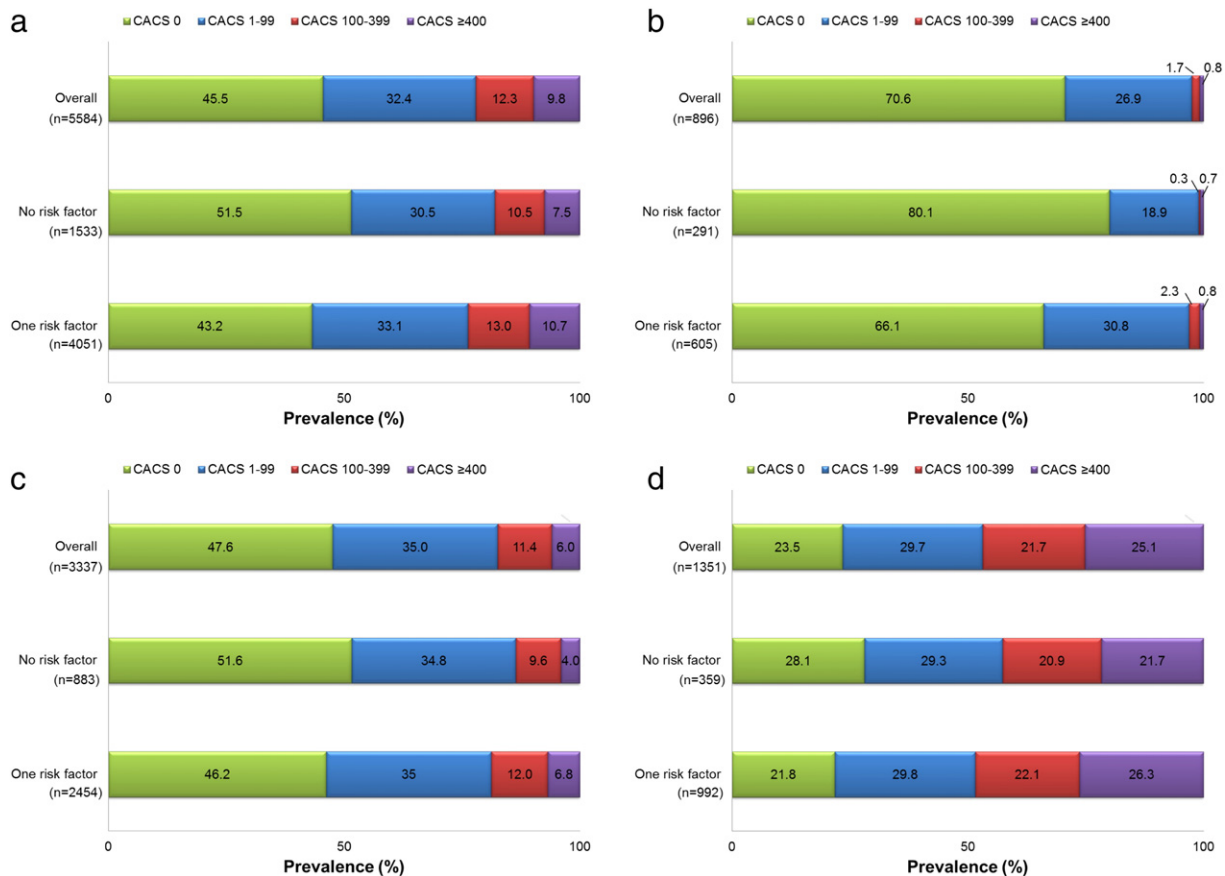


Fig. 1. a. Prevalence of CAC by no or one risk factor in the entire population. b. Prevalence of CAC by no or one risk factor among subjects aged at <45 years. c. Prevalence of CAC by no or one risk factor among subjects aged at 45–65 years. d. Prevalence of CAC by no or one risk factor among subjects aged at ≥65 years. Abbreviations: CAC—coronary artery calcium.

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