Comparison of application of 2013 ACC/AHA guideline and 2011 European Society of Cardiology guideline for the management of dyslipidemias for primary prevention in a Turkish cohort

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ABSTRACT

Objective: Atherosclerotic cardiovascular disease is a major global cause of death. The common approach in primary prevention of cardiovascular disease is to identify patients at high risk for cardiovascular disease. This article analyzes and compares the application of 2013 American College of Cardiology/American Heart Association (ACC/AHA) guideline and the 2011 European Society of Cardiology (ESC) guideline for the management of dyslipidemias for primary prevention in Turkish population.

Methods: The study included 833 patients (482 women and 351 men). Risk scores were calculated according to both guidelines and indications for statin treatment were determined according to sex and age group. Variables are presented as mean±SD or median with interquartile range for continuous data and as proportions for categorical data. Variables were analyzed by unpaired t-test, Mann-Whitney U test, chi-square or Fischer’s exact test as appropriate.

Results: The ACC/AHA would suggest statin treatment in 415 patients out of 833 (49.5%), while ESC would recommend statin for 193 patients out of 833 (23.1%) (p<0.001). Statins would be recommended for 40.4% of women and 62.6% of men for primary prevention by the ACC/AHA, while this figure was 12% for women and 38.4% for men according to the ESC guideline (p<0.001 for both).

Conclusion: When compared to the ESC guideline, the ACC/AHA guideline suggests augmented statin treatment for primary prevention in Turkish population. (Anatol J Cardiol 2017; 17: 92-6)

Keywords: guidelines, preventive cardiology, statins, dyslipidemias

Introduction

Atherosclerotic cardiovascular disease (ASCVD) is a major global cause of death (1, 2). Yet prevention of this disorder remains suboptimal. The purpose of primary prevention is to detect individuals who have high enough risk for cardiovascular events to warrant targeting them with intensive interventions that not only involve changes in lifestyle, but pharmacological approaches as well.

Risk prediction models should have good discrimination power to be clinically meaningful. Numerous algorithms use combinations of conventional risk factors to identify individuals at higher risk for cardiovascular disease (CVD) who are most likely to benefit from preventive measures (3, 4). Both the American College of Cardiology/American Heart Association (ACC/AHA) and the European Society of Cardiology (ESC) develop and continuously update their guidelines in order to influence clinical practice. These guidelines use varying approaches to CVD risk estimation and implement different criteria for therapeutic recommendations. ESC advocates the use of the Systematic Coronary Risk Evaluation (SCORE) equation for individuals aged between 40 and 65 years. According to the ESC guideline, if the estimated 10-year risk of ASCVD ≥5% and low-density lipoprotein (LDL) cholesterol level ≥100 mg/dL, or the estimated 10-year risk of ASCVD≥10% and LDL cholesterol level ≥70 mg/dL, initiation of a statin treatment is recommended for primary prevention (5). Meanwhile, the ACC/AHA developed cardiovascular risk calculator targeting individuals between 40 and 75 years of age. According to the ACC/AHA guideline, if the estimated 10-year risk of ASCVD ≥7.5% or primary LDL cholesterol level ≥189 mg/dL, initiation of a statin treatment is recommended for primary prevention (6). Different approaches to statin treatment translate
into substantial differences with respect to population qualifying for treatment, economic burden and health systems. This study is a comparison of the ACC/AHA guideline with the ESC guideline for initiation of statin treatment for primary prevention of ASCVD in the Turkish population.

**Methods**

**Study design**

All consecutive patients aged between 40–75 years admitted to Başkent University Ankara hospital on an outpatient basis between December 2013 and April 2014 were evaluated for possible enrollment in the study. The research was conducted in accordance with the Second Helsinki Declaration and was approved by the Local Ethics Committee. Patients without sufficient data in the records to calculate risk score, patients who had statin treatment indications for secondary prevention (presence of coronary artery disease, peripheral arterial disease, cerebrovascular disease, or diabetes mellitus) were excluded.

The records of 4533 patients were examined, 3700 patients were excluded from study, and the scores of 833 patients (482 women and 351 men) were calculated (Fig. 1). Patients were divided into 2 groups according to sex. Within each gender group, patients were subdivided into 4 groups according to age (40–49 years, 50–59 years, 60–69 years, and 70–75 years). Risk scores were calculated according to both guidelines and indication for immediate statin treatment was determined. If 10-year score risk of ASCVD ≥5% and LDL cholesterol level ≥100 mg/dL, or the estimated 10-year score risk of ASCVD ≥10% and LDL cholesterol level ≥70 mg/dL, ESC recommends initiation of immediate statin treatment for primary prevention in individuals 40 to 65 years of age (5). In the presence of the same other risk factors, the score risk of patients over the age of 65 was the same as those with the age of 65. We used high-risk version of the SCORE scale in this study.

ACC/AHA targeted individuals aged between 40 and 75 years. According to the ACC/AHA guideline, if the estimated 10-year risk of ASCVD ≥7.5% or primary LDL cholesterol level ≥189 mg/dL, initiation of an immediate statin treatment is recommended (6).

**Statistical analyses**

Variables are presented as mean±SD or median (range, interquartile range [IQR]) for continuous data and as proportion for categorical data. Continuous variables with normal distribution were analyzed with unpaired t-test. Continuous variables with non-normal distribution were analyzed using Mann-Whitney U test. Kolmogorov-Smirnov test was used to identify whether continuous variables were normally distributed. Categorical parameters were analyzed with chi-square or Fischer’s exact test, as appropriate. Two-sided p values <0.05 were considered significant. Statistical analysis was performed using commercially available computer program (SPSS version 21.0 for Windows; SPSS, Inc., Chicago, Illinois, US).

**Results**

We evaluated 833 patients (482 women and 351 men). Baseline characteristics of the participants are presented in Table 1. When ACC/AHA risk score was considered, 415 patients out of 833 (49.5%) were eligible for statin treatment, while this figure was 193 patients (23.1%) for the ESC SCORE system (p<0.001). We found that statins would be recommended for primary prevention for 40.4% of women and 62.6% of men by the ACC/AHA, while this was 12% for women and 38.4% for men under the ESC guideline (p<0.001 for both).

Based on ACC/AHA ASCVD risk score, median risk was 7.4% (0–48.6; IQR=9.8) for the overall study population (Fig. 2). Twenty-six patients would be eligible for statin treatment based on LDL cholesterol over 189 mg/dL. There were 389 patients whose risk was ≥7.5% (median=13.3; 7.5–48.6; IQR=10.25), thus qualifying for statin treatment according to ACC/AHA guideline. Table 2 shows the number of individuals qualifying for statin treatment stratified by empiric 5-point increase in risk.

According to the ESC, median risk score for our population was 2% (0–33; IQR=3) (Fig. 3). Fifty-two patients qualified for statin treatment based on score risk of ≥5% and LDL cholesterol
≥100 mg/dL. The total was 141 patients when risk score ≥10 and LDL cholesterol ≥70 mg/dL were considered.

There were also significant differences between the 2 guidelines for 50–59 years and 60–69 years groups of female patients (p<0.001 for both). There were no statistically significant differences in 40–49 years and ≥70 years groups (p=0.341 and p=0.634, respectively). There were significant differences in 40–49 years and 50–59 years groups in male patients. There were no statistically significant differences in 60–69 years and ≥70 years groups in men (p=0.065 and p=0.99, respectively) (Table 3).

Discussion

In this study, it was observed that compared with the ESC guideline, the ACC/AHA guideline would augment the number of individuals requiring statin treatment for primary prevention of cardiovascular disorders. ACC/AHA guideline would recommend statins for almost all male patients and more than 70% of female patients age 70 years and over for primary prevention.

There are no considerable differences between the ACC/AHA guideline (6) and the ESC guideline with respect to recommendations for statin use in secondary prevention (5). Selection of patients and determination of indications for statin use in primary prevention is a source of great debate. Different risk prediction systems exist for determination of patients at risk in primary prevention. The most commonly used scoring systems are the risk scoring tools of the ACC/AHA guideline and the ESC guideline SCORE risk system. For primary CVD prevention, based on the evidence from clinical trials of statin drugs, the new ACC/AHA guideline modified clinical decision-making and proposed recommending statin treatment solely based on a 10-year ASCVD risk greater than 7.5% (6). This distinction from previous guidelines in the United States and from current ESC guideline represents a fairly straightforward approach that deviates from risk functions of 10-year hard coronary heart disease (CHD) or CVD mortality combined with blood concentrations of LDL cholesterol (5, 7, 8).

Table 1. Characteristics of the study population

| Gender | Women (n=482) | Men (n=351) |
|--------|---------------|-------------|
| Age, years | 58.1±9.3 | 55.3±9.2 |
| Systolic blood pressure, mm Hg | 142±24 | 145±26 |
| Diastolic blood pressure, mm Hg | 73±11 | 75±13 |
| Antihypertensive treatment, n (%) | 303 (62.9) | 188 (53.6) |
| Current smoking, n (%) | 70 (14.5) | 93 (26.5) |
| Chronic kidney disease, n (%) | 2 (0.4) | 2 (0.6) |
| Total cholesterol, mg/dL | 225±42 | 215±38.4 |
| HDL cholesterol, mg/dL | 51.5±10.9 | 45.4±9.01 |
| LDL cholesterol, mg/dL | 144±36.1 | 137.7±31.5 |
| TG, mg/dL* | 125 (93–165) | 140 (102–193) |

*Data expressed as median with interquartile range. HDL - high-density lipoprotein; LDL - low-density lipoprotein; TG - triglyceride

Table 2. Subjects qualifying for statin treatment based on ACC/AHA risk level

| Stratified risk level* | Patients n, (%) |
|-----------------------|-----------------|
| 7.5–12.4 | 177 (42.6) |
| 12.5–17.4 | 86 (20.7) |
| 17.5–22.4 | 59 (14.2) |
| ≥22.5 | 67 (16.1) |
| 26 (6)** |

*Five-point increase in the risk was chosen empirically for stratification. **Patients with LDL cholesterol >189 mg/dL. ACC/AHA - American College of Cardiology/American Heart Association; LDL - low-density lipoprotein

Figure 2. The ACC/AHA calculated risk for the study population (n=833). X-axis represents percentage of risk

Figure 3. The ESC calculated score risk for the study population (n=833). X-axis represents percentage of risk

Figure 2. The ACC/AHA calculated risk for the study population (n=833). X-axis represents percentage of risk of individuals requiring statin treatment for primary prevention of cardiovascular disorders. ACC/AHA guideline would recommend statins for almost all male patients and more than 70% of female patients age 70 years and over for primary prevention.

There are no considerable differences between the ACC/AHA guideline (6) and the ESC guideline with respect to recommendations for statin use in secondary prevention (5). Selection of patients and determination of indications for statin use in primary prevention is a source of great debate. Different risk prediction systems exist for determination of patients at risk in primary prevention. The most commonly used scoring systems are the ACC/AHA guideline and the ESC guideline SCORE risk system. For primary CVD prevention, based on the evidence from clinical trials of statin drugs, the new ACC/AHA guideline modified clinical decision-making and proposed recommending statin treatment solely based on a 10-year ASCVD risk greater than 7.5% (6). This distinction from previous guidelines in the United States and from current ESC guideline represents a fairly straightforward approach that deviates from risk functions of 10-year hard coronary heart disease (CHD) or CVD mortality combined with blood concentrations of LDL cholesterol (5, 7, 8).
Usability of a risk prediction system depends on combination of its calibration and discrimination (9). Proper calibration of a risk prediction system is crucial when it is used to make a decision whether a treatment is to be initiated (9). An inaccurate risk prediction system may not only fail to correctly determine patients truly at risk, but may also lead to possible drug complications and unnecessary cost through improper patient selection. Kavousi et al. (8) showed that the 3 risk prediction systems (the ACC/AHA guideline, the National Cholesterol Education Program Adult Treatment Panel III, and the ESC guideline) provided poor calibration and moderate discrimination. This study showed that compared with the ESC guideline, the ACC/AHA guideline would increase the number of patients eligible for statins for primary and secondary prevention of cardiovascular disorders from 66.1% to 96.4% in male patients and from 39.1% to 65.8% in female patients in the European cohort (8). Additionally, this study showed that the c-statistics values of the 3 risk prediction systems were not considerably different, although the ESC guideline’s risk prediction system still had the relatively highest value (8). Similarly, Vaucher et al. (10) concluded that, relative to the ESC guideline, the ACC/AHA guideline leads to a considerable increase in the number of high-risk individuals for whom statin treatment would be recommended: 2.2 times more male patients and 1.9 times more female patients in Switzerland. Taylor et al. (11) and Mihaylova et al. (12) also reported in separate studies that the ACC/AHA guideline has a lower cut-off level for treatment. In the present study, when compared to the ESC guideline, the ACC/AHA would increase the number of individuals qualifying for statin treatment about 1.6 times in male patients and 3.36 times in female patients for primary prevention. Our study further strengthens previous findings and showed that no women aged below 60 years would be qualified for statin treatment by the ESC guideline. Similarly, the Swiss data from Vaucher et al. (10) disclosed that no women below 60 years of age required statin treatment when the ESC guideline was observed.

Table 3. Statin treatment recommendations of guidelines for different age and sex groups

| Age, years | Male | Female | Total |
|-----------|------|--------|-------|
|           | ESC  | ACC/AHA | P     | ESC  | ACC/AHA | P     | ESC  | ACC/AHA | P     |
| 40–49 (n=232) | 4 (1.7) | 17 (7.3) | 0.016 | 0 (0) | 6 (2.5) | 0.341 | 4 (1.7) | 17 (7.3) | 0.016 |
| 50–59 (n=304) | 46 (15.1) | 81 (26.6) | <0.001 | 0 (0) | 39 (12.8) | <0.001 | 46 (15.1) | 81 (26.6) | <0.001 |
| 60–69 (n=221) | 67 (30.3) | 87 (39.3) | 0.065 | 38 (17.1) | 94 (42.5) | <0.001 | 105 (47.5) | 181 (81.9) | <0.001 |
| ≥70 (n=76) | 18 (23.6) | 19 (25) | 0.99 | 20 (26.3) | 56 (73.6) | 0.634 | 38 (50) | 75 (98.6) | 0.484 |

ACC/AHA - American College of Cardiology/American Heart Association; ESC - European Society of Cardiology

There are some limitations to the present study. First, our study was not a follow-up study and it did not study calibration and discrimination of the guidelines in a Turkish population. Second, cost analysis of both guidelines was not possible due to incomplete study data. Third, it solely enrolled patients presenting at an outpatient clinic of a tertiary university hospital. Thus, the study population does not necessarily reflect the general Turkish population.

**Conflict of interest:** None declared.

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