Observational Study

Medicine

OPEN

APACHE II-ECG scoring system

A novel and strong predictor of in-hospital mortality for patients treated in intensive care unit

Sefer Aslan, MD[a], Kubilay İşsever, MD[a,*], Serdar Olt, MD[b], Emre Yılmaz, MD[c], Ersin Kuloğlu, MD[a], Ayşe Şahin Tutak, MD[b]

Abstract

Some novel electrocardiographic (ECG) parameters, such as T-wave peak to T-wave end duration (Tp-Te) and Tp-Te/Q-T interval (QT) ratios, have recently been found to be associated with cardiac ischemia and effective in predicting ventricular arrhythmias and mortality. This study examined the association between ECG repolarization parameters and mortality in intensive care unit (ICU) patients. A total of 232 ICU patients were retrospectively categorized as survivors or nonsurvivors retrospectively. Laboratory, demographic, and ECG parameters were compared between the groups. A novel ECG score was measured using the QT interval, Tp-Te, and Tp-Te/QT ratio upon admission to the ICU. We compared the ECG score, Acute Physiologic and Chronic Health Evaluation II (APACHE II)-score, and APACHE II-ECG scores (the combination of APACHE II and ECG score) regarding mortality using a biostatistical program. The mean age of the 232 patients was 69.96 ± 18.01 years, and 49.1% were male. The nonsurvivor group was significantly older and had higher ECG, APACHE II, and APACHE II-ECG scores. Multivariate Cox regression analysis revealed that higher levels of all 3 scores were independent risk factors for mortality ([hazard ratio, HR (95% CI): 1.847 (1.305–2.615), $P = .001$], [HR (95%CI): 1.146 (1.071–1.225), $P < .001$], and [HR (95% CI): 1.181 (1.117–1.249), $P < .001$], respectively). Receiver operating curve analysis of these scoring systems for predicting mortality in the ICU revealed a stronger predictive value for the APACHE II-ECG score (AUC [95% CI]: 0.872 [0.824–0.919], $P < .001$, sensitivity: 88.7%, specificity: 73.3%). Kaplan–Meier survival analysis revealed the superiority of the APACHE II-ECG score in predicting the survival of ICU patients (log rank chi-square: 80.366, $P < .001$). Our study suggests combining ECG repolarization parameters with APACHE II score offers a new, more robust system for stronger mortality prediction in ICU patients.

Abbreviations: APACHE II = Acute Physiologic and Chronic Health Evaluation II, COPD = chronic obstructive pulmonary disease, CVD = cerebrovascular disease, ECG = electrocardiography, HR = hazard ratio, ICU = intensive care unit, INR = International Normalized Ratio, Modified APACHE II score = APACHE II-ECG score, QT = Q-T interval, ROC = receiver operating curve, SOFA = Sequential (or sepsis-related) Organ Failure Assessment, Te = T wave end, Tp = T wave peak.

Keywords: APACHE- II score, ECG score, ICU mortality, QT, Tp-Te interval, Tp-Te/QT ratio

1. Introduction

The T-wave peak to T-wave end duration/Q-T interval (Tp-Te/QT) ratio assesses the electrical activity of the heart. Specifically, it shows the interval between the peak and end of the T wave on an electrocardiography (ECG) and compares it with the length of the QT interval. Ventricular repolarization parameters such as Tp-Te and Tp-Te/QT have been well studied, and higher values of these parameters have been associated with poor outcomes in patients with heart failure, acute myocardial infarction, and ventricular arrhythmias.[1–4] Furthermore, recent studies have revealed new associations between these parameters and other pathological clinical conditions such as sarcoidosis, migraine, COVID-19, and sepsis.[5–8] These associations might be explained by alterations in the autonomic nervous system in these diseases, causing an imbalance in ventricular transmural dispersion repolarization.[6,7]

Intensive care units (ICUs) are departments of hospitals where patients with life-threatening diseases are followed-up and managed. Therefore, it is vital to closely monitor and analyze the risk factors of these patients at the time of admission to take timely actions to reduce ICU mortality. Due to this reason, predictive scoring systems such as the Acute Physiologic

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

Our study was approved by the Adıyaman University Clinical Research Ethical Committee (approval no. 2018/2-20: February 2020).

[a] Department of Internal Medicine, Giresun University Faculty of Medicine, Giresun, Turkey, [b] Department of Internal Medicine, Adıyaman University Faculty of Medicine, Adıyaman, Turkey, [c] Department of Cardiology, Giresun University Faculty of Medicine, Giresun, Turkey.

** Correspondence: Kubilay İşsever, Department of Internal Medicine, Giresun University Faculty of Medicine, Aksu Mahallesi Mehmet İzmen Caddesi No: 145 Merkez, Giresun, Turkey (e-mail: kubilayissever@gmail.com).*

How to cite this article: Aslan S, İşsever K, Olt S, Yılmaz E, Kuloğlu E, Tutak AŞ. APACHE II-ECG scoring system: A novel and strong predictor of in-hospital mortality for patients treated in intensive care unit. Medicine 2024;103:52(e41121).

Received: 31 July 2024 / Received in final form: 2 December 2024 / Accepted: 11 December 2024

http://dx.doi.org/10.1097/MD.0000000000041121

and Chronic Health Evaluation II (APACHE II), Simplified Acute Physiologic Score, and Sequential (or sepsis-related) Organ Failure Assessment (SOFA) scores have been developed and widely used for ICU patients.[9,10] However, new searches are ongoing to explore better, more precise, practical, and rapidly applicable parameters to achieve perfect results for the early diagnosis and management of ICU patients. Accordingly, researchers have discovered new associations between some demographical parameters, inflammatory indexes, comorbidities, and mortality/ICU admission in COVID-19 patients even in the fourth year of the pandemic.[11] Determining these associations is crucial, especially in health facilities where many patients with various health conditions are admitted to ICUs.

ECG is an easy and cost-effective method for obtaining valuable information regarding the cardiac functions. It is routinely applied upon admission to ICUs in almost all countries. It takes a few minutes to obtain a proper 12-lead ECG from patients and calculate valuable parameters such as Tp-Te interval and Tp-Te/QT ratios. In addition, performing an ECG can be repeated at any time the physician needs during patient follow-up. These characteristics make ECG a perfect candidate as a mortality predictor in the ICU setting. Li et al[7] reported that the predictive effect of Tp-Te/QT on death was better than that of SOFA in their study of sepsis patients. Since preventing ventricular arrhythmias is vital for reducing mortality and morbidity in ICU, evaluation of ventricular repolarization parameters might be predictive for this purpose.[12,13] This study aimed to examine the association between ECG repolarization parameters and mortality and to find new scoring systems for ICU patients, if possible,.

2. Materials and Methods

In our retrospective and observational study, we included 232 consecutive patients who were followed-up in the Internal Medicine Intensive Care Unit of our tertiary care institution. We included patients aged > 18 years who did not undergo emergency surgical intervention at admission and did not present with a cardiovascular pathology. Patients hospitalized in the ICU for <24 hours, admitted from the cardiac ICU, with acute coronary syndrome, with trauma and acute surgical indications, with any electrolyte imbalances, taking drugs that prolong the QT interval, and without a 12-lead ECG analysis on admission were excluded. The main reason for excluding the patients whose causes of ICU admission were cardiac diseases and electrolyte imbalances was to avoid bias since these conditions directly affect the heart's electrical activity. The generability of the predictive performance of ECG repolarization parameters for all mortality causes (except the abovementioned ones) was also our primary endpoint for this study. We obtained data from patients who were followed-up and treated in the ICU between January 2017 and December 2018 through a file search and local hospital database. The protocol was approved by the Adıyaman University Faculty of Medicine Ethics Committee, Adıyaman, Turkey (approval no. 2018/2-20, February 2020) and conformed to the guidelines of the Declaration of Helsinki.

Laboratory tests performed during ICU admission, demographic, characteristics, and APACHE II scores were evaluated. APACHE II scoring is a routine and mandatory practice in tertiary ICU admissions at our center. In our study, the outcome was in-hospital mortality rate. All-cause mortality was assessed without differentiating between the causes of death. We divided our study patients into 2 groups: "survivors" and "non-survivors."

2.1. ECG analysis

A 12-lead ECG was performed on all patients at admission using the same device in the supine position. We analyzed the ECG images recorded at 25 mm/s for 10 seconds with 1.0 mV (10 mm) as the standard voltage. The ECGs used in the analyses were selected from the routine ECGs obtained during the ICU admission. Heart rate, PR interval, QRS complex, QT interval, Bazett formula [QT (ms)/RR (s)1/2] corrected QT (QTc), Tpeak-to-Tend interval, Tp-e/QT, and Tp-e/QTc ratios were measured. ECGs viewed from the online imaging tool were evaluated with a magnifying glass and pixel measurement ruler to improve the accuracy of the measurements. Our electrocardiography device (MAC 2000, GE Medical Systems Information Technologies, Inc, Milwaukee) provides a measurement constant of 10 mm/mV in the lower left, at the beginning of the rhythm line, as standard. Our ECGs are uploaded to our imaging system in pdf format. The pixel measurement ruler may give different results according to the zoom ratio in measurements. For this reason, it is necessary to calibrate the pixel measurement result over the measurement standard each time at the zoom depth at which the measurement will be made. In this way, it is found how many pixels correspond to how many mV and mm. Measurements were performed by a cardiologist blinded to the patient data and without any conflicts of interest. Repeated ECG measurements were performed. The intraobserver agreement coefficient was <5%.

The ECG score was calculated using repolarization markers such as QT, Tp-e, and Tp-e/QT. We determined the predictive values of these repolarization markers. We planned to assign + 1 points for measurements above the predictive value of each ECG parameter and 0 points for measurements below the predictive value. The ECG score was calculated as a minimum of 0 point and a maximum of 3 points. In the analyses, we evaluated the diagnostic value of APACHE II and ECG scores for in-hospital mortality prediction. We produced the APACHE II-ECG score (APACHE II score + ECG score) by adding the ECG score data to the APACHE II score. We compared the diagnostic power and survival analysis of the APACHE II-ECG score with other risk factors.

2.2. Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences for Windows v. 26.0 (). The normality of the distribution was determined using Kolmogorov–Smirnov analysis. Data were shown as numbers, percentages, and mean ± standard deviation. Data with non-normal distribution were expressed as median (25th–75th percentile values). Continuous variables with normal distribution were evaluated using Student *t* test, and those with non-normal distribution were evaluated using the Mann–Whitney *U* test. The Chi-square test was used to compare categorical parameters between survivors and non-survivors, including the APACHE II, ECG, and Modified APACHE II scores. Receiver operating curve (ROC) analysis was performed to determine the cutoff values for each ECG parameter and the APACHE II, ECG, and Modified APACHE II scores. Univariate and multivariate Cox regression analyses were used to determine risk factors for in-hospital mortality. The level of statistical significance was set at $P < .05$.

3. Results

The mean age of the 232 patients included in our study was 69.96 ± 18.01 years and 49.1% were male. The median in-hospital follow-up period was 116 days (min–max: 23.5–116 days) and the mortality rate was 30.6% (n = 71). The mean age of the non-survivors group patients was significantly higher than the survivors group (67.73 ± 19.80 vs 75.01 ± 11.69, respectively, $P = .004$). Inotropic support, sedation and intubation rates were significantly higher in the non-survivor group ($P < .001$ each). We found that the non-survivor group tended to have acidosis and leukocytosis,

and had higher glucose, urea, creatinine and International Normalized Ratio (INR) levels than the survivor group. ECG score (1.90 ± 0.89 vs 1.19 ± 0. 85, $P < .001$), APACHE II score (22.97 ± 5.29 vs 14.39 ± 6.26, $P < .001$) and APACHE II-ECG score (24.87 ± 5.47 vs 15.58 ± 6.27, $P < .001$) were significantly higher in the non-survivors group. The demographic, characteristics, and laboratory results of the patients and the survival subgroups are shown in Table 1.

The causes of intensive care unit admission and the survival distribution of the study patients are shown in Figure 1. The most common admissions were for chronic obstructive pulmonary disease (COPD), cerebrovascular diseases (CVD), acute respiratory distress syndrome and pneumonia. The admission diagnoses with the highest mortality rates were pulmonary embolism, COPD, CVD and pneumonia.

QT (347.62 ± 42.29 vs 335.02 ± 37.65, $P = .025$), Tp-e (77.11 ± 12.52 vs 68.15 ± 11.22, $P < .001$) and Tp-e/QT (0.22 ± 0.05 vs 0.20 ± 0.03, $P < .001$) measurements were significantly higher in the non-survivors group. No significant difference was found in other ECG measurements. The electrocardiographic findings of the study patients and survival subgroups are presented in Table 2.

We present the results of the univariate Cox regression analysis for in-hospital mortality risk factors in Table 3 and multivariate Cox regression analysis in Table 4. Three different models were used to predict in-hospital mortality using the APACHE II, ECG, and APACHE II-ECG risk scores. Multivariate Cox regression analysis revealed that the APACHE II score [hazard ratio, HR (95% CI): 1.146 (1.071–1.225), $P < .001$], ECG score [HR (95% CI): 1.847 (1.305–2.615), $P = .001$] and APACHE II-ECG risk scores [HR (95% CI): 1.181 (1.117–1.249), $P < .001$] were independent risk factors for in-hospital mortality prediction.

The cutoff values of QT, Tp-e and Tp-e/QT measurements, which have significant predictive value for in-hospital mortality, were calculated as 340.5 (AUC: 0.585, $P = .04$), 75.5 (AUC: 0.694, $P < .001$), and 0.197 (AUC: 0.610, $P = .007$), respectively. When calculating the ECG score, 1 point was given for each value above this predictive value, whereas 0 point were given for values below this predictive value. The maximum and minimum ECG score were 3 and 0, respectively.

Details of the ROC analysis of the risk scores are presented in Figure 2 and Table 5. We found that the ECG score (AUC [95% CI]: 0.708 [0.635–0.780], $P < .001$, sensitivity: 63.4%, specificity: 72%) and APACHE II score (AUC [95% CI]: 0.855 [0.804–0.905], $P < .001$, sensitivity: 87.3%, specificity: 73.9%) had significant diagnostic power in predicting in-hospital mortality. We found that the diagnostic power of the modified APACHE II (APACHE II-ECG score; AUC [95% CI]: 0.872 [0.824–0.919], $P < 0001$, sensitivity: 88.7%, specificity: 73.3%) score was superior to that of the other 2 risk scores.

Our study group was regrouped according to the cut off values obtained by ROC analysis of ECG, APACHE II and Modified APACHE II scores. For each score, binary groups

Table 1

Demographic characteristics and laboratory findings of the patients and survival subgroups.

Variables	All (n = 232)	Survivors (n = 161)	Nonsurvivors (n = 71)	*P* value
Age (yr)	69.96 ± 18.01	67.73 ± 19.80	75.01 ± 11.69	**.004**
Male gender, n (%)	114 (49.1%)	73 (45.3%)	41 (57.7%)	.082
Inotropic support, n (%)	73 (31.5%)	19 (11.8%)	54 (76.1%)	**<.001**
Intubation, n (%)	50 (21.5%)	6 (3.7%)	44 (61.9%)	**<.001**
Sedation, n (%)	54 (23.2%)	12 (7.4%)	42 (59.2%)	**<.001**
ICU follow-up (d)	4 (1.25–9)	5 (1–12)	14 (4–64)	**<.001**
pH	7.37 ± 0.13	7.38 ± 0.11	7.34 ± 0.18	**.047**
HCO_3	25.43 ± 7.74	25.57 ± 6.91	25.15 ± 9.20	.712
PaO_2	60.47 ± 12.09	58.86 ± 11.54	63.63 ± 12.23	.407
PCO_2	44.23 ± 16.37	43.57 ± 15.11	45.54 ± 18.65	.419
WBC	13.07 ± 6.16	12.43 ± 5.64	14.47 ± 7.01	**.021**
Lymphocyte	1.30 (0.82–1.91)	1.38 (0.84–1.93)	1.31 (0.78–1.89)	.114
Monocyte	0.80 (0.41–0.87)	0.78 (0.38–0.86)	0.83 (0.42–0.89)	.774
MPV	8.59 ± 2.07	8.50 ± 2.03	8.78 ± 2.16	.346
Hgb	12.38 ± 2.40	12.29 ± 2.36	12.58 ± 2.51	.415
Hct	39.22 ± 7.33	38.94 ± 7.06	39.87 ± 7.91	.371
Plt	214.42 ± 87.64	217.95 ± 82.03	206.69 ± 98.99	.374
Glucose	157.56 ± 36.01	147.52 ± 35.90	179.93 ± 40.19	**.009**
Urea	64.98 ± 17.48	56.45 ± 13.41	84.13 ± 20.85	**<.001**
Albumin	3.10 ± 0.75	3.18 ± 0.75	2.92 ± 0.71	**.018**
Creatinine	1.14 ± 0.82	1.04 ± 0.75	1.36 ± 0.93	**.008**
Sodium	139.29 ± 6.26	139.03 ± 5.34	139.89 ± 7.97	.340
Potassium	4.20 ± 0.79	4.14 ± 0.65	4.34 ± 1.02	.084
Total protein	6.30 ± 0.77	6.36 ± 0.72	6.17 ± 0.88	.199
AST	79.88 ± 15.97	54.72 ± 10.94	137.49 ± 27.49	.036
ALT	65.35 ± 13.07	46.76 ± 9.35	67.93 ± 13.58	.063
Calcium	8.55 ± 0.70	8.60 ± 0.69	8.43 ± 0.71	.182
Sedimentation	28.97 ± 5.79	24.84 ± 4.96	37.44 ± 7.48	**<.001**
CRP	2.12 (0.59–8.96)	2.3 (0.48–9.2)	5.9 (2.34–21.18)	.092
Procalcitonin	3.39 ± 0.67	3.10 ± 0.62	4.08 ± 0.81	.688
aPTT	32.36 ± 8.99	31.70 ± 8.50	33.93 ± 9.97	.110
INR	1.32 ± 0.61	1.25 ± 0.37	1.51 ± 0.93	**.007**
ECG score	1.41 ± 0.92	1.19 ± 0.85	1.90 ± 0.89	**<.001**
APACHE II score	17.01 ± 7.17	14.39 ± 6.26	22.97 ± 5.29	**<.001**
APACHE II-ECG score	18.42 ± 7.40	15.58 ± 6.27	24.87 ± 5.47	**<.001**

Bold values indicates statistically significant values at $P < .05$.

ALT = alanine aminotransferase, aPTT = activated partial thromboplastin time, AST = aspartate aminotransferase, CRP = C-reactive protein, HCO_3 = bicarbonate, Hct = hematocrit, Hgb = hemoglobin, INR = International Normalized Ratio, MPV = mean platelet volume, paO_2 = partial arterial oxygen fraction, pCO_2 = partial arterial carbondioxide fraction, Plt = platelets, WBC = white blood cell.

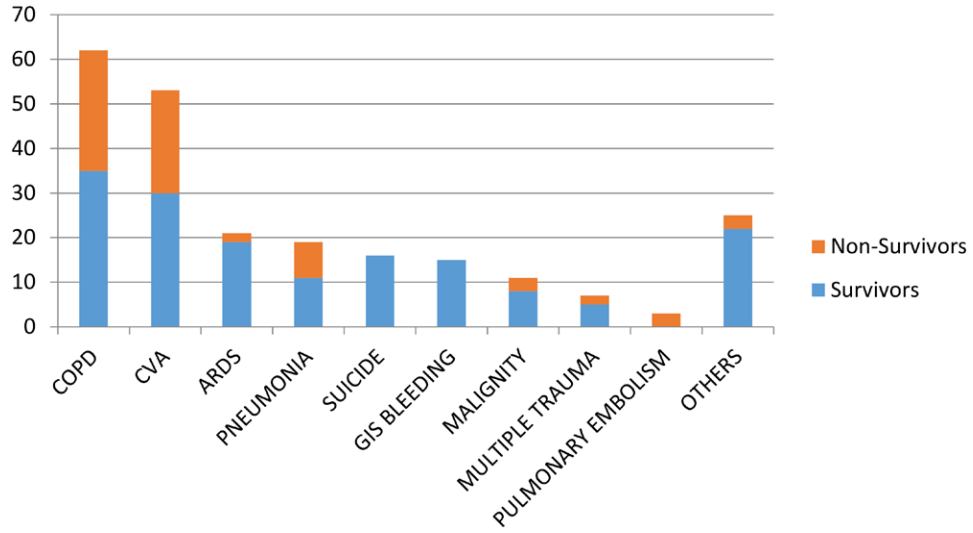

Figure 1. Distribution of patients according to the underlying cause of ICU admission and mortality rates. ARDS = acute respiratory distress syndrome, COPD = chronic obstructive pulmonary disease, CVD = cerebrovascular disease, GIS = gastrointestinal system, ICU = intensive care unit.

Table 2

Electrocardiographic findings of the patients and survival subgroups.

Variables	All (n = 232)	Survivors (n = 161)	Nonsurvivors (n = 71)	*P* value
Heart rate	103.35 ± 20.45	98.24 ± 19.64	108.46 ± 21.26	.068
PR (ms)	147.62 ± 25.25	148.26 ± 24.36	146.98 ± 26.15	.280
QRS (ms)	100.01 ± 20.21	100.16 ± 19.22	99.86 ± 21.18	.432
QT (ms)	338.88 ± 39.46	335.02 ± 37.65	347.62 ± 42.29	**.025**
QTc (ms)	421.88 ± 43.04	419.59 ± 42.94	424.18 ± 43.14	.341
Tp-e (ms)	70.89 ± 12.32	68.15 ± 11.22	77.11 ± 12.52	**<.001**
Tp-e/QT	0.20 ± 0.04	0.20 ± 0.03	0.22 ± 0.05	**<.001**
Tp-e/QTc	0.20 ± 0.05	0.20 ± 0.05	0.21 ± 0.06	.209

Bold values indicates statistically significant values at $P < .05$.

PR = P-R interval, QRS = QRS complex, QT = Q-T interval, QTc = corrected Q-T interval, Tp-e = T peak to T end interval, Tp-e/QT = T peak to T end interval/QT, Tp-e/QTc = T peak to T end interval/corrected QT.

Table 3

Results of univariate Cox regression analysis for in-hospital mortality risk factors.

	Univariable analysis			Univariable analysis	
	HR (95% CI)	*P* value		HR (95% CI)	*P* value
Age	1.022 (1.005–1.038)	**.009**	AST	1.001 (1.000–1.001)	**.003**
Gender	1.494 (0.933–2.393)	.095	ALT	1.001 (1.000–1.002)	**.007**
Ph	0.137 (0.029–0.647)	**.012**	Sedimentation	1.016 (1.006–1.026)	**.001**
PaO_2	1.004 (0.998–1.010)	.212	INR	1.571 (1.209–2.041)	**.001**
WBC	1.046 (1.011–1.082)	**.009**	QT	1.007 (1.001–1.013)	**.018**
Hct	1.017 (0.984–1.052)	.314	QTc (ms)	1.012 (1.004–1.029)	**.004**
ICU follow-up duration	1.016 (1.006–1.025)	**.001**	Tp-e (ms)	1.058 (1.037–1.080)	**<.001**
Glucose	1.003 (1.001–1.005)	**.003**	Tp-e/QT	2.014 (1.346–3.568)	**<.001**
Urea	1.007 (1.004–1.011)	**<.001**	Tp-e/QTc	1.048 (1.022–1.089)	**.006**
Creatinine	1.368 (1.115–1.678)	**.003**	APACHE II Score	1.188 (1.144–1.233)	**<.001**
Albumin	0.688 (0.510–0.927)	**.014**	ECG Score	1.951 (1.521–2.501)	**<.001**
Sodium	1.020 (0.981–1.061)	.326	APACHE II-ECG Score	1.191 (1.149–1.234)	**<.001**
Potassium	1.273 (0.968–1.676)	.085			

Bold values indicates statistically significant values at $P < .05$.

ALT = alanine aminotransferase, AST = aspartate aminotransferase, Hct = hematocrit, INR = International Normalized Ratio, paO_2 = partial arterial oxygen fraction, Plt = platelets, Tp-e = T peak to T end interval, Tp-e/QT = T peak to T end interval/QT, Tp-e/QTc = T peak to T end interval/corrected QT, WBC = white blood cell.

were formed as below and above the cut off value. We evaluated the survival of these groups by Kaplan–Meier analysis. In all 3 groups, we observed that the survival of patients above the cut off value was lower than that of patients below the cut off value. This survival estimate was statistically significant for each scoring system. The details of the Kaplan–Meier survival analysis are shown in Figure 3. We found that the Modified APACHE II (Log Rank Chi-Square: 80.366, $P < .001$) score was superior to the other 2 risk scores in predicting survival.

Table 4

Results of multivariate Cox regression analysis to identify independent risk factors for in-hospital mortality.

	Model 1	Model 2	Model 3
	HR (95% CI) *P* value	HR (95% CI) *P* value	HR (95% CI) *P* value
APACHE II score	**1.146** (1.071–1.225) *P* < .001	–	–
ECG score	–	**1.847** (1.305–2.615) *P* = .001	–
APACHE II-ECG score	–	–	**1.181** (1.117–1.249) *P* < .001

Model 1: Gender, ICU follow up duration, glucose, urea, albumin, AST, ALT, sedimentation, INR, QT, QTc, Tp-e, Tp-e/QT, Tp-e/QTc.
Model 2: Age, gender, pH, WBC, ICU follow up duration, glucose, urea, albumin, creatinine, potassium, AST, ALT, sedimentation, INR.
Model 3: Gender, ICU follow up duration, glucose, urea, albumin, AST, ALT, sedimentation, INR.
Bold values indicates statistically significant values at *P* < .05.
ALT = alanine aminotransferase, APACHE II = Acute Physiologic and Chronic Health Evaluation II, AST = aspartate aminotransferase, ECG = electrocardiography, ICU = intensive care unit, INR = International Normalized Ratio, QT = Q-T interval, QTc = corrected QT, Tp-e = T peak to T end interval, WBC = white blood cell.

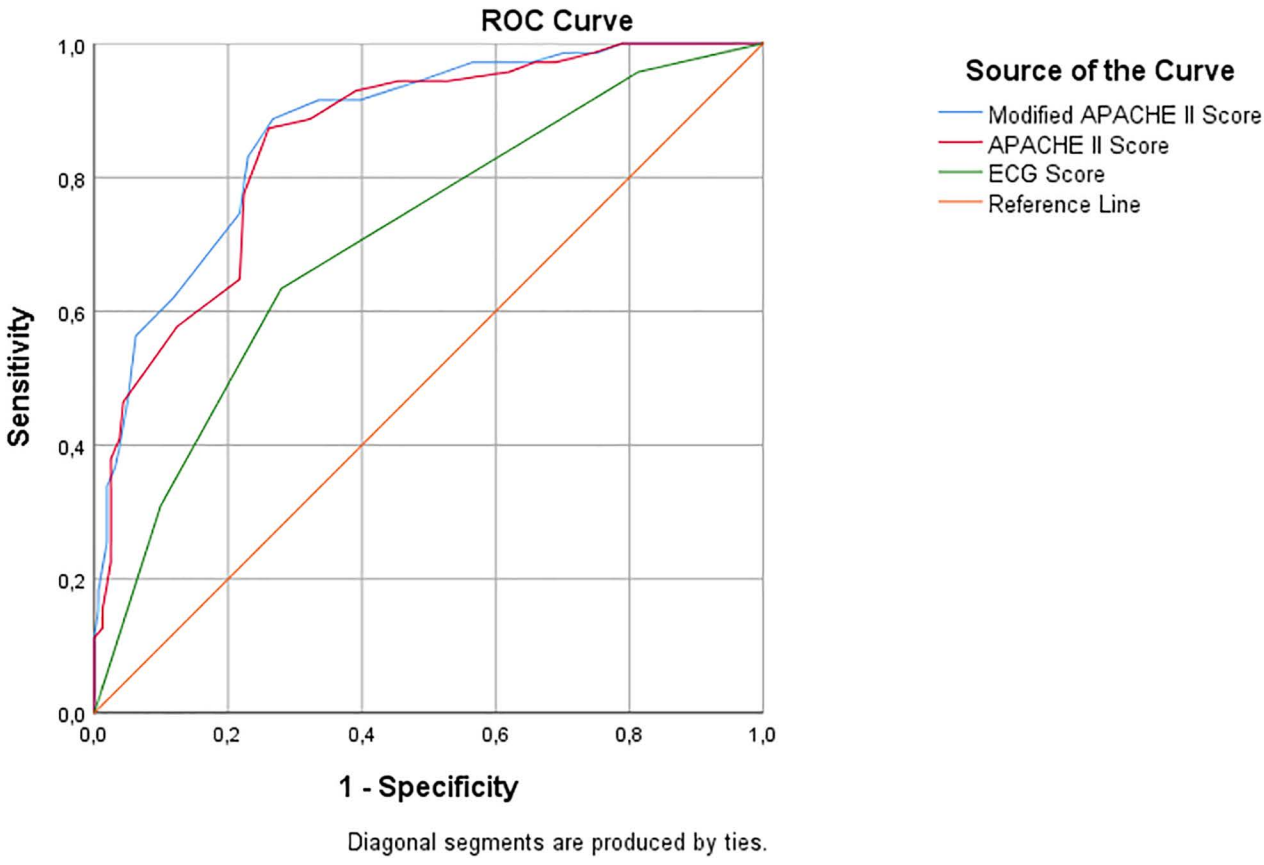

Figure 2. ROC curves of risk scores for prediction of in-hospital mortality. APACHE II = Acute Physiologic and Chronic Health Evaluation II, ECG = electrocardiography, ROC = receiver operating curve.

Table 5

Details of ROC analysis of risk scores for predicting in-hospital mortality.

	AUC	95% CI	*P* value	Sensitivity	Specificity	Youden index
ECG score	**0.708**	0.635–0.780	**<.001**	63.4	72	0.354
APACHE II score	**0.855**	0.804–0.905	**<.001**	87.3	73.9	0.612
APACHE II-ECG score	**0.872**	0.824–0.919	**<.001**	88.7	73.3	0.620

Bold values indicates statistically significant values at *P* < .05.
APACHE II = Acute Physiologic and Chronic Health Evaluation II, AUC = area under curve, ECG = electrocardiography, ROC = receiver operating curve.

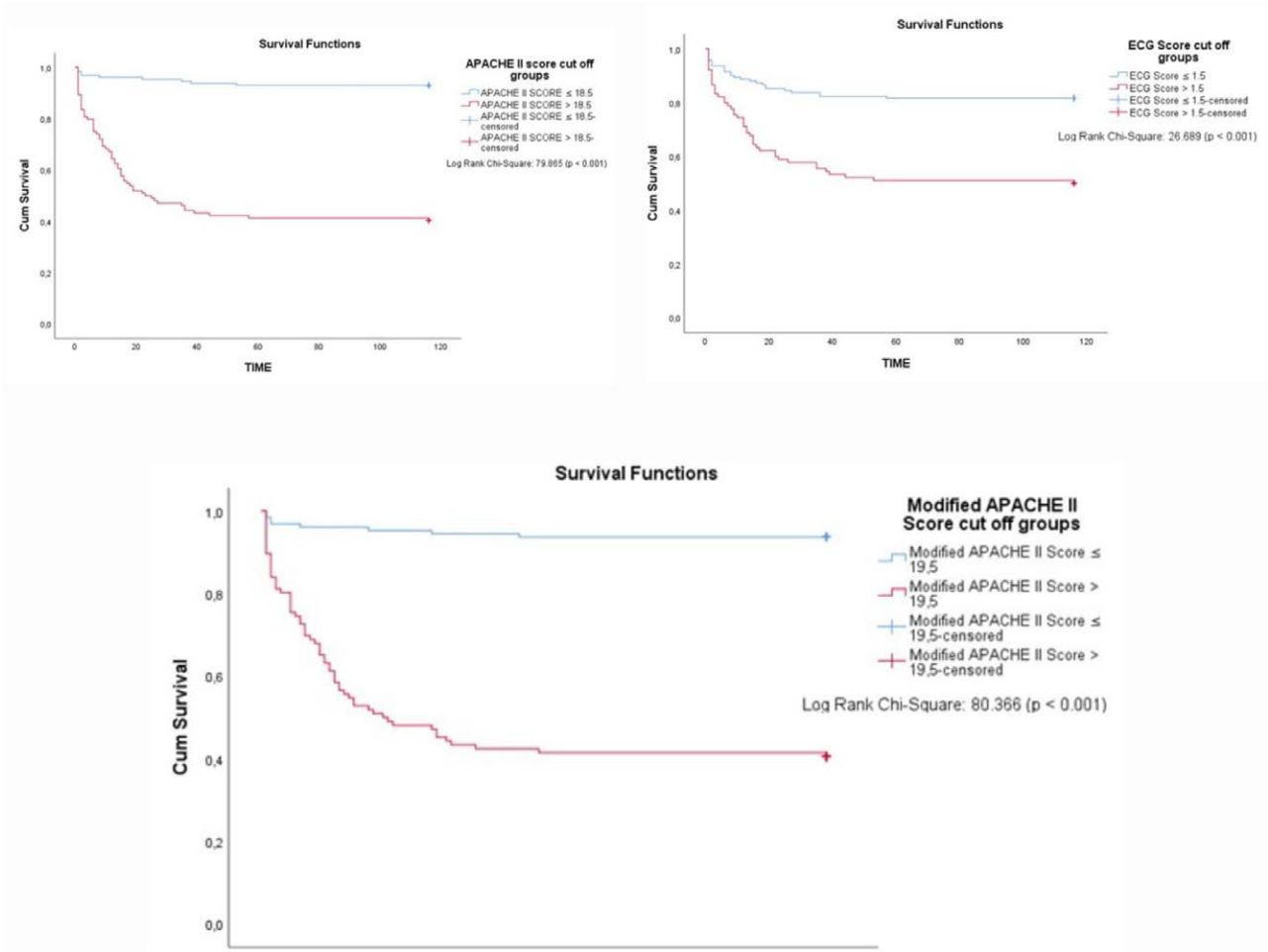

Figure 3. Survival analysis results of subgroups determined according to risk score predictive values. APACHE II = Acute Physiologic and Chronic Health Evaluation II, ECG = electrocardiography.

4. Discussion

Our results revealed a novel and precise scoring system for mortality prediction in the ICU. To our knowledge, this is the only study in the literature that evaluates the predictive performance of the combination of the APACHE II score and some ECG repolarization parameters such as QT, Tp-e, and Tp-e/QT in ICU patients. All 3 scores (APACHE II, ECG score, and APACHE II-ECG score) showed independent and significant associations with all-cause mortality in the ICU; above all, the APACHE II-ECG score had the best predictive performance. Concerning the importance of better and quicker scoring systems for risk prediction in ICU patients, our results might "teach an old dog new tricks."

The APACHE II score includes parameters such as age, rectal temperature, mean arterial pressure, heart rate, respiratory rate, oxygenation, some laboratory biomarkers (pH, sodium, creatinine, etc) and the Glasgow coma scale.[14] Among these, the heart rate is the only indicator that provides direct information regarding cardiac function. In contrast, cardiovascular diseases are the most commonly seen etiology of ICU admission and the most common cause of death in ICU.[15] In this regard, the APACHE II score might have been more powerful in terms of mortality prediction if the score included more parameters related to baseline cardiac functions regardless of the cause of admission to the ICU. At this point, our analyses revealed better results for the APACHE II-ECG score than the for the ECG and APACHE II scores alone. Although the results demonstrated a slight difference between the APACHE II and APACHE II-ECG scores, we think this difference would be more significant if our patient group was larger.

APACHE II has proved its adequacy as a mortality predictor, even more robust than SOFA, during the COVID-19 pandemic.[16] However, its efficacy needs to be studied better in cardiac ICU patients in the literature. A recent study demonstrated that the APACHE II score had a higher predictive value for in-hospital mortality than inflammatory indices in patients with acute coronary syndrome.[17] Another study comparing the predictive performance of APACHE II, Simplified Acute Physiologic Score II, and SOFA in post-cardiac arrest patients treated with therapeutic hypothermia revealed superior performance for the APACHE II score than for the SOFA score.[18] Seoane et al[19] also demonstrated the high discrimination capacity and predictive value of the APACHE II score in patients undergoing cardiac surgery. Although this score has been validated for predicting in-hospital mortality for all ICU patients regardless of the cause, these studies demonstrated that it also has a valuable performance for patients treated with severe cardiac problems. Adding the ECG scoring system to the APACHE II score will not only strengthen its predictive capacity for in-hospital all-cause mortality but also allow this combination to be used more widely for risk stratification, especially in patients treated for severe cardiovascular problems in ICU.

Several ECG scoring systems composed of different ECG parameters have been studied for diagnosis, risk prediction, follow-up, and treatment response processes in various diseases. An ECG scoring consisting of T wave inversions, S

waves, and Q wave abnormalities in different leads was shown to be effective for predicting perfusion defects in patients with acute pulmonary thromboembolism.[20] A recent study demonstrated that an ECG score including the frontal plane QRS-T angle and heart rate-corrected QT duration presented better results than cardiovascular magnetic resonance imaging (CMR) for prognosis prediction in patients with heart failure. The authors recommended combining this ECG score with cardiovascular magnetic resonance imaging results since it has been shown to improve the overall prognostic performance.[21] Concordantly, our analysis also revealed better prognostic performance for the APACHE II-ECG score. Another recent study conducted with 8417 participants revealed an important result that even in a low-risk asymptomatic population, an ECG score based on the Minnesota code classification system could independently predict cardiovascular death.[22] These promising results, along with our results, suggest that adding ECG parameters to any other risk-scoring system for any disease might increase its predictive performance. However, these associations must be studied and verified in future studies with larger populations. After ascertaining the contribution of ECG parameters for mortality prediction by various studies, applying this ECG score as an ICU admission routine in addition to other routine scores such as APACHE II might be discussed and included in the guidelines. For instance, the APACHE II-ECG score might be decisive for patients presenting on borderline levels regarding risk prediction for traditional routine risk scoring systems at admission. With these advantages, evaluating admission ECG parameters might offer additional value when clinicians struggle to manage severe patients, especially when deciding on the treatment setting (ICU vs ward).

When we analyzed the patients' demographic data, COPD and CVD were the 2 most common causes of admission to the ICU, followed by acute respiratory distress syndrome, pneumonia, suicide, gastrointestinal bleeding, malignancy, multiple trauma, and pulmonary embolism. This patient heterogeneity suggests that the APACHE II-ECG score can be used in a wide range of ICU patients regardless of the cause of admission. The non-survivor group had significantly elevated mean age, length of stay, white blood cell count, sedimentation, glucose, urea, pH, INR, and decreased albumin values, as expected and verified in the literature.[23]

Our study has some limitations. *P* values, sensitivity, and specificity values regarding the predictive effectiveness of the scores were very close to each other in the analyses. This study includes patients who had indications for being admitted to "intensive care" ICU. More studies on trauma, surgery, and cardiac ICU patients are needed to generalize these results to all ICU patients. The results could be more significant if the dataset had been more extensive. The dataset should have included more demographic and clinical information, such as comorbidities, history of drug use, and basal cardiac functions. Lastly, there could be some additional follow-up data except mortality for the survivor group to analyze whether these scores can also predict readmissions or clinical progression. Despite all of these, our study has some valuable and "game-changing" results.

5. Conclusion

Adding ECG ventricular repolarization parameters to the APACHE II score might improve its predictive capacity in ICU patients regardless of the admission cause, suggesting its ability to change the daily practices of the clinicians. This new scoring system must be validated in additional studies with larger patient groups. The addition of ECG parameters to other ICU risk-scoring systems should also be discussed in future research for better prediction results.

Author contributions

Conceptualization: Sefer Aslan, Kubilay İşsever.
Data curation: Serdar Olt, Ersin Kuloğlu.
Formal analysis: Emre Yılmaz.
Investigation: Sefer Aslan, Serdar Olt.
Methodology: Kubilay İşsever, Emre Yılmaz.
Project administration: Ayşe Şahin Tutak.
Software: Emre Yılmaz.
Supervision: Sefer Aslan, Ayşe Şahin Tutak.
Validation: Ersin Kuloğlu.
Visualization: Sefer Aslan, Serdar Olt.
Writing – original draft: Sefer Aslan, Kubilay İşsever.
Writing – review & editing: Sefer Aslan, Kubilay İşsever.

References

[1] Yayla C, Bilgin M, Akboğa MK, et al. Evaluation of Tp-E interval and Tp-E/QT ratio in patients with aortic stenosis. Ann Noninvasive Electrocardiol. 2016;21:287–93.
[2] Castro-Torres Y, Carmona-Puerta R, Katholi RE. Ventricular repolarization markers for predicting malignant arrhythmias in clinical practice. World J Clin Cases. 2015;3:705–20.
[3] Gupta P, Patel C, Patel H, et al. T(p-e)/QT ratio as an index of arrhythmogenesis. J Electrocardiol. 2008;41:567–74.
[4] Castro Hevia J, Antzelevitch C, Tornés Bárzaga F, et al. Tpeak-Tend and Tpeak-Tend dispersion as risk factors for ventricular tachycardia/ventricular fibrillation in patients with the brugada syndrome. J Am Coll Cardiol. 2006;47:1828–34.
[5] Ucsular F, Karadeniz G, Karadeniz C, Yalnız E, Demir M. Evaluation of Tpeak-Tend interval and Tpeak-end/QT ratio in patients with sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis. 2016;33:151–6.
[6] Selvi F, Korkut M, Bedel C, Kuş G, Zortuk O. Evaluation of Tpeak-end interval, Tpeak-end/QT, and Tpeak-end/Qtc ratio during acute migraine attack in the emergency department. Acta Neurol Belg. 2024;124:949–55.
[7] Li D, Weng Y, Zhen G, Jiang L. Tp-Te interval and Tp-Te/QT ratio are valuable tools in predicting poor outcome in sepsis patients. Front Cardiovasc Med. 2022;9:879085.
[8] Sit O, Oksen D, Atici A, et al. Prognostic significance of Tp-e interval and Tp-e/QTc ratio in patients with COVID-19. Eur Rev Med Pharmacol Sci. 2021;25:3272–8.
[9] Pellathy TP, Pinsky MR, Hravnak M. Intensive care unit scoring systems. Crit Care Nurse. 2021;41:54–64.
[10] Kaur H, Chandran VP, Rashid M, et al. The significance of APACHE II as a predictor of mortality in paraquat poisoning: a systematic review and meta-analysis. J Forensic Leg Med. 2023;97:102548.
[11] Foroughi P, Varshochi M, Hassanpour M, Amini B, Nikniaz Z, Amini H. The predictive role of age and the systemic inflammation indexes on ICU admission and mortality in patients with COVID-19. Int J Aging. 2023;1:e10.
[12] Senaratne JM, Sandhu R, Barnett CF, Grunau B, Wong GC, Van Diepen S. Approach to ventricular arrhythmias in the intensive care unit. J Intensive Care Med. 2021;36:731–48.
[13] Özbek SC, Sökmen E. Usefulness of Tp-Te interval and Tp-Te/QT ratio in the prediction of ventricular arrhythmias and mortality in acute STEMI patients undergoing fibrinolytic therapy. J Electrocardiol. 2019;56:100–5.
[14] Omer E, Zaghla H. Adrenal insufficiency in cardiogenic shock: incidence and prognostic implication. World J Cardiovasc Dis. 2019;09:562–71.
[15] Orban JC, Walrave Y, Mongardon N, et al; AzuRéa Network. Causes and characteristics of death in intensive care units: a prospective multicenter study. Anesthesiology. 2017;126:882–9.
[16] Mahmoodpoor A, Imani F, Soleimanpour H. COVID-19 is not over and needs prediction scores: an endless road! Anesth Pain Med. 2021;11:e121654.
[17] Kahraman F, Yılmaz AS, Demir M, Beşiroğlu F. APACHE II score predicts in-hospital mortality more accurately than inflammatory indices in patients with acute coronary syndrome. Kardiologiia. 2022;62:54–9.
[18] Choi JY, Jang JH, Lim YS, et al. Performance on the APACHE II, SAPS II, SOFA and the OHCA score of post-cardiac arrest patients treated with therapeutic hypothermia. PLoS One. 2018;13:e0196197.
[19] Seoane LA, Espinoza J, Burgos L, et al. Valor pronóstico del sistema de calificación APACHE II en el postoperatorio de cirugía cardíaca [Prognostic value of APACHE II score in postoperative of cardiac surgery]. Arch Cardiol Mex. 2020;90:398–405.

[20] Iles S, Le Heron CJ, Davies G, Turner JG, Beckert LE. ECG score predicts those with the greatest percentage of perfusion defects due to acute pulmonary thromboembolic disease. Chest. 2004;125:1651–6.
[21] Maanja M, Schlegel TT, Fröjdh F, et al. An electrocardiography score predicts heart failure hospitalization or death beyond that of cardiovascular magnetic resonance imaging. Sci Rep. 2022;12:18364.
[22] Kim WD, Lee Y, Kim BS, et al. Electrocardiography score based on the Minnesota code classification system predicts cardiovascular mortality in an asymptomatic low-risk population. Ann Med. 2023;55:2288306.
[23] Odabasi MS, Ozkaya G, Serin E, Akkus A, Yilmaz P, Sayan I. Laboratory findings in predicting intensive care need and death of COVID-19 patients. Int J Med Biochem. 2021;4:77–84.