

# Computed Tomographic Measurement of Coronary Artery Calcification in the Assessment of Cardiovascular Risk: A Descriptive Study

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**Introduction and objectives.** Measurement of coronary artery calcification (CAC) is used in the evaluation of cardiovascular risk. We investigated its usefulness by comparing CAC assessment with that of various risk charts.

**Methods.** We determined cardiovascular risk in patients without known atherosclerosis using the 1998 European Task Force (ETF), REGICOR (*Registre Gironí del Corazón*) and SCORE (Systematic Coronary Risk Evaluation) charts. CAC was assessed by computerized tomography and measurements were classified as low risk (i.e., score <1), intermediate risk (ie, score 1-100), or high risk (ie, score >100).

**Results.** The study included 331 patients (mean age 54 [8.5] years, 89% male). In 44.1%, CAC was detected (mean score 96 [278]). The degree of agreement between the cardiovascular risk derived from the CAC score and that derived from the SCORE and ETF charts was acceptable:  $\kappa=0.33$  ( $P<0.05$ ) and  $\kappa=0.28$  ( $P<0.05$ ), respectively, but agreement was poor with the REGICOR chart:  $\kappa=0.02$  ( $P=0.32$ ). The SCORE and ETF charts, respectively, classified 45.0% and 38.3% of patients with a CAC score >100 as high risk, whereas the REGICOR chart did not classify any of these patients as high risk. Male sex, older age, smoking history, and a family history of coronary heart disease were all associated with the detection of CAC.

**Conclusions.** Measurement of CAC demonstrated calcification in 44.1% of patients without known atherosclerosis. By regarding those with a CAC score >100 as high-risk, 10.4% of patients evaluated using the SCORE chart would be reclassified as high risk, as would 11.6% of those evaluated using the ETF chart, and 18.9% of those evaluated using the REGICOR chart. Consequently, more patients would be eligible for preventative treatment.

**Key words:** Atherosclerosis. Coronary disease. Calcification. Tomography.

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## La determinación de calcio coronario con tomografía computarizada en la evaluación del riesgo cardiovascular: un estudio descriptivo

**Introducción y objetivos.** La cuantificación de calcio coronario (CCC) es una herramienta que evalúa el riesgo cardiovascular. Hemos valorado su utilidad mediante la comparación de distintas tablas de riesgo con la CCC.

**Métodos.** Se midió el riesgo cardiovascular (Task Force Europea de 1998 [TFE], Registre Gironí del Cor [REGICOR] y Systematic Coronary Risk Evaluation [SCORE]) de individuos sin arterioesclerosis conocida. Se realizó una CCC con tomografía computarizada y se clasificaron en función de la CCC en riesgos bajo (< 1), medio (1-100) y alto (> 100).

**Resultados.** Se incluyó a 331 personas (edad media  $54 \pm 8,5$  años, 89% varones). En el 44,1% se detectó calcio en la CCC (mediana  $96 \pm 278$ ). El grado de acuerdo entre el riesgo cardiovascular calculado según CCC y las tablas SCORE y TFE fue aceptable ( $\kappa = 0,33$ ;  $p < 0,05$  y  $\kappa = 0,28$ ;  $p < 0,05$ ) y escaso para REGICOR ( $\kappa = 0,02$ ;  $p = 0,32$ ). SCORE y TFE clasificarían como de riesgo elevado al 45,0 y al 38,3% de aquellos con valores de calcio > 100, mientras que REGICOR no identificaría como de alto riesgo a ninguno de ellos. El sexo masculino, la edad avanzada, el tabaquismo y los antecedentes familiares de cardiopatía isquémica se asociaron con la detección de calcio coronario.

**Conclusiones.** La CCC detectó calcio en el 44,1% de los pacientes sin historia de cardiopatía isquémica. Estos individuos con un índice de calcio coronario > 100 podrían reclasificarse como pacientes de riesgo alto, lo que ocurriría en el 10,4% de las personas analizadas con SCORE, el 11,6% con TFE y en el 18,9% con REGICOR e incrementaría el número de individuos candidatos a un tratamiento preventivo.

**Palabras clave:** Aterosclerosis. Enfermedad coronaria. Calcio. Tomografía.

**ABBREVIATIONS**

CC: coronary calcium  
 REGICOR: Framingham equation calibrated for the Spanish population by the Registre Gironí del Cor (REGICOR)  
 SCORE: 10-year risk tables for fatal cardiovascular disease derived from the European SCORE project in 2003  
 ETF: Framingham equation derived from the 1998 European Task Force

**INTRODUCTION**

Screening for clinically silent coronary artery disease is a challenge for health services as half the first coronary events, including sudden death, occur in asymptomatic individuals.<sup>1</sup> The stratification of cardiovascular risk at 10 years should be the initial tool that enables us to determine the next step in the clinical evaluation and that helps guide us on decisions about preventative measures in asymptomatic subjects.<sup>2</sup> It is recommended to make aggressive therapeutic decisions such as primary prevention for patients above the high-risk threshold (>20% cardiovascular events in the next 10 years if we use the equations derived from the Framingham study, or risk of death  $\geq 5\%$  if we use the SCORE tables<sup>3</sup>). This cut-off point corresponds to the risk of a new event in subjects with established ischemic heart disease.<sup>4</sup> These are the patients who stand to benefit most from an early change in their lifestyle and treatment with drugs that have been shown to slow disease progression (antiplatelet agents,<sup>5</sup> lipid-lowering drugs,<sup>6</sup> renin-angiotensin system blockers,<sup>7</sup> and  $\beta$ -blockers<sup>8</sup>).

Quantification of coronary calcium (CC) allows assessment of calcium deposition in coronary arteries and has been shown to be a useful tool in cardiovascular risk stratification.<sup>9-11</sup> Currently, recommendations limit use of quantification of CC in asymptomatic patients to those considered at intermediate risk and to those with insufficient data available to guide the subsequent therapeutic strategy.<sup>12</sup>

But some important questions have yet to be answered: Are estimates of cardiovascular risk based on functions that only take into account major risk factors acceptable? Does quantification of CC provide any additional benefit in the risk calculation according to the established equations?<sup>13</sup>

This present study aimed to provide an answer to these questions. Our main objective was to assess the usefulness of quantifying CC in studying cardiovascular risk by comparing different risk tables with the CC results. Secondary objectives were to provide CC data for a sample Spanish population and to identify factors associated with detection of CC.

**METHODS****Design and Participants**

This was a descriptive observational study in which all consecutive subjects who attended the department of preventative medicine of the CIMA Clinic, Barcelona, between July 2003 and January 2006 were invited to participate, regardless of whether they attended on their own initiative, whether they were referred by other family doctors or specialists for a cardiology examination, or whether they were referred from our own service. Table 1 shows the exclusion criteria.

The local ethics committee approved the study and all patients gave written informed consent.

**Interventions and Measurements**

All participants attended an outpatient appointment to record their medical history, carry out a physical examination, and extract blood samples after 12 hours of fasting for characterization of their cardiovascular risk factors. The following variables were analyzed: Age, sex, obesity (BMI>30), smoking (smokers were taken to be daily smokers of any number of cigarettes and ex-smokers were those who had not smoked for at least 1 year), and systolic and diastolic blood pressure (mm Hg). We also investigated whether they were diagnosed with hypertension (3 readings >140/90 mm Hg), hypercholesterolemia (2 values >250 mg/dL), or diabetes mellitus according to the criteria of the American Diabetes Association.<sup>14</sup>

Total cholesterol, triglycerides, and high-density lipoprotein cholesterol (HDL-C) concentrations were measured by enzymatic techniques, and the low-density lipoprotein cholesterol (LDL-C) concentration was calculated using the Friedewald equation.<sup>15</sup> Other parameters measured included C-reactive protein (CRP),<sup>16</sup> homocysteine,<sup>17</sup> and lipoprotein (a) concentrations.<sup>18</sup>

From the information obtained, the cardiovascular risk was calculated by applying the tables derived from the Framingham study: The 1998 European Task Force (ETF)<sup>4</sup> and the calibration of the REGICOR group,<sup>19</sup>

**TABLE 1. Study Exclusion Criteria\***

1. Prior diagnosis of coronary arteriosclerosis or clinical signs and symptoms indicative arteriosclerosis
2. Diagnosis of arteriosclerosis in other territories (carotid, cerebrovascular accident, or peripheral arteriopathy)
3. Age <35 years or >74 years
4. Presence of any of the contraindications described for quantification of CC: Atrial fibrillation, claustrophobia, or inability to hold breath for at least 15 s

\*CC indicates coronary calcium

who assessed the risk of all cardiovascular events, and the equation from the SCORE project<sup>3</sup> for low-risk European countries, which assesses the probability of cardiovascular mortality. These tables estimate the 10-year cardiovascular risk on the basis of the following variables: age, sex, smoking habit, blood pressure, total cholesterol, and presence of diabetes mellitus. The REGICOR also includes HDL-C. From the values obtained with the ETF and REGICOR equations, the risk was reclassified as low (<10% at 10 years for coronary events), intermediate (10%-20%), and high (>20%). The values obtained with the SCORE equation was reclassified as low (10-year risk  $\leq$ 1% for fatal coronary events), intermediate (2%-4%), and high ( $\geq$ 5%).

### Quantification of Coronary Calcium

In addition to exercise testing done according to the Bruce protocol on a treadmill,<sup>20</sup> CC was quantified for all patients with a 16 MX 8000 IDT Philips multidetector row computed tomograph, with the support of specific programming according to the method of Agatston,<sup>21</sup> applied retrospectively, for a 70% relative risk with a slice thickness of 3 mm and a threshold for calcium definition of 130 Hounsfield units, on a workstation with specialized software (Extended Brilliance™ Workspace software).

To allow comparison of CC with risk calculations from the different risk equations, low cardiovascular risk was defined as individuals with CC less than 1, intermediate risk as those with values between 1 and 100 inclusive, and high risk as those with values above 100 in a conservative and fully arbitrary fashion on the basis of observations made in previous studies that have shown the predictive capacity of CC events.<sup>9-11</sup>

### Statistical Analysis

Descriptive analysis of all variables was carried out according to their nature. Patients were excluded from the analysis if information was missing that prevented risk calculation according to the equations used. The presence of classic risk factors among patients with CC equal to 0 and greater than 0 was compared with the Fisher exact test and a logistic regression model was constructed to predict CC greater than 0 (dependent variable). As independent variables, the model included the classic age groups for men (>55 years) and women (>65 years) and other determining factors. Individuals with C-reactive protein (CRP) greater than 10 mg/L were excluded from the analysis (12 individuals in all) as participants with such levels are considered to have an exogenous acute-phase stimulus.<sup>16</sup> Pharmacological treatments were also excluded. All the traditional risk factors were included in the construction of the model, and none were excluded. Agreement between

cardiovascular risk predicted by the risk equations and CC was evaluated by contingency tables for calculating the  $\kappa$  statistic.

All statistical analyses were done with the SPSS Package for Windows (version 14.0).

## RESULTS

In total, 840 individuals who underwent quantification of CC agreed to participate. The following patients were excluded from the analysis because they did not meet the inclusion criteria: 445 patients had prior diagnosis of coronary arteriosclerosis, 6 had clinical signs and symptoms indicative of ischemic heart disease at the time of inclusion, 4 had peripheral artery disease in their legs, 2 had silent carotid arteriosclerosis, and 1 had cerebrovascular accident. In addition, 4 subjects were excluded from the analysis because they were under 36 years old and 18 because they were over 74 years old. Furthermore, it was impossible to calculate cardiovascular risk due to lack of data in 29 cases (8 because blood cholesterol concentrations were missing, 19 because no blood pressure readings were available, and 2 because of lack of information on smoking habit).

Of the remaining subjects who met no exclusion criteria and who had sufficient data to calculate cardiovascular risk ( $n=331$ ), 297 (89.7%) had complete data. In the 34 remaining individuals, some but not all information on a study variable was missing. In these individuals, a mean of 1.85 pieces of information were missing per individual. Comparison between the 297 subjects with complete data and the 34 with some piece of information missing showed no statistically significant differences between the 2 groups with respect to the primary variables, which are listed in Table 2 along with the prevalence of the different risk factors, the laboratory values, and the treatments followed by the patients.

The mean (SD) age of the 331 patients in the study was 54 (8.7) years and 89% were men. In all cases, the findings from conventional exercise testing were negative.

Coronary calcium was detected in 146 patients (44.1%), with a median value of 96.0 (interquartile range, 15.0-275.0).

Hypertension, hypercholesterolemia, obesity, and belonging to age and gender groups of risk showed a statistically significant association with detection of CC (Table 3). These associations were later reproduced in the regression model, which had a limited predictive power ( $R^2=0.316$ ), and which yielded an odds ratio (OR) greater than 2 only in the case of family history of ischemic heart disease and for men aged over 55 years. In contrast, sedentary lifestyle, smoking, diabetes mellitus, and family history of heart disease did not show a significant association with the detection of CC.

The strength of agreement between cardiovascular risk calculated according to CC and according to the

**TABLE 2. Clinical Characteristics of the Patients (n=331)\***

|                                     |              |
|-------------------------------------|--------------|
| Men                                 | 297 (89.2)   |
| Age                                 | 54.6 (8.5)   |
| Smoking habit (smoker or ex-smoker) | 227 (68.2)   |
| Sedentary lifestyle                 | 79 (23.7)    |
| Hypercholesterolemia                | 121 (36.3)   |
| HT                                  | 91 (27.3)    |
| Diabetes mellitus                   | 17 (5.1)     |
| Obesity                             | 50 (15.0)    |
| Family IHD                          | 28 (8.4)     |
| Men >55 years                       | 123 (36.9)   |
| Women >65 years                     | 31 (9.3)     |
| Total cholesterol, mg/dL            | 214.6 (42.6) |
| LDL-C, mg/dL                        | 132.2 (35.5) |
| HDL-C, mg/dL                        | 55.9 (18.3)  |
| Triglycerides, mg/dL                | 137.1 (91.1) |
| CRP, mg/dL                          | 0.76 (1.6)   |
| Homocysteine, $\mu$ m/L             | 2.8 (4.1)    |
| Lipoprotein (a), mg/dL              | 8.0 (19.6)   |
| Active Agents                       |              |
| Statins                             | 40 (12.0)    |
| $\beta$ -blockers                   | 21 (6.3)     |
| ACE inhibitors                      | 22 (6.6)     |
| ARA-II                              | 9 (2.7)      |
| ASA                                 | 18 (5.4)     |

\*ASA indicates acetylsalicylic acid; ARA-II, angiotensin II receptor antagonists; IHD, ischemic heart disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HT, hypertension; ACE, angiotensin-converting enzyme; CRP, C-reactive protein.

Values are expressed as number (percentage) or mean (SD).

risk equations was acceptable for SCORE ( $\kappa=0.33$ ;  $P<.05$ ) and for ETF ( $\kappa=0.28$ ;  $P<.05$ ) but not for REGICOR ( $\kappa=0.02$ ;  $P=.32$ ). Thus, the SCORE and ETF functions would class as high risk only 45.0% and 38.3% of those with calcium levels above 100, respectively, whereas REGICOR would not identify any of them (Table 4; Figure). On the other hand, REGICOR did not

classify as high risk any patients with low risk CC (<1), whereas the other functions did (SCORE, 4.1%; ETF, 10.2%).

## DISCUSSION

Our study shows that, despite the acceptable strength of agreement between cardiovascular risk calculated according to CC and the risk tables, these tables have a low capacity for identifying patients with high CC. These patients probably also have a high risk.

Our study has also helped identify what factors are associated with presence of CC. The strongest predictor for the presence of CC was belonging to the risk age groups for each sex (men >55 years, women >65 years), followed by hypertension, hypercholesterolemia, and obesity. These factors can help define which patients are at greatest risk of presenting with subclinical arteriosclerosis and in which patients quantification of CC may be indicated.

Of note is the large number of subjects in whom CC could be detected; many of these were assessed as low or intermediate risk according to the different risk equations used. Thus, 44.1% of our patients had clinically silent CC, with a median CC level of 96. These results are somewhat lower than those in the study by Kondos et al<sup>22</sup> who detected calcium in the coronary arteries of 74% of the 4151 healthy men studied, with a mean value of 137. If we accept that CC values less than 1 indicate a low risk of cardiovascular events and values above 100 indicate high risk,<sup>9,10,23</sup> the ETF, SCORE, and REGICOR risk equations have failed to correctly classify 46.6%, 43.2%, and 38.8% of the subjects, respectively. These data support the usefulness of quantification of CC for screening asymptomatic patients, as identification of these individuals with a CC index above 100 could lead to their reclassification as high-risk patients. This would be the case for 11.6% of those analyzed with the ETF

**TABLE 3. Clinical Characteristics of the Patients According to Whether or Not Coronary Calcium Was Detected\***

|                        | CC            |               | P†   | Odds ratio (95% CI) |
|------------------------|---------------|---------------|------|---------------------|
|                        | QCC=0 (n=168) | QCC>0 (n=146) |      |                     |
| Male                   | 149 (88.7%)   | 130 (89.0%)   | 1    | —‡                  |
| Smokers and ex-smokers | 108 (64.3%)   | 104 (71.2%)   | .23  | 1.17 (0.69-1.98)    |
| Sedentary lifestyle    | 38 (22.6%)    | 34 (23.3%)    | .89  | 0.82 (0.45-1.47)    |
| Hypercholesterolemia   | 52 (31.0%)    | 63 (43.2%)    | .03  | 1.36 (0.8-2.29)     |
| HT                     | 33 (19.6%)    | 55 (37.7%)    | 0    | 1.87 (1.06-3.30)    |
| Diabetes mellitus      | 6 (3.6%)      | 11 (7.5%)     | .14  | 1.32 (0.41-3.26)    |
| Obesity                | 17 (10.1%)    | 27 (18.5%)    | .04  | 1.22 (0.57-2.61)    |
| Family IHD             | 9 (5.4%)      | 15 (10.3%)    | .14  | 2.06 (0.81-5.28)    |
| Men >55 years          | 35 (20.84%)   | 81 (55.5%)    | <.01 | 3.68 (2.12-6.38)    |
| Women >65 years        | 6 (3.6%)      | 22 (15.1%)    | <.01 | 1.73 (0.61-4.87)    |

\*IHD indicates ischemic heart disease; CC, coronary calcium; HT, hypertension; CI, confidence interval.

†Fisher exact test.

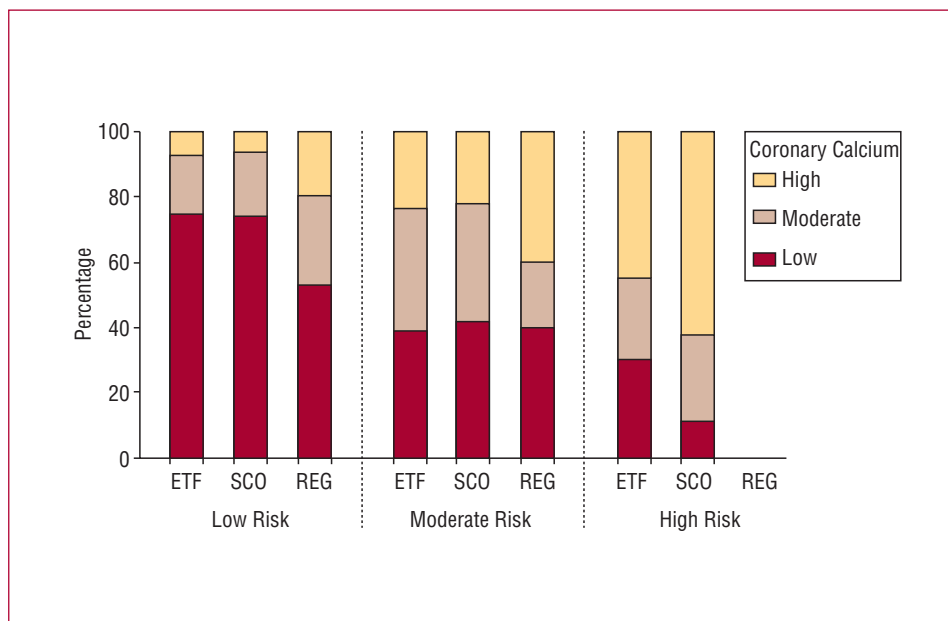
‡The variable sex was not included in the final regression model because of colinearity with the variables "men >55 years" and "women >65 years."



**TABLE 4. Cardiovascular Risk According to Coronary Calcium and Risk Equations\***

|           |            | ETF           |          |      |       | REGICOR       |          |      |       | SCORE         |          |      |       |
|-----------|------------|---------------|----------|------|-------|---------------|----------|------|-------|---------------|----------|------|-------|
|           |            | Low           | Moderate | High | Total | Low           | Moderate | High | Total | Low           | Moderate | High | Total |
| Low       | Number     | 100           | 51       | 17   | 168   | 162           | 6        | 0    | 168   | 108           | 54       | 5    | 167   |
|           | Percentage | 74.6          | 38.9     | 30.4 | 52.3  | 52.9          | 40.0     | 0    | 52.3  | 74.0          | 42.2     | 11.1 | 52.4  |
| Moderate  | Number     | 25            | 49       | 14   | 88    | 85            | 3        | 0    | 88    | 29            | 46       | 12   | 87    |
|           | Percentage | 18.7          | 37.4     | 25.0 | 27.4  | 27.8          | 20.0     | 0    | 27.4  | 19.9          | 35.9     | 26.7 | 27.3  |
| High      | Number     | 9             | 31       | 25   | 65    | 59            | 6        | 0    | 65    | 9             | 28       | 28   | 65    |
|           | Percentage | 6.7           | 23.7     | 44.6 | 20.2  | 19.3          | 40.0     | 0    | 20.2  | 6.2           | 21.9     | 62.2 | 20.4  |
| Total     |            | 134           | 131      | 56   | 321   | 306           | 15       | 0    | 321   | 146           | 128      | 45   | 319   |
| Agreement |            | $\kappa=0.33$ |          |      |       | $\kappa=0.02$ |          |      |       | $\kappa=0.28$ |          |      |       |

\*REGICOR indicates the Framingham equation calibrated for the Spanish population; SCORE, risk tables from the project to estimate the risk of fatal cardiovascular disease in Europe in 2003; ETF, Framingham equation derived from the 1998 European Task Force.



**Figure.** Cardiovascular risk according to coronary calcium and risk equations. REG indicates REGICOR, the Framingham equation calibrated for the Spanish population; SCO, SCORE, risk tables from the project to estimate the risk of fatal cardiovascular disease in Europe in 2003; ETF, Framingham equation derived from the 1998 European Task Force.

equation, for 10.4% in the case of the SCORE risk tables, and for 18.9% in the case of REGICOR. All these subjects would be candidates for preventative treatment that included measures with proven efficacy in primary cardiovascular prevention.

This affirmation is supported by a number of studies done in asymptomatic populations. In these studies, assuming that calcification only appears in atherosclerotic arteries and is absent from normal vessel walls,<sup>23</sup> addition of CC to the calculation of cardiovascular risk with the Framingham risk equations has been shown to increase or decrease the estimated probability of further clinical ischemic heart disease.<sup>10</sup> For an individual with an intermediate risk according to the risk functions, this probability is lower with a CC of 0 and higher for a high CC.<sup>24</sup> Arad et al<sup>25</sup> studied a sample of 1172 asymptomatic subjects for a follow-up period of 3.6 years and showed

that CC greater than or equal to 80 had a sensitivity of 0.85 and a specificity of 0.75 for coronary artery events, showing that an estimated risk of 6% at 10 years increased to greater than 20% when CC was greater than or equal to 80, and that this positive predictive value increased as the calcium levels increased. Detrano et al<sup>26</sup> monitored 1196 asymptomatic patients for 3.4 years and observed that 68% of them already had calcium in their coronary arteries (mean score, 44) and had an annual rate of events (myocardial infarction or death) of 1.6%. Therefore, determination of cardiovascular risk with imaging techniques can better identify patients at high and low risk, thus reducing the number of individuals classed as intermediate risk.

Due to the lack of risk equations for Spain, equations from the United States of America and/or Europe are used, and there is still debate about which of these best

approximates risk in this country. Equations from European populations, such as SCORE for Mediterranean countries are unlikely to overestimate risk in Spanish patients, as they are based mainly on Italian cohorts with a similar coronary mortality to Spain. Recent data indicate that application of SCORE classifies as high risk 3 times as many men as when the Framingham function is applied.<sup>27</sup> These differences are even higher if we apply the REGICOR calibrated equation,<sup>28</sup> which may underestimate risk in the Spanish population, given that the incidence of myocardial infarction in Girona is 15% lower than the average for Spain.<sup>29</sup> For this reason, the applicability to other areas of Spain should be treated with caution. Our study agrees with the REGICOR equation in the sense that coronary risk is very much lower, particularly in terms of the proportion of patients with high risk. In view of these results, and bearing in mind that the present study had 65 subjects with CC greater than 100 who were classified as low or moderate risk according to the REGICOR equation, perhaps the cutoff points for risk stratification according to the REGICOR equation should be reconsidered to ensure that low-risk patients are more appropriately classified.

The degree of agreement between cardiovascular risk calculated according to CC and according to the risk equations was acceptable for SCORE ( $\kappa=0.33$ ;  $P<.05$ ) and for ETF ( $\kappa=0.28$ ;  $P<.05$ ) but not for REGICOR ( $\kappa=0.02$ ;  $P=.32$ ). The interpretation of nonextreme values of the  $\kappa$  coefficient incorporates qualitative aspects, and so it is common to use interpretation rules proposed by experts. In this article, we selected those of Landis et al,<sup>30</sup> as these are the most cited ( $<0.00$ , almost nonexistent; 0.00-0.20, weak; 0.21-0.40, acceptable; 0.41-0.60, moderate; 0.61-0.80, substantial; 0.81-1.00, almost perfect).

Given that the predictions of the SCORE tables correspond best with CC, we might think that this is the most suitable equation, but the lack of specific prognostic data for the study population precludes a recommendation along these lines. In addition, SCORE has a disadvantage with respect to REGICOR in that it can only be used up to the age of 65 years and that it does not take into account HDL-C, unlike REGICOR, which, in addition, has been shown to be useful up to 74 years. This may mean the ETF and SCORE equations underestimate risk in patients with low HDL-C or triglycerides above 180 mg/dL, variables which were shown not to influence the finding of CC in our study.

It may be that the Framingham equations have a weak predictive power because they are based on classic risk factors which only explain 50% of atherosclerosis risk<sup>31,32</sup> and do not include emerging risk factors such as CRP,<sup>16</sup> homocysteine,<sup>17</sup> or lipoprotein (a),<sup>18</sup> which may contribute to identification of individuals at high risk.

Our study should be interpreted with caution due to certain limitations. It was not a study objective or our

intention to recommend quantifying CC as an ideal method for screening for coronary arteriosclerosis; this technique does not provide definitive evidence for ruling out the disease given that noncalcified plaques may elude detection. In addition, it is not known in what population CC should be quantified as a preventative measure and what information it actually contributes to traditional risk estimation based on risk functions. Likewise, it has not been shown that use of these noninvasive techniques has a good cost-benefit ratio for predicting cardiovascular risk. In addition, we should not forget the limitations of the technique itself,<sup>33</sup> which is currently costly, not widely available, and exposes the subject to radiation.

Despite the proven usefulness of CC as a prognostic factor in studies done in Anglo Saxon countries, we do not know the implications of detecting calcium in the coronary arteries in Spanish populations. Therefore, it is necessary to evaluate the true prognostic implication of the presence of silent CC in the Spanish population with studies that measure the predictive capacity of CC with quantification of coronary events and that might even assess the usefulness of preventative pharmacological treatment. In the meantime, common sense suggests that treatment for these patients should be similar to that of subjects with clinical manifestations. And, while prospective trials are pending, if the current risk equations actually predict low or moderate risk in patients who already have CC, perhaps we should reconsider the risk values for which primary prevention activities are indicated.

The high prevalence of CC detected could be due to a selection bias in our sample, given that these are individuals who came voluntarily for a medical examination. But such individuals are generally more concerned about their health and carry out preventative activities. It is also possible that a bias towards healthy workers is in operation, given that those able to stay in their job enjoy better health than the general population. Therefore, it is a limitation that our selected sample is not representative of the general population; however, it is very difficult to determine the difference in cardiovascular risk between this population and the general population.

Our sample is made up mainly of men, and so we cannot extrapolate our results to women, given that women have a lower incidence of ischemic heart disease than men of the same age.<sup>34</sup>

## CONCLUSIONS

Despite the acceptable strength of agreement between cardiovascular risk calculated according to CC and the SCORE and ETF risk equations (the results for REGICOR were not acceptable or significant), these tables have a low capacity for identifying patients with high CC, who probably also have a high risk. Measurement of CC could

reclassify cardiovascular risk estimated with the risk equations in a high percentage of individuals, increasing the number of individuals who would benefit from preventative treatment.

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