An evaluation of the different clinical practice guidelines for dyslipidemia treatment in outpatient primary prevention patients

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Abstract

Introduction: cardiovascular disease is the main cause of morbidity and mortality worldwide. There are several assessment scales to estimate cardiovascular risk and thus make treatment decisions aimed at primary prevention. The objective of this study was to evaluate the concordance between the AHA/ACC, ESC/EAS, USPSTF and GPC guidelines in determining cardiovascular risk and the decision to prescribe statins as primary prevention.

Methods: this was an analytical observational concordance study. Patients between 40 and 75 years old with no history of cardiovascular disease, who were seen at Hospital San José as outpatients in the Department of Internal Medicine between January 2019 and January 2021, were included. The Framingham, adjusted Framingham and SCORE scales were applied to the eligible patients to determine their correlation in evaluating cardiovascular risk. The AHA/ACC, ESC/EAS, USPSTF and GPC guidelines were also applied to evaluate concordance in the decision to begin statins as primary prevention.

Results: a total of 288 patients were included, with an average age of 60.5 years; of these, 63.2% were female, 46.2% had a history of hypertension and 25% had a history of diabetes mellitus. The concordance in the risk assessment using Lin's coefficient was 0.59 for AHA and SCORE, 0.67 for AHA and Framingham, 0.53 for AHA and modified Framingham, 0.63 for Framingham and SCORE, 0.72 for modified Framingham and SCORE, and 0.91 for modified Framingham and Framingham. As far as the decision to give statins, the agreement between the AHA/ACC and ESC/EAS guidelines was low, with a kappa coefficient of 0.48.

Conclusions: for patients with no documented cardiovascular disease who were seen by internal medicine as outpatients at Hospital San José, there was moderate concordance in the cardiovascular risk assessment and low concordance in the decision to give or not give statins as primary prevention. (Acta Med Colomb 2024; 49. DOI: https://doi.org/10.36104/amc.2024.2757).

Keywords: *cardiovascular disease, primary prevention, statin, metabolic syndrome, correlation.*

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Introduction

Cardiovascular disease (CVD) is considered the main cause of morbidity and mortality worldwide. In 2015, there were 17.7 million deaths related to cardiovascular causes, and mortality rates of 104 to 511 per 100,000 inhabitants, and 43 to 199 per 100,000 inhabitants, have been found in 55-74-year-old men and women, respectively (1, 2). In Colombia, according to statistics reported by the National Administrative Department of Statistics (DANE, in Spanish), CVDs accounted for 17% of the mortality in 2018 (3). These diseases generate high care costs for healthcare facilities. In the United States, this cost reached 13% of the total health costs between 2016 and 2017. Thus, the control of CVD risk factors is an essential topic that can reduce the individual costs mentioned by up to 50% (1).

Identifying classical cardiovascular risk factors like dyslipidemia, sex, age, smoking and hypertension, has led to the development of various scales to estimate the 10-year probability of experiencing clinical events related to coronary and cerebrovascular disease (4). The one most recognized and used is the Framingham scale, derived from the study by the same name and proposed in the late 90s, with multiple validations around the world (5). The Systematic Coronary Risk Evaluation (SCORE) is the scale recommended by the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) (6), while the Pooled Cohort Equations have been recommended by the American College of Cardiology/American Heart Association (ACC/AHA) since 2014 (7). In Colombia, a validation study of these scales produced a recommendation of the "recalibrated" Framingham scale to estimate the risk in our population, which consists of multiplying the score obtained on the Framingham scale by a correction factor of 0.75 (8). These scales are important elements in the design of clinical practice guidelines for the approach to and management of dyslipidemia and cardiovascular risk (6, 9-11).

One objective of these guidelines is to determine the treatment goals and most appropriate pharmacological strategies to control cardiovascular risk, including the use of statins as the main option. While there is general agreement on the approach to patients who have already had cardiovascular events (secondary prevention patients) and those with diabetes or LDL cholesterol > 190 mg/dL, the guidelines differ in their recommendations for patients who have not had prior events (primary prevention patients) and who do not have the conditions mentioned above. The main differences lie in the classification of cardiovascular risk and the indications for the use of statins in this patient population. These distinctions can have a significant impact on the percentage of patients for whom statins are recommended, the related costs and the potential benefit obtained.

The main objective of this study is to determine the concordance in the calculated cardiovascular risk between the Framingham, SCORE, Pooled Cohort Equation and "recalibrated" Framingham scales. It also seeks to evaluate the decision to prescribe statins between the AHA/ACC, ESC/EAS, and US Preventive Services Task Force (USPSTF) Recommendation Statement guidelines and the Ministry of Social Protection (MPS, in Spanish) guidelines for managing dyslipidemia in adults in Colombia (CPG), in a cohort of patients with no history of cardiovascular disease seen as outpatients in the internal medicine service of a quaternary care hospital in Bogotá.

Materials and method

An observational, analytical concordance study was conducted. The patients enrolled were those who were seen between January 2019 and January 2021 in the outpatient department of the internal medicine service at Hospital San José in Bogotá, were 40 to 75 years old, with no history of clinical atherosclerotic cardiovascular disease (myocardial infarction, acute coronary syndrome, stable or unstable angina, coronary or peripheral artery revascularization, stroke, transient ischemic attack, and peripheral artery disease including aortic aneurysm, all with an atherosclerotic origin), and who had had a lipid profile taken within the three months prior to the study. Patients who were already on statins, pregnant women, patients on steroids and those with a history of autoimmune disease were excluded.

The patients were assessed by an internal medicine specialist who collected the variables on a predetermined data collection form. The tools used to measure the clinical variables, such as a measuring tape, scale and blood pressure monitor were previously calibrated to avoid measurement errors.

The 10-year cardiovascular risk was calculated for all patients, applying the Pooled Cohort Equation, SCORE system, Framingham scale and recalibrated Framingham scale. The level of cardiovascular risk for the AHA/ACC guidelines was classified as "low risk" (< 5%), "borderline risk" (5 -7.5%), "intermediate risk" (7.6-19.9%), and "high risk" (≥ 20%), according to the Pooled Cohort Equations. For the ESC/EAS guidelines it was classified as "low" (<1%), "moderate" (1-5%), "high risk" if 6-9% and "very high risk" if ≥10%, according to the SCORE score.

The indications for administering statins were determined for each guideline. Three categories were defined in the AHA/ACC guideline: a) an indication for statins for patients with diabetes, LDL cholesterol > 190 mg/dL, and those categorized as "high risk" or "intermediate risk" with an additional risk factor (family history of premature CVD, chronic kidney disease, cholesterol ≥ 160 mg/dL, metabolic syndrome, preeclampsia, premature menopause, psoriasis, human immunodeficiency virus infection, and rheumatoid arthritis) (9); b) no indication for patients with "low risk" and c) an individualized plan in the rest of the patients. Three categories were established for the ESC/EAS guideline: give, do not give, and lifestyle changes, according to the calculated risk and level of LDL cholesterol, as described in the document's annotated tables (6). There were two categories for the USPSTF guideline: a) administer statins in patients with dyslipidemia, diabetes, hypertension, smoking and a risk ≥10% as calculated by the Pooled Cohort Equation; and b) other approaches if the previous conditions were not met (10). The decision was also dichotomous for the Colombian guideline: give statins to patients with diabetes, LDL cholesterol > 190 mg/dL, or a risk ≥10% as calculated by the recalibrated Framingham scale; and do not give statins in the rest of the cases.

The sample size was calculated with 95% confidence (α=0.05), 80% statistical power (β=0.2), and an expected kappa index of 0.6 (12), which resulted in 288 participants. For the statistical analysis, the categorical variables were described as percentages and absolute frequencies, while the continuous variables were described through averages and standard deviation if they were normally distributed, and as medians and interquartile range if they were not normally distributed, which was examined using the Shapiro-Wilk test of normality.

The concordance between the risk scores obtained through the Framingham, recalibrated Framingham, Pooled Cohort Equation and SCORE scales was evaluated using

Lin›s Concordance Correlation Coefficient. The concordance between the different guidelines in deciding to prescribe statins for primary prevention was determined considering the decision categories proposed in each guideline. The kappa index was used as the statistical technique. The analysis was done using STATA 13.0 statistical software.

In this study, the participants› medical charts were reviewed; therefore, according to the Colombian regulations established by the Ministry of Health through Resolution 8430 of 1993, it was considered to be a no-risk study. The study was approved by the Human Research Ethics Committee at Hospital San José, with reference document 0674-2020. Informed consent was not required.

Results

A total of 3,159 patients were screened, 288 of whom were included (Figure 1). The average age was 60.5 ± 9.2 years, 182 (63.2%) were women, 136 (46.2%) were patients with hypertension and 72 (25.0%) were patients with diabetes. Other demographic characteristics are described in Table 1.

Regarding the risk classification, the AHA/ACC guideline classified 45 patients (15.6%) as "high risk" and 91 (31.6%) as "low risk", while the ESC/EAS guideline classified 31 (10.76%) as "very high risk" and 35 (12.15%) as "low risk". The complete classification for these two guidelines can be found in Figure 2.

Among the risk assessment scales, the highest concordance, 0.91, was found between the Framingham and recalibrated Framingham scales, followed by the recalibrated Framingham and SCORE (0.72) and Framingham and ACC/AHA scales (0.67) (Table 2).

Regarding the decision to prescribe statins, the AHA/ACC guideline established the indication in 107 patients (37.5%), the ESC/EAS guideline in 136 (47.22%), the USPSTF guideline in 143 (49.65%), and the Colombian guideline in 132 (45.83%). Statins were not indicated in 65 patients (22.57%) according to the AHA/ACC guideline, 36 (12.50%) according to the ESC/EAS guideline, and 156 (54.17%) according to the Colombian guideline (Table 3).

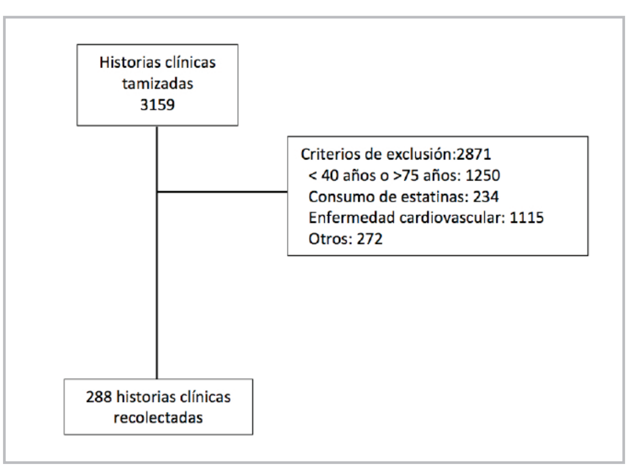

Figure 1. *Screening and decision tree.*

The decision to prescribe statins showed modest concordance, with the highest concordance between the Colombian and USPSTF guidelines (0.607), and the lowest concordance between the AHA/ACC and USPSTF guidelines, at 0.099 (Table 4).

Discussion

The results of this study showed that there is a moderate concordance in the cardiovascular risk score among the evaluated scales, and low to moderate concordance regarding the indication for statins according to the evaluated guidelines, in patients with no previously recorded cardiovascular events.

Over the last few years, various clinical practice guidelines have been created which, while they examine the same clinical studies as evidence, use different cardiovascular risk prediction models, classify the risks differently, present different LDL cholesterol thresholds, and vary in the way they determine the indication for statins (13). Overall, there has

Table 1. *Clinical and demographic characteristics.*

Variable	
Age, median (IQR)	60.5 (14.8)
Gender (f) Nº (%)	182 (63.2)
Weight, median (IQR)	68 (17)
Height, mean (SD)	159.2 (9.0)
Body mass index, median (IQR)	26.6 (6.04)
Race Nº (%)	
White	174 (60.4)
Black	2 (0.78)
Mestizo	111 (38.5)
Other	1 (0.39)
Hypertension, n (%)	133 (46.2)
Diabetes mellitus, n (%)	72 (25.0)
Smoking, n (%)	55 (19.1)
Systolic arterial pressure, median (IQR)	125 (20)
Diastolic arterial pressure, median (IQR)	80 (14)
Mean arterial pressure, median (IQR)	93.3 (14.3)
Total cholesterol, median (IQR)	203 (60)
HDL cholesterol, median (IQR)	45.4 (14)
LDL cholesterol, median (IQR)	122 (52.8)
Triglycerides, median (IQR)	162 (104)
AHA-ACC, median (IQR)	8.5 (13.1)
SCORE, median (IQR)	3 (5)
Framingham, median (IQR)	6 (10)
Modified Framingham, median (IQR)	4.5 (7.5)

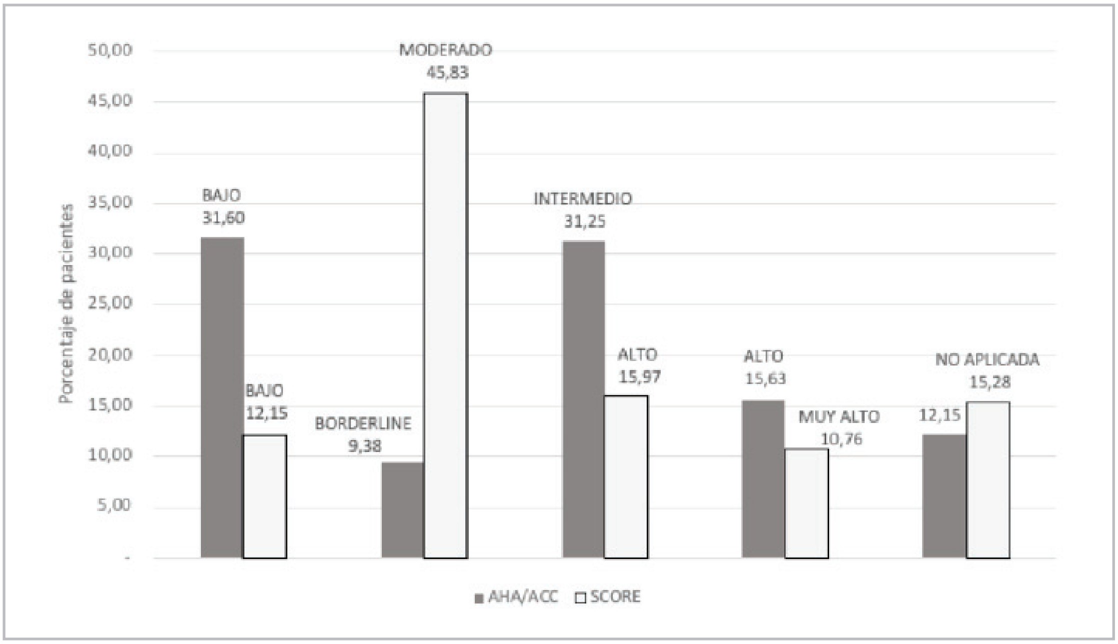

Figure 2. *Risk classification for the ACC/AHA and ESC scales.*
Not applied: refers to patients in whom the cardiovascular risk could not be calculated by the scale; in SCORE, patients over the age of 70, and in the ACC/AHA pooled cohort, due to total cholesterol <130 mg/dL, HDL < 20 mg/dL and LDL < 70 or >190 mg/dL.

Table 2. *Concordance between the risk scales.*

Scale	Lin's Concordance Coefficient			
	ACC - AHA	SCORE	Framingham	Modified Framingham
ACC- AHA	1			
SCORE	0.59, 95%CI (0.529 - 0.660)	1		
Framingham	0.67, 95%CI (0.613 – 0.733)	0.63, 95%CI (0.572 – 0.698)	1	
Modified Framingham	0.53, 95%CI (0.474 – 0.596)	0.72, 95%CI (0.664 – 0.782)	0.91, 95%CI (0.904 – 0.927)	1

been a transition from treatments based on a cardiovascular risk category plus an LDL value to a global approach that considers other cardiovascular conditions that increase the risk, making the approach more comprehensive (12, 14).

One of the most relevant aspects in applying the guideline recommendations is risk stratification using scales that estimate cardiovascular risk, which differ in aspects like the definition of outcomes and their external validity (15). The Framingham scale, SCORE and Pooled Cohort Equation (ACC/AHA) are widely used; however, they do not have an adequate concordance. Pennells et al. recently published a meta-analysis in which they compared these scales, finding significant differences in the median cardiovascular risk scores and the classification of high-risk patients, and proposing a recalibration of the scales, which improves their predictive ability (16). In Colombia, in 2018, Mancera et al. found a moderate concordance (Kappa= 0.47) in patients with high cardiovascular risk between the modified Framingham scale and SCORE, and a weak concordance (Kappa= 0.3497) between the modified Framingham and ACC/AHA 2013 (17). Muñoz et al. also found low concordance between the modified Framingham and SCORE scales (Kappa=0.28 and 0.22) (18). Furthermore, in a concordance study in women with type 2 diabetes, Navarro et al. found low concordance between the Framingham scale and ACC/AHA 2013 (Kappa= 0.3 95%CI 0.18 – 0.43) with age and the cholesterol level having the greatest effect on the variation in the different scales (19). Our results concur more with those of Pennells et al.'s meta-analysis, considering the risk medians established for the evaluated scales, which are highest in the Pooled Cohort Equation (ACC/AHA), followed by the Framingham scale, and lowest for SCORE, with similar differences between them. However, the risk values were higher in our study, considering that the study

Table 3. *Decision to prescribe statins, by treatment guideline.*

AHA/ACC guideline	n (%)
Prescribe (LDL > 190 mg/dL or diabetes mellitus)	90 (31.25)
Prescribe (cardiovascular risk >20%+)	18 (6.25)
Individualize for the patient	105 (36.46)
No indication for statins	65 (22.57)
Clinical guideline not applied	10 (3.47)
ESC/EAS	**n (%)**
Prescribe statins	136 (47.22)
Lifestyle changes and probable statin prescription	88 (30.56)
No indication for statins	36 (12.50)
Clinical guideline not applied	28 (9.72)
Colombian CPGs	**n (%)**
Prescription (LDL > 190 mg/dL or diabetes mellitus)	92 (31.94)
Prescription (cardiovascular risk > 10%*)	40 (13.89)
No indication for statins	156 (54.17)
USPSTF	**n (%)**
Prescription(LDL > 190 mg/dL)	21 (7.29)
Prescription (Cardiovascular risk factors + cardiovascular risk > 10%+)	103 (35.76)
Prescription (Cardiovascular risk factors + cardiovascular risk 7.5 – 10%+)	19 (6.60)
No indication for statins	131 (45.49)
Clinical guideline not applied	14 (4.86)
+ *ACC/AHA Pooled Cohort Scale*. * **Modified** *Framingham*.	

Table 4. *Concordance in the indication for statins according to the guideline studies.*

Guidelines	Kappa value	Standard error	Exact significance
AHA/ACC– ESC/EAS	0.488	0.040	0.000
AHA/ACC – CPG	0.358	0.031	0.000
AHA/ACC – USPSTF	0.099	0.033	0.000
ESC/EAS - CPG	0.367	0.028	0.000
ESC/EAS - USPSTF	0.325	0.029	0.000
CPG - USPSTF	0.607	0.047	0.000

population had a higher proportion of patients with diabetes and HTN, which increases this risk. The slightly different concordance in our study compared to the Colombian studies mentioned may be related to the type of study population. The high concordance between the Framingham and modified Framingham scales is to be expected, as the latter is the Framingham scale itself, adjusted by a calibration factor.

It has also been documented that statin prescription varies according to the recommendations of the different guidelines. Many studies show low concordance between the guidelines in the decision to administer statins (12). Pagidipati et al. showed that the USPSTF guideline identified 16% of the population 40 - 75 years old as having an indication for statins vs. 24% using the AHA/ACC guidelines (20). Likewise, Mortensen et al. documented that 42% of the population was eligible for statin use if the AHA/ACC guideline was used, 31% if the USPSTF guideline was applied, and 15% if the ESC/EAS guidelines was used (21). In Colombia, the study by Muñoz et. al. showed concordance in the indication for the use of statins (Kappa 0.57) comparing the AHA/ACC guideline, which indicated statins for 40.8% of the patients, vs. the Colombian guideline, which indicated statins for 50.7% (18). These results concur with our study, which shows the low concordance of the different guidelines regarding statin indications (kappa index 0.09-0.6). In our study, the USPSTF, Colombian and ESC guidelines identified more patients with an indication for statins compared to the AHA/ACC guideline, contrary to the studies by Pagidipati et al. and Mortensen et al. However, we must remember that, in our study, the AHA/ACC guidelines identified a majority group of patients in whom the decisions needed to be individualized, as there was incomplete data to evaluate the "risk-increasing" factors, a key component of this guideline, and therefore many of these would end up receiving statins. Consequently, this guideline identified the lowest percentage of patients with no indication for statins.

This discussion has important implications for health. On the one hand, using a guideline which finds a greater number of people with an indication for statins may lead to overprescription of these medications with direct cost overruns and the risk of possible adverse reactions (22, 23). On the other hand, identifying more patients with an indication for statins leads to increasing the population which would potentially benefit from this treatment, as documented by Mortensen et al. in their comparison of the different versions of the ESC guidelines, in which the percentage of patients eligible for statins increases from 15.4% (CI:15.1 -15.7%) in the 2016 guidelines to 32.3% (CI 31.8-32.7) with the 2019 guidelines (24, 25). The guidelines have been changing in this regard, mainly since 2014, when the AHA guideline made significant changes that affected the number of patients eligible for statins, especially among those over the age of 60, going from 21- 33% in a study by Echavarría et al., and from 37.5 - 48.6% in one reported by Pencina et al. (26, 27). This debate between cost overruns and potential benefits has different perspectives (28), with degrees of complexity that are difficult to resolve definitively.

This study has some limitations. First, it is a single-center study, which limits its external validity. Second, ambulatory care was restricted during the data collection period due to the epidemiological changes at that time, which may have caused selection bias. Third, the evaluated guidelines were published in 2019 and, considering the data collection period, the primary prevention care the physicians offered these patients may have still been guided by the concepts of previous guidelines. Finally, some risk factors that are important for the AHA/ACC guideline in the criteria for selecting statins, such as CRP and the ankle-brachial index, were not evaluated.

Conclusion

This study showed moderate concordance between the scores of the different risk scales, highlighting the existence of factors that directly affect cardiovascular risk stratification apart from the scales (family history, female sex), which could be the topic of future studies. The concordance between the evaluated guidelines in the indication for statins was low.

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