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Predictive Value of the SCORE, SCORE2, and Pooled Cohort Risk Equation Systems in Patients with Hypertension

Hipertansiyon Hastalarında SCORE, SCORE2 ve Pooled Kohort Risk Değerlendirme Sistemlerinin Prediktif Değeri

ABSTRACT

Objective: The objective of this study is to assess and compare the accuracy of old and new versions of the European Society of Cardiology Systematic Coronary Risk Evaluation (SCORE and SCORE2) American Heart Association/American College of Cardiology Pooled Cohort Risk Assessment Evaluation (PCE) in predicting long-term cardiovascular events in patients with hypertension.

Methods: This retrospective study consisted of 788 patients diagnosed with hypertension between 2009 and 2018. The absolute risk for 10-year cardiovascular events was calculated with SCORE, SCORE2, SCORE-OP, and PCE systems based on patients' data obtained on the date of hypertension diagnosis. The study group was followed for the occurrence of major adverse cardiac and cerebrovascular events. The differences between observed and predicted risk calculated using SCORE, SCORE2, and PCE systems and their prognostic value were assessed.

Results: The mean age of the 788 patients included in the study, of whom 426 (54.1%) were female, was 54 ± 9 years. During a mean follow-up of 6 years, 173 (22.0%) patients experienced a major adverse cardiac and cerebrovascular event. In predicting the occurrence of major adverse cardiac and cerebrovascular events in hypertension patients over the long-term, PCE had a predictive power comparable and slightly superior to "SCORE2—SCORE-OP (AUC 0.732 vs. 0.724, respectively)" whereas SCORE (AUC 0.689) was inferior to "SCORE2–SCORE-OP."

Conclusion: In this study, the Pooled Cohort Risk Assessment Equation risk-scoring system was superior to the old and new versions of Systematic Coronary Risk Evaluation risk system in predicting the cardiovascular and cerebrovascular events that developed in patients with hypertension.

Keywords: Arterial hypertension, cardiac and cerebrovascular events, cardiovascular risk scores, PCE, SCORE

ÖZET

Amaç: Bu çalışmanın amacı, Avrupa Kardiyoloji Derneği Sistematik Koroner Risk Değerlendirmesinin eski ve yeni versiyonlarının (SCORE ve SCORE2) ile American Heart Association/American College of Cardiology Pooled Cohort Risk Değerlendirme Denklemi'nin (PCE), hipertansiyonu (HT) olan hastalarda uzun vadeli kardiyovasküler olayları tahmin etmede doğruluğunu değerlendirmek ve karşılaştırmaktır.

Yöntem: Bu retrospektif çalışmaya, 2009-2018 yılları arasında HT tanısı alan 788 hasta alındı. HT teşhisi tarihinde elde edilen hasta verilerine dayalı 10 yıllık kardiyovasküler olay mutlak riski SCORE, SCORE2, SCORE-OP ve PCE sistemleri ile hesaplandı. Çalışma grubu, major advers kardiyak ve serebrovasküler olayların (MACCE) oluşumu açısından takip edildi. SCORE, SCORE2 ve PCE sistemleri kullanılarak hesaplanan skorlara göre; gözlenen ve tahmin edilen risk arasındaki farklar ve bunların prognostik gücü değerlendirildi.

Bulgular: Çalışmaya dahil edilen 426'sı (%54,1) kadın, 788 hastanın yaş ortalaması 54 ± 9 idi. Bu hastalardan ortalama 6 yıllık takipte 173'ünde (%22.0) MACCE gelişti. Uzun vadede HT hastalarında MACCE oluşumunu saptamada PCE, "ESC SCORE2–SCORE-OP" ile karşılaştırılabilir ve hafifçe üstün (AUC 0.732'ye karşı AUC 0.724) bir tahmin gücüne sahipken; SCORE ise daha düşük bir tahmin gücüne (AUC 0.689) sahipti.

Sonuç: Bu çalışmada PCE risk skorlama sistemi, HT'li hastalarda gelişen kardiyovasküler ve serebrovasküler olayları öngörmede SCORE risk sisteminin eski ve yeni versiyonlarına göre daha üstündü.

Anahtar Kelimeler: Arteriyel hipertansiyon, kardiyak ve serebrovasküler olaylar, kardiyovasküler risk skorları, PCE, SCORE

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

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Hypertension (HT) is the most prevalent chronic disease in the world and carries a high risk for cardiovascular morbidity and mortality.[1] In patients with HT, the initial approach in primary prevention includes assessment of the global cardiovascular disease risk and management strategy is determined based on the calculated risk.[2-5] Various studies demonstrated the effectiveness and benefits of risk-scoring systems in assessing the risks for major adverse cardiac and cerebrovascular events (MACCE).[6,7] Nonetheless, risk-scoring systems do not produce equally effective results for different patient groups, ethnicities, and countries. Therefore, studies with long-term follow-ups are required to evaluate the prognostic value of different risk-scoring systems in different patient groups.[8]

American Heart Association/American College of Cardiology Pooled Cohort Risk Equation (AMA/ACC PCE), previously European Society of Cardiology Systematic Coronary Risk Evaluation (SCORE), currently SCORE2 and SCORE-OP systems, are the most frequently used risk-scoring systems to assess 10-year absolute global cardiovascular risk.[6,7] After a major change in the 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice, the SCORE2 and SCORE-OP systems were recommended to calculate the risk of both fatal and non-fatal cardiovascular events, as opposed to the former SCORE system that estimated the risk of fatal cardiovascular events only.[6] Before 2021, risk assessment of patients over the age of 69 could not be performed with ESC SCORE, however, with the introduction of the 2021 guidelines, risk assessment in these age groups has begun using the SCORE2-SCORE-OP method.[6] The objective of this study is to evaluate and compare the prognostic value of PCE, SCORE, and SCORE2–SCORE-OP models in predicting long-term cardiovascular events in patients with HT.

Material and Methods

Study Design

The sample of this retrospectively designed study consisted of 788 patients diagnosed with HT between 2009 and 2018. Patients with a history of coronary artery disease (CAD) and cerebrovascular disease were excluded from the study. We also excluded patients <40 years of age or >80 years of age. On the other hand, the fact that diabetic patients and patients who have been using statins were not excluded from this study unlike large cohort studies might be deemed a strength of this study over other comparable studies available in the literature. There were no research termination criteria other than reaching the planned number of volunteers.

The study protocol was approved by the Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Clinical Research Ethics Committee (Approval number: KAEK/2019-02, Approval Date: 08/01/2019). Necessary permissions were obtained from the hospital management to conduct the study. The authors met the ethical standards in the Helsinki Declaration of 1975, as revised in 2000, as well as the national law.

Patients' demographic and clinical characteristics including history of diabetes, HT, dyslipidemia, smoking habits, cardiovascular medications, results of their ambulatory blood pressure (BP) monitoring measurements, hematological and biochemical measurements, and their echocardiographic parameters were obtained from the hospital's electronic medical records system and archive files.

Blood Pressure Measurements and Hypertension Diagnosis

Systolic and diastolic BPs were measured from the right arm by a trained healthcare professional using a calibrated device, while patients were in a sitting position. Blood pressure measurements were repeated once in patients with BP >140/90 mmHg, whereas twice in cases where deemed necessary, and the average of these measurements was taken. A 24-hour Holter BP measurement was performed in all patients. Patients who have been using antihypertensive medications and with mean daytime (or awake) BP ≥135 mmHg and/or ≥85 mmHg, mean nighttime (or asleep) BP ≥120 mmHg and/or ≥70 mmHg, mean 24-hour BP ≥130 mmHg and/or ≥80 mmHg based on 24-hour ambulatory BP monitoring were considered hypertensive.[9] Blood pressure has a stable circadian pattern that is 10%-20% lower at night than during the day owing to endogenous neuroendocrine oscillations and other factors.[10] Dipper HT is defined as a reduction in systolic and diastolic BPs of more than 10% from day to night. Non-dipper HT is defined as a reduction in systolic and diastolic BPs of less than 10%.[11] Moreover, patients with reverse dipper HT are described as having higher nighttime BP averages than day BP averages.[12] Resistant hypertension (RH) is defined by the 2018 American Heart Association (AHA) guidelines as the BP of a hypertensive patient that remains above goal despite concurrent use of 3 or more anti-hypertensive agents of different classes administered at maximally tolerated doses and appropriate dosing frequency.[13]

Laboratory Tests

Blood samples were taken from all patients on admission to the outpatient clinic. Blood chemistry tests and lipid parameters were measured using a Roche Cobas 8000 C502 autoanalyzer system (Roche Diagnostics, Indianapolis, Ind, USA). Total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride levels were

ABBREVIATIONS

AC	American College of Cardiology
AHA	American Heart Association
AMA	American Heart Association
CAD	Coronary artery disease
ECG	Electrocardiography
eGFR	Estimated glomerular filtration rate
HDL-C	High-density lipoprotein cholesterol
HT	Hypertension
IVS	Interventricular septum
LDL-C	Low-density lipoprotein cholesterol
LVEDd	Left ventricular enddiastolic diameter
LVEF	Left ventricular ejection fraction
LVESd	Left ventricular end-systolic diameter
MACCE	Major adverse cardiac and cerebrovascular events
PCE	Pooled Cohort Risk Equation
PWD	Posterior wall thickness
RH	Resistant hypertension
SCORE	Systematic Coronary Risk Evaluation
TIA	Transient ischemic attack

calculated by direct measurement method.[3] In patients receiving lipid-lowering therapy, pre-treatment total cholesterol and LDL-C values were estimated based on the post-treatment values and the expected tapering in the respective drug dosage, as described earlier (http://www.fda.gov/Drugs/DrugSafety, e.g., if 20 mg simvastatin is expected to reduce LDL-cholesterol by 38%, basal LDL-C is obtained by dividing the post-treatment value by 0.62).[14]

The estimated glomerular filtration rate (eGFR) was calculated using the GFR equation of Modification of Diet in Renal Disease (MDRD) Study. Hematological tests were carried out using Mindray BC-6000 (Shanghai International Holding Corp. GmbH, Hamburg, Germany).

Twelve-lead electrocardiography (ECG) was performed at a speed of 25 mm/s, height of 10 mm/mV, and filter range of 0.16-100 Hz in all patients, while they were at rest in the supine position, using a 12-lead ECG device (Nihon Kohden, Tokyo, Japan). The patients' heart rates were evaluated on ECG.

Transthoracic echocardiography was performed by 2 experienced cardiologists on all patients using a Philips HD 11 XE ultrasound machine (Andover, MA, USA). The parameters measured within the scope of transthoracic echocardiography included left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDd), left ventricular end-systolic diameter (LVESd), interventricular septum (IVS), and posterior wall thickness (PWD). All echocardiographic measurements were performed according to the guidelines set forth by the American Society of Echocardiography.[15]

Major Adverse Cardiovascular and Cerebrovascular Events During Follow-up

The follow-up data were obtained from the hospital records or through phone interviews conducted with the patients, their relatives, or family physicians. Major adverse cardiovascular and cerebrovascular events consisted of CAD, stroke, transient ischemic attack (TIA), and cardiovascular death that occurred during the follow-up period.

Coronary artery disease was diagnosed based on the presence of a ≥50% occlusive plaque in the coronary arteries after diagnostic coronary angiography, fatal or non-fatal acute coronary syndrome, sudden cardiac arrest, or ischemia in non-invasive stress tests.[16]

Cerebrovascular disease diagnosis was made based on the presence of intracranial hemorrhage, TIA, and stroke in long-term follow-up.[17] Since our study is a retrospective study, diagnoses of TIA and stroke were obtained from the medical history of the patients and the control examinations of the patients.

Cardiovascular Risk Models

Risk scores of the patients were obtained through online calculation links (https://www.heartscore.org and https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/).[6]

Absolute 10-year cardiovascular event risk was calculated using the SCORE, SCORE2, SCORE-OP, and PCE risk-scoring systems based on patients' data obtained at the time of HT diagnosis. The optimal cutoff values of these risk-scoring systems in predicting long-term cardiovascular events in HT patients were determined by ROC analysis, and their efficacies were compared.

Statistical Analysis

Statistical analyses were carried out using the SPSS 24.0 (Statistical Product and Service Solutions for Windows, Version 24.0, IBM Corp., Armonk, NY, USA, 2016) software package. The normal distribution characteristics of continuous variables were assessed using visual (histograms, probability curves) and analytical methods (Kolmogorov–Smirnov and Shapiro–Wilk tests). Numerical variables with and without normal distribution were expressed as mean ± SD values and median (interquartile range) values, respectively. Categorical variables were expressed as percentage (%) values. Statistical analyses of numerical variables such as the risk ratios between independent groups were carried out using student's *t*-test or Mann–Whitney *U* test, whereas the statistical analyses of categorical variables were carried out using Pearson's chi-squared test. The efficacies of the models used by risk-scoring systems in predicting MACCE during the long-term follow-up were compared with the multiple logistic regression analysis (stepwise backward elimination). The variables which were found to be significant ($P < 0.2$) in the univariate analysis were further analyzed using the multivariate model.[18] The correlations between the risk ratios obtained using the risk-scoring systems and other variables were analyzed by Spearman's correlation analysis. The predictive values of the risk ratios in predicting MACCE during long-term follow-up were determined by ROC analysis. Probability (*P*) statistics of <0.05 were deemed to indicate statistical significance.

Results

The study group consisted of 788 patients [426 (54.1%) female, mean age 54 ± 9 years], of whom 173 (22.0%) experienced MACCE during a mean follow-up duration of 5.9 ± 1.3 years. Coronary artery disease was diagnosed in 149 (18.9%) patients: 130 (87%) had a history of acute coronary syndrome (ACS); 19 (13%) had chronic coronary syndrome (CCS); 32 (4.1%) patients had stroke; 14 (1.8%) patients had TIA; and 7 (0.9%) patients died. The patients were divided into 2 groups based on the occurrence of MACCE.

The distribution of the demographic characteristics of the patients by the MACCE groups is shown in Table 1. There was no significant difference between the two groups in mean body mass index and rates of patients with smoking and alcohol consumption (Table 1). On the other hand, the mean age, percentage of male patients, and hyperlipidemia (HL) were significantly more frequent in the MACCE (+) group (Table 1). There was no significant difference between the groups in terms of antihypertensive drug use, except for calcium channel blockers and beta blockers, which were used more frequently in the MACCE (+) group (Table 1). Additionally, the use of acetylsalicylic acid (ASA) and statin was significantly higher in the MACCE (+) group (Table 1). Left ventricular ejection fraction was significantly lower, whereas LVESd, IVS, and PWD were significantly higher in the MACCE (+) group. Twenty-four-hour SBP and DBP, daytime SBP, and nighttime SBP and DBP values, as well as reverse dipper HT, resistant HT and isolated systolic HT ratios, were significantly higher in the MACCE (+) group (Table 1).

Table 1. Demographic Characteristics of Hypertensive Patients According to the Presence of MACCE

n=788	MACCE (–) (n=615)	MACCE (+) (n=173)	*P*
Age (years) (mean ± SD)	52.51 ± 8.78	57.69 ± 9.00	**<0.001**
Gender (male), n (%)	271 (44.1)	91 (52.6)	0.047
Body mass index, (kg/m²) (mean ± SD)	30.55 ± 4.99	30.55 ± 4.60	0.998
Smoking, n (%)	80 (13.0)	32 (18.5)	0.068
Alcohol, n (%)	19 (3.1)	9 (5.2)	0.185
Diabetes mellitus, n (%)	94 (15.3)	59 (34.1)	**<0.001**
Hyperlipidemia, n (%)	287 (46.7)	99 (57.2)	0.007
Blood pressure medication, n (%)	290 (47.2)	94 (54.3)	0.294
ACEi or ARB, n (%)	259 (42.1)	79 (45.7)	0.923
Calcium channel blocker, n (%)	146 (23.7)	62 (35.8)	**<0.001**
Beta-blocker, n (%)	111 (18.0)	56 (32.4)	0.007
Diuretic, n (%)	186 (30.2)	67 (38.7)	0.087
Acetylsalicylic acid, n (%)	54 (8.8)	42 (24.3)	**<0.001**
Statin, n (%)	30 (4.9)	29 (16.8)	**<0.001**
Hemoglobin, g/dL (mean ± SD)	13.80 ± 1.63	13.89 ± 1.70	0.538
Leukocyte, 10^3/ uL (mean ± SD)	7.59 ± 1.87	8.00 ± 2.06	**0.017**
Platelet, 10^3/ uL (mean ± SD)	267.6 ± 73.0	263.2 ± 66.5	0.483
Creatinine, mg/dL (mean ± SD)	0.80 ± 0.20	0.86 ± 0.23	**<0.001**
Glucose, mg/dL	98 (91-109)	107 (95-138)	**<0.001**
LDL-C, mg/dL (mean ± SD)	129.9 ± 36.6	131.6 ± 35.8	0.609
HDL-C, mg/dL (mean ± SD)	47.8 ± 13.6	44.1 ± 10.6	**0.002**
Total cholesterol, mg/dL (mean ± SD)	203.7 ± 41.8	208.1 ± 41.0	0.251
Triglyceride, mg/dL	133 (98-189)	159 (119-245)	**<0.001**
C-reactive protein, mg/L	2.8 (1.4-6.0)	3.7 (1.9-6.1)	0.141
Uric acid, mg/dL (mean ± SD)	5.34 ± 1.40	5.78 ± 1.39	**0.002**
LVEF,% (mean ± SD)	63.68 ± 4.12	61.99 ± 4.09	**<0.001**
LVEDd, mm (mean ± SD)	47.19 ± 4.24	47.63 ± 4.77	0.275
LVESd, mm (mean ± SD)	28.13 ± 4.04	30.03 ± 4.06	**0.016**
IVS, mm (mean ± SD)	11.09 ± 1.82	11.99 ± 2.41	**<0.001**
PWD, mm (mean ± SD)	10.30 ± 1.47	10.82 ± 1.79	**<0.001**
Heart rate, beats/min (mean ± SD)	75.45 ± 13.40	75.30 ± 14.23	0.919
24 hours SBP, mmHg (mean ± SD)	142.7 ± 17.4	149.9 ± 16.6	**<0.001**
24 hours DBP, mmHg (mean ± SD)	88.8 ± 11.9	90.9 ± 12.1	**0.045**
Daytime SBP, mmHg (mean ± SD)	144.8 ± 17.5	151.5 ± 16.9	**<0.001**
Daytime DBP, mmHg (mean ± SD)	91.1 ± 12.2	92.8 ± 12.5	0.112
Night SBP, mmHg (mean ± SD)	135.7 ± 19.4	143.9 ± 18.5	**<0.001**
Night DBP, mmHg (mean ± SD)	81.7 ± 12.6	84.2 ± 12.7	**0.024**
Non-dipper HT, n (%)	394 (64)	117 (67.6)	0.321
Reverse dipper HT, n (%)	94 (15.2)	43 (24.8)	**0.003**
Resistant HT, n (%)	87 (14.2)	48 (28.1)	**<0.001**
Isolated systolic HT, n (%)	34 (5.6)	18 (10.4)	**0.019**

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HT, hypertension; IVS, interventricular septum; LDL-C, low-density lipoprotein cholesterol; LVEDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESd, left ventricular end-systolic diameter; MACCE, major adverse cardiovascular and cerebrovascular event; PWD, diastolic posterior wall thickness; SBP, systolic blood pressure.
Statistically, values below $P < 0.05$ are indicated in bold in the text.

The distribution of hypertensive patients' risk scores calculated from the ESC and ACC/AHA risk-scoring systems by the MACCE groups is shown in Table 2. All risk ratios were significantly higher in the MACCE (+) group than in the MACCE (–) group. Although all 3 models were found to be significant in predicting the occurrence of MACCE –2 Log likelihood value was lower, whereas Cox&Snell R2 and Nagelkerke R^2 values were higher in the PCE model. Therefore, it was concluded that the PCE model was superior to the SCORE model in predicting the occurrence of MACCE [3.50% value for the ESC risk-scoring system and 9.45% value for the ACC/AHA risk-scoring system (P=0.001)].

The distribution of patients' risk groups determined using the SCORE and PCE risk-scoring systems by the MACCE groups is

Table 2. The Distribution of Hypertensive Patients' Risk Scores Obtained from the ESC and ACC/AHA Risk-Scoring Systems by the MACCE Groups

	Study Sample (n=788)		
Risk-Scoring Systems	MACCE (–) (n=615)	MACCE (+) (n=173)	*P*
PCE, %	5.8 (2.7-11.2)	13.3 (7.3-24.3)	**<0.001**
SCORE, %	2.0 (1.0-4.0)	4.0 (2.0-7.0)	**<0.001**
SCORE2 and SCORE-OP, %	4.0 (2.5-8.0)	9.50 (5.0-15.0)	**<0.001**

ACC/AHA, American College of Cardiology/American Heart Association; ESC, European Society of Cardiology; MACCE, major adverse cardiovascular and cerebrovascular event; n, number; PCE, Pooled Cohort Risk Assessment Equation; SCORE, Systemic Coronary Risk Evaluation.

shown in Table 3. Receiver operating characteristic (ROC) curves created using the risk ratios obtained from the ESC SCORE, ACC AHA PCE, and SCORE2–SCORE OP are shown in Figure 1. Receiver operating characteristic curves were developed using the risk scores calculated from the SCORE, SCORE2–SCORE-OP, and PCE risk-scoring systems to detect the presence of CAD, stroke, TIA, and MACCE. In comparison of their accuracy in predicting MACCE, PCE risk-scoring system had a higher predictive value than SCORE in all endpoints (AUC: 0.688 vs. 0.724 for CAD, 0.662 vs. 0.714 for stroke, 0.690 vs. 0.757 for TIA, and 0.689 vs. 0.732 for MACCE) (Table 4 and Figure 1). The optimal predictive values for the PCE, SCORE and SCORE2-SCORE-OP systems in predicting MACCE in HT patients during the follow-up period were determined as 9.45% (69.4% sensitivity and 68% specificity) 3.50% (58.7% sensitivity and 72.5% specificity), and 2% (46.82% sensitivity and 85.2% specificity) respectively ($P = 0.001$) (Figure 1).

The comparison of the groups created according to the optimal predictive values of the ESC and ACC/AHA risk-scoring systems in terms of endpoints is shown in Figure 2. The presence of MACCE according to the risk categories of the scores is shown in Figure 3. In detecting the occurrence of MACCE, PCE was more successful than the "SCORE-2–SCORE-OP" risk-scoring system (Table 4).

Table 3. Distribution of Patients' Risk Groups Determined Using the ESC SCORE and AHA/ACC PCE Risk-Scoring Systems by the MACCE Groups

Risk-Scoring Systems	MACCE (–)	MACCE (+)	Fatal MI and Stroke	Non-Fatal MI and Stroke
PCE 0%-5%, n (%)	290 (91.2)	28 (8.8)	3 (27.3)	313 (41)
PCE 5%-7.5%, n (%)	81 (83.5)	16 (16.5)	0 (0)	96 (12.4)
PCE 7.5%-20%, n (%)	170 (71.1)	69 (28.9)	2 (18.2)	233 (30.5)
PCE >20%, n (%)	74 (55.2)	60 (44.8)	6 (54.5)	121 (15.9)
SCORE <1%, n (%)	278 (89.1)	34 (10.9)	3 (27.3)	306 (40.1)
SCORE 1%-5%, n (%)	253 (75.3)	83 (24.7)	6 (54.5)	324 (42.5)
SCORE 5%-9%, n (%)	60 (69.8)	26 (30.2)	2 (18.2)	83 (10.9)
SCORE >10%, n (%)	24 (44.4)	30 (55.6)	0 (0)	50 (6.6)
SCORE2/SCORE OP (low–moderate risk)	340 (55.3)	45 (26)	3 (27.3)	379 (49.7)
SCORE2/SCORE OP (high risk)	184 (29.9)	47 (27.2)	2 (18.2)	224 (29.4)
SCORE2/SCORE OP (very high risk)	91 (14.8)	(81 (46.8)	6 (54.5)	160 (21)

ACC/AHA, American College of Cardiology/American Heart Association; ESC, European Society of Cardiology; MACCE, major adverse cardiovascular and cerebrovascular event; n, number; PCE, Pooled Cohort Risk Assessment Equation; SCORE, Systemic Coronary Risk Evaluation .

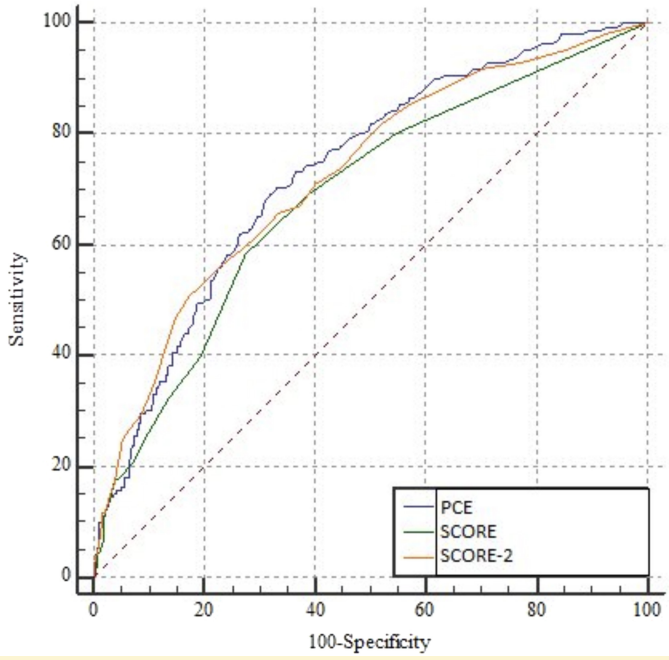

Figure 1. Receiver operating curves created using the risk ratios obtained from the ESC SCORE, ACC/AHA PCE, and SCORE-2-SCORE-OP risk-scoring systems for the detection of MACCE.

Discussion

The findings of this study revealed a significant relationship between MACCE and widely used risk scores. The prognostic values of all risk-scoring systems in predicting the occurrence of MACCE in HT patients during the follow-up period were slightly significant. However, AHA/ACC PCE risk-scoring system was slightly superior to both the former ESC SCORE and the updated new ESC SCORE2 and SCORE-OP risk-scoring systems. The comparison of the older and updated versions of the ESC risk-scoring systems revealed that the revised version of SCORE improved prediction of MACCE risk compared to former version in hypertensive patient population.

Atherosclerotic cardiovascular and cerebrovascular diseases are among the leading causes of morbidity and mortality in today's world, particularly in developing countries.[19] Therefore, estimating the risk of developing cardiovascular disease in adults is very important in terms of tailoring both preventive approaches and treatment modalities. The fact that atherosclerotic cardiovascular and cerebrovascular diseases often occur as a result of multiple risk factors render predicting the risk of MACCE in asymptomatic individuals even more important. All risk calculation systems are designed to identify the total risk created by common risk factors.[20] A successful risk calculation system is expected to help identify individuals with an increased risk for atherosclerotic cardiovascular and cerebrovascular diseases, assess the cumulative effects of existing risk factors on the individual, take into account variables such as lifestyle changes, and enable the evaluation of alternative medications through individualization of patient follow-up.[21]

Table 4. Area Under the Curve Values of PCE, SCORE, and SCORE2/SCORE-OP Models for the Detection of Endpoints

	SCORE		SCORE2/SCORE-OP		PCE	
Study Endpoints	**AUC (CI 95%)**	***P***	**AUC (CI 95%)**	***P***	**AUC (CI 95%)**	***P***
Coronary artery disease	0.688 (0.640-0.736)	**<0.001**	0.721 (0.676-0.766)	**<0.001**	0.724 (0.680-0.769)	**<0.001**
Stroke	0.662 (0.571-0.752)	**0.002**	0.666 (0.566-0.765)	**<0.001**	0.714 (627-0.800)	**<0.001**
Transient ischemic attack	0.690 (0.526-0.853)	**0.015**	0.704 (0.531-0.877)	0.009	0.757 (0.640-0.875)	**0.001**
Fatal MI and stroke	0.576 (0.412-0.739)	**<0.001**	0.533 (0.357-0.709)	**<0.001**	0.689 (0.497-0.882)	**<0.001**
MACCE	0.689 (0.644-0.735)	**<0.001**	0.724 (0.692-0.755)	**<0.001**	0.732 (0.691-0.773)	**<0.001**

AUC, area under curve; CI, confidence interval; MACCE, major adverse cardiovascular and cerebrovascular event; OR, odds ratio; PCE, Pooled Cohort Risk Assessment Equation; SCORE, Systemic Coronary Risk Evaluation.

In line with the literature data, the findings of this study indicated that advanced age and male gender were major risk factors for developing atherosclerotic cardiovascular events.[22] Diabetes mellitus is another important risk factor for cardiovascular diseases. The presence of DM alone increases the risk of developing cardiovascular diseases 2 to 4 times and is thus associated with a higher incidence of heart failure and death.[23,24] It should be noted that the presence of DM is queried only in the PCE risk model. The SCORE system evaluates diabetic patients directly in the high- or very-high risk categories depending on the associated conditions. Therefore, Mortensen et al and Tralhao et al excluded diabetic patients from their studies.[25,26] In numerous clinical studies, the PCE risk-scoring system has been demonstrated to be more accurate than the SCORE risk-scoring system for predicting atherosclerotic cardiovascular disease. However, it is not possible to prove its superiority by excluding an important risk factor such as DM. For this reason, diabetic patients were also included in the ESC risk-scoring systems and analyzed as such. Scoring systems such as ADVANCE and DIAL recommended in the guidelines for diabetic patients were not utlized in this study because of the methodological issues and their infrequent use in daily practice. Hence, it was hypothesized that the model applied in this study for predicting the development of MACCE, will be more compatible with real-life data. Despite including diabetic patients to all scoring groups the PCE system was again superior to the old and new versions of SCORE Qureshi et al and Mortensen et al excluded patients with statin use from their studies.[26,27] Given that such a study design may disrupt the evaluation of dyslipidemia, which is an important risk factor in the development of cardiovascular disease, and that the inclusion of patients with statin use would be more compatible with real-life data, statin use was not considered an exclusion criterion in this study.

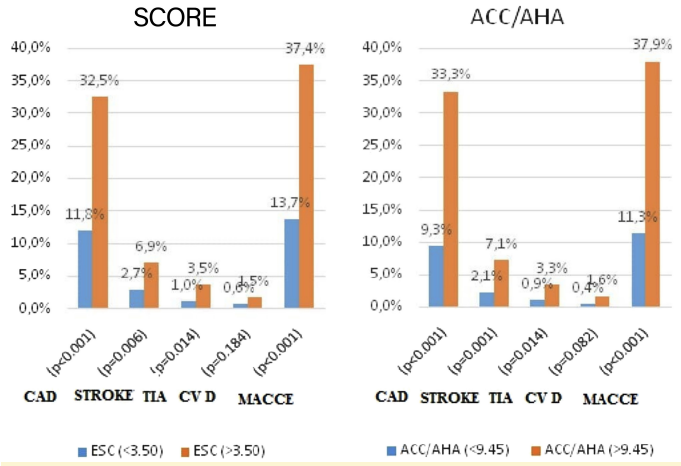

Figure 2. The comparison of the groups created according to the optimal predictive values of the SCORE and ACC/AHA risk-scoring systems in terms of endpoints. CAD, coronary artery disease; TIA, transient ischemic attack; CVD, cardiovascular death; MACCE, major adverse cardiovascular and cerebrovascular event.

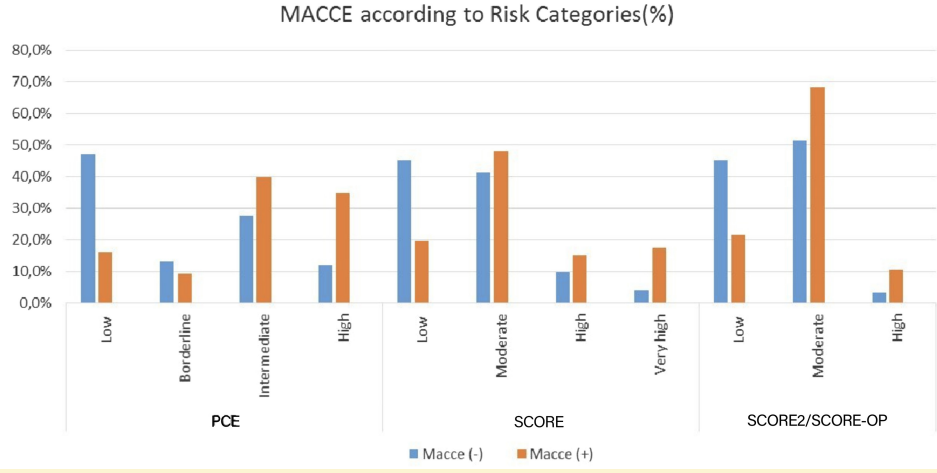

Figure 3. Major adverse cardiovascular and cerebrovascular event according risk categories (%).

Twenty-four-hour SBP and DBP, daytime SBP, and nighttime SBP and DBP values, as well as reverse dipper HT, resistant HT, and isolated systolic HT ratios were significantly higher in the MACCE (+) group. As a matter of fact, the relationships between these hypertensive patterns in the context of cardiovascular diseases and mortality has been shown in prospective studies with large patient populations.[28]

The efficacies of PCE and SCORE risk systems have been previously compared in terms of prognostic values in predicting the atherosclerotic cardiovascular and cerebrovascular events in large cohort studies conducted with the general population in different countries.[27,26] The findings of these studies, which partially excluded DM and dyslpidemic patients, revealed that the PCE risk system was superior to the SCORE risk system. However, the predictive values of these risk-scoring systems during long-term follow-ups in specific patient groups are still unclear. In a study conducted with 327 patients aged 40-75 years without DM and CAD, Tralhao et al[25] compared the PCE and SCORE risk systems based on the endpoints of obstructive CAD and coronary calcium scores with computed tomography (CT) angiography due to suspected ischemic heart disease and found that the predictive power of the PCE was superior to the SCORE. This study successfully explained the prognostic power of community-based risk-scoring systems in a specific patient group. In addition to the accurate prediction of MACCE by the SCORE and PCE risk-scoring systems, this trend was associated with more MACCE in the higher-risk group than in the lower-risk group, consistent with risk groups. However, a prospective study design is needed to determine the prognostic power of these risk-scoring systems in predicting the long-term cardiovascular events in specific patient groups. In this context, our study was designed to determine the prognostic value of PCE and SCORE risk-scoring systems in predicting long-term MACCE development in hypertensive patients, a risk group for cardiovascular and cerebrovascular events. Consequently, the PCE risk-scoring system was found to be superior to the SCORE risk system in predicting the occurrence of MACCE in hypertensive patients as well as in general population-wide cohorts.

To the best of this study's authors' knowledge, this is the first study to compare AHA/ACC PCE risk-scoring system with the ESC SCORE risk-scoring system also including the updated new ESC SCORE2 and SCORE-OP risk-scoring tools in the hypertensive patient population. In conclusion, AHA/ACC PCE risk-scoring system was found to be superior to both the former SCORE and the updated new SCORE2 and SCORE-OP models. Nevertheless, the increase in the predictive accuracy of SCORE2 compared to SCORE indicates an improvement in the model and risk stratification of the patients.

Limitations of the Study

The study's main limitations were its relatively small sample size and single-center methodology, both of which restricted the study's ability to generalize its findings to the entire population of hypertension patients. On the other hand, the fact that diabetic patients and patients who have been using statins were not excluded from this study unlike large cohort studies might be deemed a strength of this study over other comparable studies available in the literature. While risk assessment is recommended for patients aged 40-69 in the former SCORE risk-scoring system, patients over 70 years of age can be evaluated in the updated new SCORE-2 and SCORE-OP risk-scoring systems, in order to compare these risk-scoring systems in this age group, over 70 years of age. The former SCORE risk scores of the patients were also calculated and included in the study. Finally, treatment continuity was not evaluated in the statin-using group at a mean follow-up of 6 years.

Conclusion

The study findings indicated that the predictive values of all risk-scoring systems, i.e. PCE, SCORE and SCORE2, in predicting MACCE in hypertensive patients in the long term were moderately significant. On the other hand, pairwise comparisons of these risk-scoring systems revealed that PCE risk-scoring system was superior to the old and new versions of SCORE risk system in predicting the cardiovascular and cerebrovascular events that developed in patients with HT.

Ethics Committee Approval: The study protocol was approved by the Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Clinical Research Ethics Committee (Approval Number: KAEK/2019-02, Date: 08.01.2019).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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Declaration of Interests: The authors have no conflict of interest to declare.

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