Atherosclerosis 290 (2019) 80–86

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Predictive validity of the risk SCORE model in a Mediterranean population with dyslipidemia

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HIGHLIGHT

- Hypercholesterolemia is one of the main cardiovascular risk factors.
- Recommendations on the initiation of lipid-lowering treatment depend on the level of cardiovascular risk, as calculated using SCORE.
- SCORE does not accurately predict the appearance of cardiovascular events in patients with hypercholesterolemia and no lipid-lowering treatment.
- Using SCORE in clinical practice can derive in the undertreatment of patients with hypercholesterolemia.

ARTICLE INFO

Keywords:
Hypercholesterolemia
SCORE
Cardiovascular disease
Cardiovascular risk

ABSTRACT

Background and aims: Cholesterol treatment for the primary prevention of cardiovascular disease is based on cardiovascular risk, as assessed by the SCORE (Systematic COronary Risk Evaluation) scale. This study aimed to assess the predictive value and clinical utility of the SCORE scale for preventing cardiovascular events and all-cause mortality in people with dyslipidemia and no lipid-lowering treatment.

Methods: Patients with dyslipidemia and no lipid-lowering treatment were included from the ESCARVAL-RISK cohort. Cardiovascular risk was calculated by means of the SCORE scale. All deaths and cardiovascular events were recorded for up to five years of follow-up. We calculated sensitivity, specificity and other predictive values for different cut-off points and assessed the effect of different risk factors on the diagnostic accuracy of the SCORE charts.

Results: In the final cohort of 18,853 patients, there were 1565 cardiovascular events and 268 deaths. The risk value recommended to initiate pharmacological treatment (5%) presented a specificity of 86% for death and 90% for cardiovascular events, and a sensitivity of 53% for death and 32% for cardiovascular events. In addition, the scale classified as low risk 62.8% of the patients who suffered a cardiovascular event and 46.6% of those who died. Antithrombotic treatment, diabetes, hypertension, heart failure, peripheral artery disease and chronic kidney disease were associated with a reduction in the predictive capability of the SCORE scale, whereas metabolic syndrome was related to better risk prediction.

Conclusions: The predictive capability of the SCORE scale for cardiovascular disease and total mortality in patients with dyslipidemia is limited.

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https://doi.org/10.1016/j.atherosclerosis.2019.09.007
Received 16 July 2019; Received in revised form 15 September 2019; Accepted 19 September 2019
Available online 23 September 2019
0021-9150/

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide [1]. Ischemic heart disease is responsible for most of the cardiovascular deaths (27%), followed by cerebrovascular disease (23%).

Hypercholesterolemia is one of the primary CVD risk factors and the most frequent hereditary disease; indeed, more than half of the population in the largest European countries (Germany, France, Italy, Spain and the UK) aged 25 years or older have high cholesterol levels (≥5 mmol/l or 193 mg/dl) [2]. But despite the high prevalence and the unequivocal relationship with CVD and all-cause mortality, treatment rates and fulfillment of therapeutic objectives are suboptimal [3]. The reduction of low-density lipoprotein (LDL) cholesterol with statins is variable, with larger reductions achieved in people with higher cholesterol, so treatment objectives are based not only on achieving target levels but also on the relative reduction from baseline. Different studies suggest that lowering LDL cholesterol by about 1 mmol/L (38.67 mg/dl) with standard statin regimens reduced the 5-year incidence of major coronary events, revascularizations, and ischemic strokes by a fifth [4,5].

CVD prevention should take an integrated approach, including behavioral changes in diet and physical activity as well as pharmacological treatment. Cardiovascular risk scales have the dual purpose of establishing a patient's overall risk for CVD as well as selecting patients who would benefit from specific treatments. The SCORE (Systematic COronary Risk Evaluation) project was developed to estimate the total cardiovascular risk and to guide in clinical practice for primary prevention of CVD in Europe [6]. In Spain, the SCORE chart for low-risk countries is recommended as an integrated approach for controlling cardiovascular risk factors. Statins are the cornerstone drug treatment for hypercholesterolemia, however, adherence to the recommendations on when or at what dose they should be administered is still low [7]. Moreover, there is no evidence that using this strategy has a clinical benefit, and there are also doubts about the efficiency of statins treatment for primary prevention in certain populations [8,9]. Thus, the aim of the present study is to assess the predictive value and clinical utility of the SCORE risk scale for preventing ischemic cardiopathy, stroke, and all-cause mortality in people with hypercholesterolemia and no lipid-lowering treatment.

2. Materials and methods

This observational cohort study included patients from the ESCARVAL-RISK study [10,11], a prospective cohort study in people with cardiovascular risk factors (arterial hypertension, hypercholesterolemia, or diabetes mellitus) but without established CVD. The aim of that study is to investigate associations between major CVD risk factors and CVD incidence in a real-world setting.

Our study was performed in line with international recommendations on clinical research (Declaration of Helsinki of the World Medical Association, as amended in October 2013). The Committee for Ethics and Clinical Trials of the Center for Public Health Research approved the ESCARVAL-RISK study [10]. All patient data were collected from the electronic clinical history (ECH) in the ABUCASIS health information system. Patients were recruited during January 2008 and were followed until 31 December 2012; data were anonymized and handled in compliance with the cognizant legislation on data protection (Organic Law 15/1999). Moreover, all researchers with access to the study data were required to sign a document guaranteeing the confidentiality of patient information. Patients' informed consent was not necessary to carry out the study.

2.1. Study population

Included patients were recruited from the primary care centers run through the Valencian Region's public health system. Each user of the national health system has a unique patient identifier through which their ECH can be accessed. The ESCARVAL-RISK registry included 73,302 people of both sexes who met the study's inclusion criteria: aged 30 or older; no known CVD; presenting to their local health center for routine care; with at least one of the following CVD risk factors: hypertension, diabetes mellitus, and/or hypercholesteremia. The latter condition was defined as a concentration of total cholesterol of 200 mg/dL or more, a registered diagnosis of hypercholesteremia (International Classification of Diseases (ICD) code E78), or the use of lipid-lowering treatment. For the present study, we included the subgroup of patients with hypercholesterolemia who were not receiving any drug treatment to control the condition. Exclusion criteria were ECHs with missing data for any of the variables needed to calculate cardiovascular risk using the SCORE chart for low-risk countries; serious comorbidities limiting the patient's life expectancy to less than five years; other diseases that could, based on medical criteria, distort the study results; or any other mental or social factor that the research team believed could interfere with follow-up (Supplementary Fig. 1).

2.2. Study variables

The health information system of the Valencian Region (ABUCASIS II) maintains ECHs that record the main epidemiological variables, anthropometric and clinical examination data, CVD risk factors, comorbidities, electrocardiogram (ECG) data, blood and urine analytical data, and any prescribed drug treatments. For our study, we extracted the following variables: sex, age, body mass index (BMI), medical history, drug treatments, tobacco use, systolic blood pressure (mmHg), and total cholesterol (mg/dL). The diagnosis of metabolic syndrome was assessed when three or more of the following criteria were present: waist circumference > 102 cm in men or > 88 cm in women; triglyceride level ≥150 mg/dl; HDL cholesterol < 40 mg/dL in men or < 50 mg/dL in women; systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg; fasting glucose ≥100 mg/dL. We then calculated the risk of experiencing a cardiovascular event using the SCORE chart for low-risk countries, following the working methodology proposed by the European Society of Cardiology [6].

2.3. Follow-up

Follow-up was from January 2008 to December 2012. Participants were followed up by means of annual reviews of hospital records up to the first admittance for ischemic cardiopathy or stroke, or to death from any cause. We undertook separate analyses for predicting all-cause mortality and the composite outcome of cardiovascular events. Mortality data were obtained by linking the ESCARVAL database to the Valencian Region Death Registry, and the reason for hospitalization was determined based on the ICD codes assigned (9th revision: ICD-9 410–414 for ischemic cardiopathy or ICD-9 430–438 for stroke).

2.4. Statistical analysis

Descriptive statistics were calculated for CVD risk as a percentage, according to the SCORE system. Receiver operating characteristic (ROC) curves were plotted with the SCORE risk against the observed incidence of cardiovascular events or all-cause mortality. We also calculated the sensitivity, specificity, Youden index and predictive values for different cutoff points. The maximum value of the Youden index was used to identify the cutoff point with the best sensitivity and specificity.

The risk calculation was both quantitative (risk for cardiovascular mortality at 10 years) and qualitative, according to whether the risk was less than 5% [6]. We assessed the sensitivity, specificity, predictive values and total diagnostic effectiveness for each scale (percentage of correct classifications for each observed event). Finally, we identified the patients whom the scale had accurately classified (that is, they were classified as being at low risk and did not experience an event, or as

high risk and had) as well as those classified inaccurately. Multivariable logistic regression models were fitted to calculate the odds ratio (OR) and 95% confidence intervals (CIs) for a patient being inaccurately classified with the SCORE chart, according to different factors associated with the predictive capacity of the scale. These models did not include the variables used to construct the SCORE scale, such as age, sex, systolic blood pressure, total cholesterol, or tobacco use.

Explanatory variables in the model were BMI; treatment with antiplatelet drugs, anticoagulants, insulin, oral antidiabetics or antihypertensives; and comorbidities like diabetes mellitus, heart failure, proteinuria, peripheral arteriopathy, atrial fibrillation, arterial hypertension, kidney disease, left ventricular hypertrophy, retinopathy, and metabolic syndrome. Variables with missing data for more than 25% of the total tests were excluded from the model. All the analyses were repeated after the exclusion of diabetic patients. Analyses were undertaken using SPSS v.18 and R v.3.5.0 statistical software.

3. Results

Of the 73,302 patients included in the ESCARVAL-RISK registry [10], 57,645 had hypercholesterolemia. After excluding the patients being treated for the condition, the number of eligible patients dropped to 36,521. Following exclusion of patients with missing data for the variables needed to construct the risk score, the final sample size was 18,853 (Fig. 1). The risk of suffering a cardiovascular event was calculated using SCORE for all included patients.

Table 1 shows the baseline characteristics for the study population. Just over half (53.4%, n = 10,065) of the sample were women, and the mean age was 57.9 (standard deviation [SD] 13.3) years. Mean concentration of total cholesterol was 222.5 (SD 40.5) mg/dL; mean BMI, 29.4 (SD 4.9) kg/m^2; and mean systolic blood pressure, 135.4 (SD 19.4) mmHg. Mean cardiovascular risk was 2.3% (SD 2.6%; range 0%–20.5%), with 85.5% (n = 16,120) of the sample presenting a risk of less than 5% and the remaining 14.5% (n = 2733) showing a risk of 5% or more. Fig. 1 shows the distribution of estimated SCORE risk.

The follow-up period in the study was five years, with a mean period of 4.0 (SD 1.4) years and a median of 4.9 years achieved. By study end, there was a registered total of 1565 cardiovascular events and 268 total deaths. Fig. 2A and B show the area under the ROC curve (AUC) for the prediction of cardiovascular events (AUC 0.736, 95% CI 0.724–0.748) and death (AUC 0.790, 95% CI 0.763–0.817). No differences between sexes were apparent in terms of the predictive power of the charts. Tables 2 and 3 show the sensitivity and specificity of the SCORE table for the prediction of cardiovascular events or mortality. The points of maximum sensitivity and specificity were 2.0% for the prediction of a cardiovascular event (sensitivity 69%, specificity 66%) and 2.3% for the prediction of all-cause mortality (sensitivity 76%, specificity 68%). The cutoff used in clinical practice of 5% has a high specificity (86% for death and 90% for cardiovascular events) but low sensitivity (53% for death and 32% for cardiovascular events).

The distribution of patients with events in the overall sample, according to the risk attributed by the SCORE charts, is shown in Table 4. Those who suffered either a cardiovascular event or death, 62.8% and 46.6%, respectively, had been classified as being at low risk. Table 5 shows the results of the multivariable logistic regression, reporting ORs and 95% CIs for inaccurate SCORE classification based on cardiovascular events and death. Variables that reduced the predictive power of

Table 1
Baseline characteristics of study population (N = 18,853).

Variable		
Age, years (SD)	57.9	(13.3)
Female sex	10,065	(53.4)
Tobacco use	5,130	(27.2)
BMI	2.3	(2.6)
Medical history		
Arterial hypertension	10,583	(56.1)
Systolic blood pressure, mmHg (SD)	135.4	(19.4)
Diastolic blood pressure, mmHg (SD)		
Total cholesterol, mg/dl (SD)	222.5	(40.5)
Left ventricular hypertrophy	10	(0.1)
Diabetes mellitus	4,891	(25.9)
Retinopathy	64	(0.3)
Metabolic syndrome	77	(0.4)
Kidney disease	241	(1.3)
Proteinuria	168	(0.9)
Atrial fibrillation	91	(0.5)
Heart failure	342	(1.8)
Peripheral arteriopathy	421	(2.2)
Treatments		
Antiplatelet therapy	1,365	(7.2)
Insulin	142	(0.8)
Oral antidiabetics	781	(4.1)
Anticoagulants	632	(3.4)
Antihypertensives	2,412	(12.8)

BMI: body mass index; SD: standard deviation.

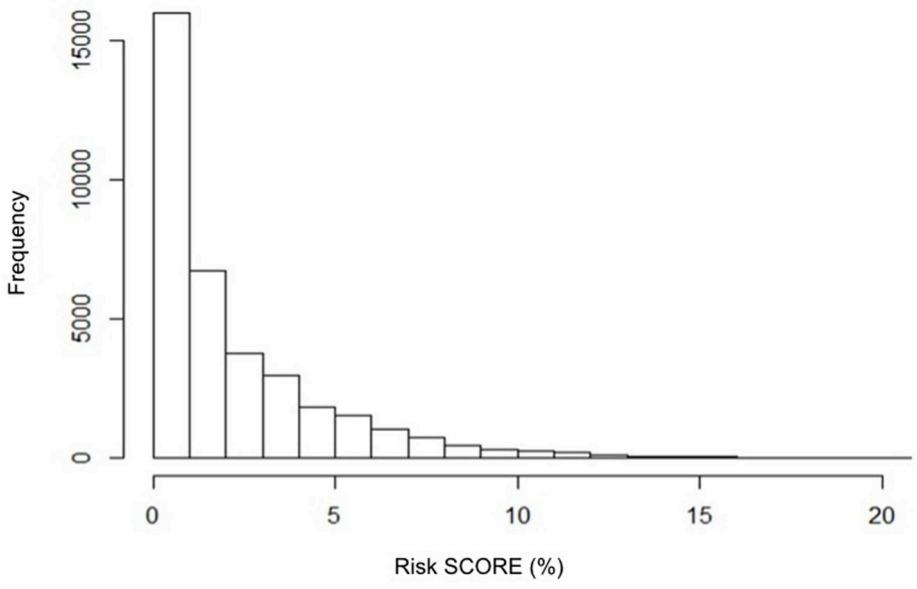

Fig. 1. Histogram of risk distribution for fatal cardiovascular event in the population according to the SCORE risk index.

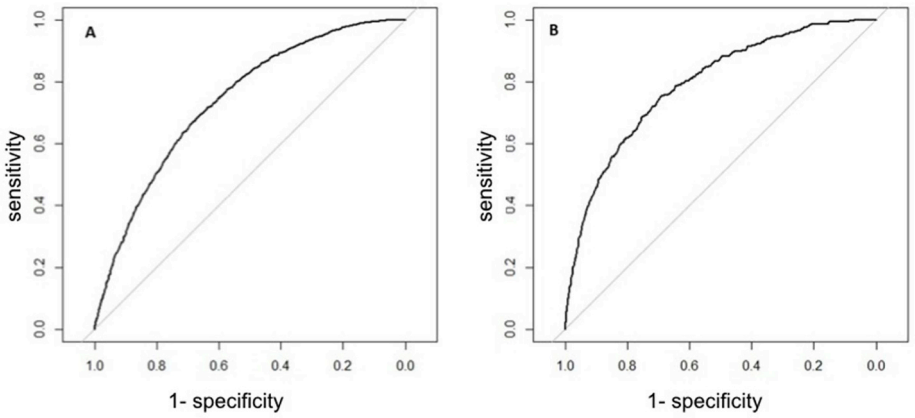

Fig. 2. ROC curves for the prediction of cardiovascular events (A) and all-cause mortality (B), according to SCORE risk charts.

Table 2
Sensitivity, specificity, and positive and negative predictive values for the prediction of cardiovascular events at each SCORE cutoff point.

Cutoff (%)	Sensitivity	Specificity	Youden index	Positive predictive value	Negative predictive value
0.1	0.996	0.083	0.079	0.084	0.996
0.2	0.969	0.212	0.181	0.094	0.988
0.4	0.937	0.303	0.240	0.102	0.983
0.6	0.904	0.380	0.284	0.110	0.979
0.8	0.879	0.433	0.312	0.116	0.977
1.0	0.844	0.487	0.331	0.122	0.974
1.1	0.822	0.516	0.338	0.126	0.972
1.2	0.810	0.527	0.337	0.127	0.970
1.3	0.784	0.556	0.340	0.130	0.968
1.4	0.776	0.571	0.347	0.133	0.968
1.5	0.761	0.583	0.344	0.134	0.966
1.6	0.737	0.610	0.347	0.138	0.965
1.8	0.716	0.636	0.352	0.143	0.964
1.9	0.705	0.648	0.353	0.145	0.963
2.0	0.693	0.661	0.354	0.148	0.962
2.5	0.615	0.728	0.343	0.161	0.957
3.0	0.546	0.775	0.321	0.171	0.953
4.0	0.437	0.843	0.280	0.191	0.946
5.1	0.318	0.897	0.215	0.208	0.939
8.0	0.115	0.970	0.085	0.246	0.928
10.9	0.035	0.993	0.028	0.287	0.924
14.0	0.007	0.999	0.006	0.333	0.922
17.3	0.001	1.000	0.001	0.333	0.922
18.0	0.001	1.000	0.001	0.286	0.922
20.5	0.000	1.000	0.000	0.000	0.922

Table 3
Sensitivity, specificity, and positive and negative predictive values for the prediction of all-cause mortality at each SCORE cutoff point.

Cutoff (%)	Sensitivity	Specificity	Youden index	Positive predictive value	Negative predictive value
0.0	0.998	0.078	0.076	0.013	1.000
0.2	0.986	0.200	0.186	0.015	0.999
0.4	0.954	0.287	0.241	0.016	0.998
0.6	0.934	0.361	0.295	0.018	0.998
0.8	0.916	0.413	0.329	0.019	0.997
1.0	0.890	0.466	0.356	0.020	0.997
1.1	0.884	0.494	0.378	0.021	0.997
1.2	0.870	0.505	0.375	0.021	0.997
1.4	0.847	0.548	0.395	0.023	0.997
1.5	0.836	0.561	0.397	0.023	0.996
1.6	0.815	0.588	0.403	0.024	0.996
1.8	0.804	0.614	0.418	0.025	0.996
1.9	0.795	0.626	0.421	0.026	0.996
2.0	0.788	0.639	0.427	0.026	0.996
2.1	0.772	0.654	0.426	0.027	0.996
2.2	0.760	0.669	0.429	0.028	0.996
2.3	0.758	0.682	0.440	0.029	0.996
2.5	0.731	0.706	0.437	0.030	0.995
2.7	0.721	0.717	0.438	0.031	0.995
2.8	0.703	0.731	0.434	0.031	0.995
3.0	0.678	0.755	0.433	0.033	0.995
4.0	0.591	0.826	0.417	0.040	0.994
5.1	0.534	0.861	0.395	0.053	0.992
5.9	0.418	0.918	0.336	0.060	0.992
8.0	0.233	0.966	0.199	0.078	0.990
10.1	0.116	0.988	0.104	0.105	0.989
20.5	0.000	1.000	0.000	0.000	0.988

the SCORE chart included antithrombotic treatment, diabetes mellitus, arterial hypertension, heart failure, peripheral arteriopathy, and kidney disease, whereas having metabolic syndrome improved event prediction using the scale.

The analyses performed after the exclusion of diabetic patients showed similar results. Again, the cutoff of 5% showed a high specificity (88% for death and 90% for cardiovascular events) but low sensitivity (48% for death and 33% for cardiovascular events). Out of the non-diabetic patients who suffered either a cardiovascular event or death, 67.1% and 51.9%, respectively, had been classified as being at low risk (Supplementary Tables 1–5).

4. Discussion

The present study shows that the SCORE cardiovascular risk chart does not accurately predict the appearance of cardiovascular events in a

Table 4
SCORE risk classification for cardiovascular mortality: (expected) cutoff of 5% *versus* (observed) incidence of cardiovascular events and mortality.

		Cardiovascular event		Mortality	
	Total	Event	No event	Exitus	No exitus
High risk ≥ 5%, n (%)	2,733 (14.5%)	582 (37.2%)	2,151 (12.4%)	143 (53.4%)	2,590 (13.9%)
Low risk < 5%, n (%)	16,120 (85.5%)	983 (62.8%)	15,137 (87.6%)	125 (46.6%)	15,995 (86.1%)
Total	18,853	1565	17,288	268	18,585

Table 5
Variables related to inaccurate prediction of cardiovascular event and mortality using SCORE.

	Inaccuracy of SCORE prediction for cardiovascular event	Inaccuracy of SCORE prediction for acute coronary syndrome	Inaccuracy of SCORE prediction for stroke	Inaccuracy of SCORE prediction for all-cause mortality
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
BMI (kg/m^2)	0.98 (0.97–0.98)	0.97 (0.97–0.98)	0.97 (0.96–0.98)	0.95 (0.95–0.96)
Antiplatelet therapy	NS	NS	1.21 (1.04–1.41)	1.39 (1.19–1.62)
Anticoagulant therapy	1.79 (1.48–2.17)	2.07 (1.71–2.50)	1.74 (1.43–2.11)	1.59 (1.30–1.94)
Arterial hypertension	2.40 (2.17–2.65)	2.63 (2.38–2.92)	2.82 (2.54–3.13)	2.61 (2.35–2.91)
Left ventricular hypertrophy	NS	5.16 (1.22–21.83)	NS	NS
Diabetes mellitus	1.51 (1.38–1.65)	NS	NS	1.59 (1.45–1.75)
Metabolic syndrome	NS	NS	NS	0.34 (0.13–0.87)
Heart failure	2.26 (1.76–2.91)	2.84 (2.21–3.66)	3.11 (2.47–4.05)	2.82 (2.19–3.62)
Peripheral artery disease	3.98 (3.19–4.98)	4.63 (3.70–5.80)	1.78 (1.40–2.25)	1.56 (1.22–1.99)
Atrial fibrillation	2.47 (1.51–4.03)	2.67 (1.63–4.38)	3.43 (2.10–5.59)	3.55 (2.17–5.78)
Kidney disease	1.62 (1.20–2.19)	1.83 (1.36–2.47)	2.32 (1.73–3.09)	2.49 (1.85–3.37)
n	15,870	15,870	15,870	15,870
LRT (*p*-value)	893.6 (< 0.001)	932.7 (< 0.001)	784.3 (< 0.001)	845.3 (< 0.001)
Nº inaccurate predictions	2,781	2,679	2,524	2,407
AUC (95% CI)	0.669 (0.658–0.680)	0.667 (0.656–0.679)	0.659 (0.647–0.670)	0.676 (0.665–0.688)

AUC: area under the receiver operating characteristics curve; BMI: body mass index; OR: odds ratio; CI: confidence interval; LRT: log ratio test; NS: not significant.

non-selected Mediterranean population with hypercholesterolemia not receiving lipid-lowering treatment. Our results raise doubts as to whether the SCORE index is valid for predicting cardiovascular risk and guiding treatment decisions in patients with hypercholesterolemia, as 62.8% of the patients with hypercholesterolemia who suffered a cardiovascular event were not classified as being at high risk according to SCORE. Thus, using this tool in clinical practice may lead to undertreatment of patients, depriving them of effective preventive medicine. More research advances are needed to develop better risk scores capable of accurately identifying the patients at high risk of suffering a cardiovascular event.

Cardiovascular risk indexes are useful tools in clinical practice, but a requirement for their generalized use is their validity. The SCORE charts have been widely evaluated, and most studies have shown good discrimination performance, with AUCs oscillating from 0.70 to 0.80 [12–14]. However, the SCORE charts for low-risk countries have shown acceptable results when applied to high-risk populations, while the high-risk version overestimates their cardiovascular risk [15]. In Spain, Baena-Diez et al. [16] found that even with an acceptable discrimination capacity, the SCORE index significantly overestimated the observed cardiovascular mortality. Furthermore, Kutkiene et al. [17] have already highlighted the importance of the fact that using the SCORE risk charts could underestimate cardiovascular risk in patients with atherogenic hypercholesterolemia.

A number of factors could explain the ill fit of the SCORE charts to the study population:

1. The Spanish population shows different behavioral patterns compared to northern European countries and even to neighboring countries in southern Europe [18–20].
2. The extremes are not well represented. When risk factors present very high values, for example if a patient has severe hypercholesterolemia, the SCORE charts do not allow a corresponding adjustment to the cardiovascular risk. In fact, the charts do not increase risk in people presenting systolic blood pressure over 180 mmHg or total cholesterol of 300 mg/dL, even though cardiovascular risk does continue to increase above these values.

3. Some ages fall outside the scales' range of validity. This is probably one of the weakest points of the risk scale. The population of this study had a mean age of 57.9 years, but 35% were older than 64, so the SCORE charts should not be applied to them. However, SCORE is often the only tool clinicians use to estimate cardiovascular risk and guide treatment decisions in older patients. A chart for people over the age of 65 has been recently added [21], and although it has yet to be validated, it could contribute to solving this problem. For people under the age of 40, the charts' predictive power also decreases, making their use inadvisable. This circumstance contrasts with the fact that onset of atherosclerosis can begin as early as adolescence [22]. Thus, optimal CVD prevention should begin at a young age, with early risk identification and effective treatment [23,24].

4. SCORE does not consider the presence of some risk factors. The results of this study show how factors like kidney disease, peripheral arterial disease, and heart failure can influence the appearance of CVD. Their absence on the charts reduces the predictive capacity of the index. By contrast, arterial hypertension is included on the SCORE charts, but it is actually associated with inaccurate classification for the prediction of events in our population. This is probably due, at least in part, to the persistence of high blood pressure in some patients despite having an established diagnosis and therefore being under treatment. BMI shows an inverse relationship with the charts' predictive capacity, with predictive power increasing for patients who are more overweight. Diabetes increases CVD incidence to the point where the former was for years considered equivalent to the latter; however, there is a wide risk spectrum associated with diabetes, depending on the patient's age, duration of the disease, degree of control, and other modifiers [25–27]. Kidney disease is also a recognized modulator of cardiovascular risk, and its presence should be considered in patients at intermediate risk [28]. The increased risk associated with the presence of microalbuminuria or with a reduced glomerular filtration rate is well documented [29]. Other variables that SCORE does not consider but which have shown to influence the development of CVD are a family history of CVD, chronic inflammatory disease, ankle-brachial index, hypertriglyceridemia, or the presence of biomarkers like apo B, lipoprotein (a), or C-reactive protein.

5. The charts are used poorly. Many of the limitations of the tables are attributable simply to clinicians not following the recommendations for their use. The clearest examples relate to their application in patients whose age is outside the range for which the charts were designed, but there are other circumstances that also entail an increased risk, for example, sedentarism and obesity; a family history of early CVD; social vulnerability or ethnic minority status; type 2 diabetes; type 1 diabetes with a target-organ lesion; low values of high-density lipoprotein (HDL) cholesterol; high values of triglycerides, apo B, fibrinogen, or lipoprotein(a); evidence of atherosclerosis on imaging tests; or a glomerular filtration rate of less than 60 mL/min/1.73 m^2. In our population, variables like diabetes mellitus, chronic kidney disease, or peripheral arterial disease were associated with lower predictive

capacity.

Additional strategies have also been considered for estimating cardiovascular risk, including the determination of serum biomarkers (C-reactive protein, lipoprotein(a), and apo B, among others) and the assessment of coronary calcium by means of computerized tomography (CT) [30–32]. In light of our results, the estimation of cardiovascular risk could be improved by adding several variables to the SCORE risk charts. In the past, a good cardiovascular risk score needed to include only a selection of clinical or analytical variables to make the index applicable in any context. However, with the advent of ECHs and big data, CVD risk estimation should be optimized by including the maximum amount of information at our disposal. Thus, there is a need for more studies on cardiovascular risk evaluation and its validation, along with good coding for diagnoses on the ECH. Pending the realization of these studies, we would propose adjusting the cutoff point used for making decisions on lipid-lowering treatment. Tables 2 and 3 show that by decreasing the risk cutoff, it is possible to improve sensitivity without substantially compromising specificity; in our study the optimal cutoff points for maximizing both measures of accuracy were 2.0% for the prediction of a cardiovascular event and 2.3% for the prediction of death.

4.1. Limitations and strengths

Our registry was prospective but given its population-based nature we cannot rule out diagnostic errors on the ECH or their correction as CVD. To minimize the risk of this bias, all professionals participating in the ESCARVAL study completed an online training course in cardiovascular care, accredited by the Spanish National Health System, as well as specific training in the ABUCASIS II system and ECHs used in the Valencian Region [33]. Moreover, selection bias could be an issue if we selected patients with low motivation for CVD prevention or if the sample composition was determined by professionals who were not committed to primary prevention. However, this is unlikely given the large sample of patients and quantity of participating professionals. Finally, the SCORE risk charts are not designed to predict CVD but rather cardiovascular mortality, and the risk period is 10 years. Such long-term predictions do not tend to motivate the patient to change behaviors or take prophylactic drugs, so shorter-term predictions could help to identify the many patients who, as in this study, could experience an event within five years despite being considered at low risk. This could help to improve physical activity levels, intensify interventions, avoid clinical inertia, and improve adherence to treatment. With regard to this study's strengths, it has a high statistical power and was performed in a routine clinical practice setting, with the participation of a large number of both patients and professionals.

4.2. Conclusion

The SCORE risk charts have a limited predictive capacity for CVD and all-cause mortality in patients with hypercholesterolemia from the primary care setting. Different tools are needed to guide indications for lipid-lowering treatment for primary CVD prevention.

Conflicts of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

Acknowledgements

This work was supported in part by a grant from CIBERCV 16/11/00420, an initiative from Carlos III Health Institute Madrid and the Spanish Ministry of Economy and Competitiveness.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atherosclerosis.2019.09.007.

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