Relationship Among Risk Score Systems and Coronary Atherosclerosis Determined by Multislice Computed Tomography

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Background: Risk score systems (RSS) were designed to estimate the risk of cardiac events. Their ability to predict coronary atherosclerosis (CA) has not been established.

Hypothesis: Risk score systems can predict presence of CA in patients without typical symptoms or ischemia. Because design of each RSS is different, their predictive value could also differ.

Methods: A retrospective analysis was done on patients from a low-risk region referred for cardiac multislice computed tomography (MSCT). The sample included low- to intermediate-risk patients with nontypical chest pain and asymptomatic high-risk patients. Patients with documented ischemia were excluded. Three RSS were determined: Framingham Risk Score (FRS), Regicor (FRS calibrated for Spanish population), and Systematic Coronary Risk Evaluation (SCORE). Coronary arteries were investigated to determine calcium score and presence of protruding atheromas.

Results: We analyzed 582 patients (53.8% male; mean age 51 ± 11.5 years). Their mean estimated risk was intermediate: 15.6 ± 10.4 by FRS, 6.3 ± 4.3 by Regicor, and 3.9 ± 4.1 by SCORE. The MSCT showed no CA in 38.8%, nonobstructive plaques in 28.7%, and obstructive ones in 32.5%. The ability of the RSS to predict CA was not significantly different, with moderate diagnostic value (areas under ROC curves, 0.72–0.65). The prevalence of CA was high in low-risk patients: 40%, 47%, and 53% in FRS, Regicor, and SCORE low-risk patients, respectively.

Conclusions: Risk score systems have only moderate diagnostic value to predict presence of CA, without significant differences among them. Coronary artery disease is highly prevalent in patients considered low risk.

KEYWORDS

Imaging, computed tomography, Preventive cardiology, Ischemic heart disease, acute coronary syndromes

1 | INTRODUCTION

Identification of patients at risk of cardiac events is one of the goals of prevention in cardiovascular medicine. For this purpose, several risk scoring systems (RSS) that include demographic and clinical

characteristics have been developed.^{1–4} Most of them were designed to assess the future risk of events due to coronary artery disease (CAD),^{1–3} whereas Systematic Coronary Risk Evaluation (SCORE) was designed to assess the risk of cardiovascular death.⁴ Coronary artery disease is considered a continuum that begins early in life with

minimal changes and ends with clinical events, sometimes lethal ones.⁵ Due to the “hard” nature of the endpoints used to design RSS, to prevent previous stages of the disease, it seems reasonable to look for the relationship among RSS and silent atherosclerosis. Several authors have demonstrated the relationship between the Framingham Risk Score (FRS) and subclinical atherosclerosis detected by carotid intima-media thickness^{5,6} or by detection of coronary lesions using multislice computed tomography (MSCT).^{7,8} Multislice computed tomography offers a noninvasive window to explore the presence of CAD, both investigating calcium score⁷ or plaques.⁹ Studies comparing the value of different RSS to predict subclinical CAD are lacking. The aim of this study was to compare the ability of 3 RSS to predict CAD as determined with MSCT coronarography.

2 | METHODS

2.1 | Study Population

This retrospective study was conducted in a university hospital that serves a region of 260 000 inhabitants in southern Europe from December 2012 to January 2015. The population screened included 656 outpatients referred for MSCT following a previously designed protocol. Patients could be referred for (1) nontypical chest pain with low or intermediate cardiovascular risk, or (2) high cardiovascular risk without cardiac symptoms and programmed high-risk noncardiac surgery. The protocol excluded patients with atrial fibrillation, typical angina, previous acute coronary syndrome, revascularization, ischemia documented by noninvasive testing, and/or angiographically documented severe coronary artery stenosis. Contraindications for MSCT were allergy to iodinated contrast, glomerular filtration rate <30 mL/min, pregnancy, and hyperthyroidism. All patients gave written consent before the testing was done. Investigations were in accordance with the Declaration of Helsinki.

2.2 | Risk Factors

The presence of coronary risk factors (diabetes mellitus, blood pressure, serum lipids, family history of CAD, cigarette smoking, and use of antihypertensive agents) and demographic data (age, sex) were recorded in the clinical history. Patients were classified as active smokers if they had smoked during the previous 12 weeks. Those treated with a hypoglycemic agent or with fasting plasma glucose ≥ 126 mg/dL were classified as diabetic. Patients taking antihypertension drugs were classified as hypertense. The values of blood pressure and lipids included in the RSS equations were those obtained in the outpatient clinic during the visit previous to the MSCT.

2.3 | Risk Estimation

Cardiovascular risk was estimated using 3 different scores: the Framingham Risk Score (FRS)¹; Regicor, a version of FRS calibrated for the Spanish population³; and HeartSCORE calculator,⁴ using the low-risk version, as indicated for the Spanish population. Because SCORE

was not designed for patients age >70 years, those patients were excluded from analysis. Using FRS, patients were considered at low risk when the 10-year risk of events was $\leq 10\%$, intermediate risk when the risk was between 10% and 20%, and high risk when the estimated risk was $\geq 20\%$.¹² Using Regicor, patients were considered at low risk when the risk of events at 10 years was <5%, moderate risk if it was between 5% and 10%, and high risk if it was $\geq 10\%$.³ Using SCORE, patients were at low risk when the 10-year risk of cardiovascular death was <1%, intermediate risk if it was between 1% and 5%, and high risk if it was $\geq 5\%$.¹³

2.4 | Imaging Techniques

The cardiac MSCT coronary angiography was performed with a 64-slice MSCT scanner (Brilliance CT; Philips, Eindhoven, The Netherlands). In the absence of contraindications, patients with a heart rate >65 bpm received intravenous β -blockers before the examination. A prospective coronary calcium scan without contrast was performed, followed by the coronary angiography, with retrospective electrocardiograph gating and according to protocols.¹⁰ Iodinated infusion for coronary artery CT angiography was injected at a dose of 1.2 mL/kg at a flow rate of 5 mL/sec. Data were subsequently transferred to dedicated workstations for postprocessing (Brilliance Workspace Portal and Cardiac Viewer; Philips).

The MSCT coronary angiograms were evaluated by 2 radiologists and 2 cardiologists. The original axial dataset and curved multiplanar reconstructions were used for this purpose. Coronary artery calcium was identified as a dense area affecting ≥ 4 contiguous pixels of >130 Hounsfield units.¹¹ Atherosclerotic lesions were identified as structures >1 mm² within and/or adjacent to the coronary artery lumen, clearly distinguished from the lumen and the surrounding pericardial tissue.¹¹ Lesions were considered obstructive when they occupied $\geq 50\%$ of the luminal diameter, as determined by quantitative coronary angiography. Patients were classified into 3 groups according to the severity of lesions: without coronary lesions, with nonobstructive lesions (including any degree of stenosis of <50% or calcification), and with ≥ 1 obstructive lesion, irrespective of its location. According to the extension of CAD, patients were classified into 3 groups: without lesions; 1-vessel disease (occlusive or not); and multivessel disease, including left main.

2.5 | Statistical Analysis

Continuous variables are expressed as mean $\pm$ SD. Categorical variables are expressed as percentages. The area under the receiver operating characteristic (ROC) curves was determined to assess the performance of RSS. To compare among different ROC curves, the asymptotic 95% confidence interval was calculated. The performance of one measure could be considered better if its area under the curve was significantly greater. Analysis of variance was used to compare prevalences among groups. Pearson correlation coefficients were estimated to analyze correlation between continuous variables. A 2-tailed *P* value of <0.05 was considered statistically significant. Statistical analyses were performed using SPSS 11.0 (SPSS Inc., Chicago, IL).

TABLE 1 Baseline Characteristics and Main Findings in MSCT

Parameter	Value
Male sex	313 (53.8)
Age, y	51.3 ± 11.5
HTN	380 (65.3)
DM	114 (19.6)
Smoker	235 (40.4)
Hypercholesterolemia	239 (41.1)
Total cholesterol, mg/dL	185.8 ± 42.2
LDL-C, mg/dL	113.9 ± 35.7
HDL-C, mg/dL	47.8 ± 12.4
Patients on statins	207 (35.6)
FRS	15.6 ± 10.4
SCORE	3.9 ± 4.1
Regicor risk score	6.3 ± 4.3
Cardiac MSCT findings	
No lesions	226 (38.8)
Nonsignificant lesions	167 (28.7)
Significant lesions	189 (32.5)

Abbreviations: DM, diabetes mellitus; FRS, Framingham risk score; HDL, high-density lipoprotein cholesterol; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; MSCT, multislice computed tomography; SCORE, Systematic Coronary Risk Evaluation; SD, standard deviation.

Results are shown as n (%) for noncontinuous variables and mean ± SD for continuous variables.

3 | RESULTS

Seventy-four patients were age >70 years and were excluded. A final sample of 582 patients was analyzed. Most patients were referred for nontypical chest pain (547/94%). Thirty-five (6%) were patients with high cardiovascular risk and programmed high-risk noncardiac surgery. Patient characteristics are shown in the Table 1. The mean age was 51.3 ± 11.5 years, and 313 (53.8%) patients were male. The average risk for the whole group was moderate, with mean values of FRS of 15.6 ± 10.4, Regicor 6.3 ± SD 4.3, and SCORE 3.9 ± 4.1. Risk classification was markedly different depending on the RSS used (Figure 1).

The MSCT showed obstructive lesions in 189 patients (32.5%), nonobstructive ones in 167 (28.7%), and no lesions or coronary calcium in 226 (38.8%). Among those with coronary lesions, 268 (46%)

had 1-vessel disease (obstructive or not) and 88 (15%) had multivesel disease. Patients without lesions had lower risk, estimated by any of the 3 RSS, than those with any degree of lesion (Figure 2A). The estimated risk of patients with obstructive lesions was also higher than the risk of those with nonobstructive lesions, but the differences were smaller and even nonsignificant if estimated by Regicor. Patients with no lesions had much lower risk than those with any extent of coronary disease (obstructive or not; Figure 2B). No significant differences were observed among those with ≥1-vessel disease.

Patients classified as low-risk ones by any of the 3 RSS frequently had coronary atherosclerosis (CA): 53.4% by SCORE, 47.2% by Regicor, and 40% by Framingham. On the opposite hand, patients considered at high risk were rarely free of coronary lesions: 14.7% by Regicor, 14.5% by SCORE, and 18.8% by FRS. The correlation of the 3 RSS systems with the coronary calcium score was $r = 0.35$ for FRS, $r = 0.26$ for SCORE, and $r = 0.26$ for Regicor, all of them with $P < 0.001$.

The ability of the 3 RSS to predict CA was analyzed by ROC curves. Figure 3 shows the curves for any coronary lesion or only obstructive ones. The areas under the ROC curves did not differ significantly and ranged from 0.72 to 0.65, which means a moderate predictive value for the 3 RSS.

4 | DISCUSSION

Our study shows that the ability of the 3 RSS to predict CAD was only moderate and not significantly different among them. We found that CA is a common condition in individuals considered at low or intermediate risk to develop cardiovascular events. In our sample, MSCT showed coronary lesions in 61.2% of cases, half of them with obstructive plaques (≥50% narrowing of lumen), even in the absence of typical symptoms of CAD and once ischemia was excluded using other noninvasive tests. The percentage of patients considered at low risk who had coronary lesions was high (from 40% to 53%, depending on the RSS used), and high-risk patients were rarely free of CA.

Other studies addressed to detect CAD in patients referred for MSCT have found similar results. In these samples, approximately two-thirds of patients have CA,^{8,14} 25% to 33% of them with obstructive lesions. The high prevalence of CA in the adult population

FIGURE 1 Percentage of patients in each risk category depending on the RSS used. (A) Framingham Risk Score. (B) SCORE (low-risk population). (C) Regicor (Framingham calibrated). Abbreviations: RSS, risk scoring system; SCORE, Systematic Coronary Risk Evaluation.

FIGURE 2 Average risk of patients by (A) the degree of stenosis and (B) by the number of vessels affected.

FIGURE 3 Receiver operating characteristic curves to show the diagnostic accuracy of the 3 RSS to predict (A) any coronary plaque and (B) only obstructive lesions. The AUC and its CI appear at the right of the lines for each RSS. Abbreviations: AUC, area under the curve; CI, confidence interval; RSS, risk scoring system.

from developed countries has been widely demonstrated with other techniques. In a sample of necropsies of patients age <35 years who died accidentally, in a low-risk region (Spain), 34% of men and 22% of women had atherosclerosis.¹⁵ Necropsy studies have found atherosclerosis affecting different arterial territories in 93% of Mexican patients age 23 to 66 years, all of them dead due to noncardiovascular causes.¹⁶

Other studies, performed on populations from different risk regions using similar methods, have shown similar results.^{8,14} Risk scoring systems were not been designed to assess the presence of coronary disease, but to predict events. The 3 RSS made different risk classifications: using previously established cutoff points, SCORE classified as low-risk patients three times more cases than FRS. Because FRS was designed for a higher-risk population, it could be supposed that FRS can overestimate risk in lower-risk regions. This can explain 2 of our results: FRS found fewer patients at low risk (35.2% vs 66.4% by SCORE; Figure 1), while those classified as low risk by FRS were more frequently free of atherosclerosis (60% by FRS, vs 46.6% by SCORE).

Our study shows relationships among the risk estimated by the RSS and the degree of obstruction. Park et al¹⁷ demonstrated that

the finding of obstructive plaques in true asymptomatic patients was a predictor of cardiovascular events. Maddox et al¹⁸ analyzed the outcome of 37 674 patients 1 year after a MSCT scan was done. They found that the presence of nonobstructive plaques was associated with a worse prognosis, and that the prognosis worsened as the severity of lesions and the number of affected vessels increased. Fujimoto et al¹⁹ have demonstrated that calcium score and the presence of nonculprit high-risk plaques detected by MSCT predict future events in revascularized patients. More recently, Breuckmann et al²⁰ have shown that calcium score can be used as a surrogate marker of risk in patients with chest pain and atrial fibrillation admitted to a chest pain unit. Our work, as these other studies, shows that atherosclerosis is very common in patients considered at low or intermediate risk, even in a low-risk region such as ours.

4.1 | Study Limitations

This study was retrospective. The high prevalence of atherosclerosis in our sample could be attributed to a bias in the selection of the patients referred for MSCT. Even though most of them had nontypical pain, some could have real angina. To reduce this possibility, we

excluded those with demonstrated ischemia. We did not use plaque analysis to determine the presence of nonprotruding atheromas, and density of plaques was not analyzed to assess their vulnerability. Events were recorded during a mean follow-up of 26 ± 3 months, but the absolute number was so small (11 episodes of cardiac death or acute coronary syndrome, none of them in patients with normal vessels) that an in-depth analysis was not possible.

5 | CONCLUSION

From a clinical point of view, our study can provide 2 conclusions. First, RSS have only a moderate value to predict for CAD, without differences among the 3 RSS analyzed. Second, coronary atherosclerosis is highly prevalent, even in those people considered at low risk by scoring systems in a low-risk region. Our findings support the clinical relevance of nonobstructive CAD even in low-risk populations. Being in a low-risk group does not mean a person has healthy arteries; this can only be affirmed using imaging techniques, such as MSCT. For this reason, preventive interventions cannot be relaxed even in low-risk groups. Further investigation is needed to design strategies to more accurately assess risk using imaging techniques and to decide interventions to improve the outcome of patients with silent atherosclerosis.

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