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A Simple Clinical Model Composed of ECG, Shock Index, and Arterial Blood Gas Analysis for Predicting Severe Pulmonary Embolism

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Abstract

Background: Objective diagnosis of severe pulmonary embolism (PE) is obligatory because of its considerable mortality.
Aim: To assess the abilities of electrocardiography (ECG) score (sECG) and the newly generated scoring system composed of the scores obtained from arterial blood gas (ABG) analysis and shock index (SI) in addition to sECG in predicting severe PE.
Material and Methods: The degree of pulmonary vascular obstruction (sPVO) and the right ventricular dysfunction (RVD) were determined with spiral computed tomography (CT) in 53 consequent patients with PE. Twelve-lead ECG taken within a day of PE event and ABG values were evaluated according to ECG scoring system and original Geneva system, respectively.
Results: The mean age of patients was 62.6 $\pm$ 13.4 years. Right ventricular dysfunction, sPVO $\geq$ 50%, hypoxemia, and SI were present in 34 (64.2%), 27 (50.9%), 50 (94.3%), and 22 (41.5%) patients, respectively. The mean sECG, 5.9 $\pm$ 5.1, was correlated with sPVO, maximum diameter of right ventricle (RV), and right ventricle to left ventricle (RV/LV) ratio ($r = .385$, $r = .415$, and $r = .329$, respectively). The mean newly generated score was 10.9 $\pm$ 5.5 and correlated with sPVO, maximum diameter of RV, and RV/LV ratio ($r = .394$, $r = .483$, and $r = .393$, respectively). Receiver operator characteristic (ROC) curve analyses revealed that sECG $\geq$ 3.5, s (ECG + SI) $\geq$ 4.5, and s (ECG + SI + ABG) $\geq$ 9.5 predict the severe PE patients with 70.6%, 61.8%, 58.8% sensitivities and 52.6%, 63.2%, 73.7% specificities, respectively. **Conclusion:** Adding the scores obtained from SI and ABG to the sECG enhances the specificity of sECG in predicting RVD (+) or severe PE patients, although a lesser degree decreasing in sensitivity may occur.

Keywords

ECG, pulmonary embolism, severity, spiral thorax CT, scoring, shock index, arterial blood gas analysis

Introduction

Pulmonary embolism (PE) is a common clinical problem, and objective diagnosis of the severe form is obligatory because of its considerable morbidity and mortality. The incidence of fatal PE vary from <1% to 7%.[1-3] Two-week mortality or in-hospital clinical worsening in patients with undiagnosed PE ranges between 25% and 38%, while mortality in properly treated patients is lower, as it ranges from less than 1% to 20%.[4] These results highlight the importance of determining the patients' mortality risk in the management of acute PE. The clinical markers such as presence of shock or hypotension, elevated brain natriuretic protein (BNP) or *N*-terminal proBNP, or markers of myocardial injury such as elevated cardiac troponin T or I are the principle markers useful for risk stratification of patients with acute PE.[5] Echocardiographic findings suggesting dysfunction of the right ventricular dysfunction (RVD) have been reported to occur in at least 25% of patients with PE.[6] In literature, there are discordant results about RVD in acute PE. Some authors proposed that RVD is a prognostic marker of complications and death,[7,8] but the others showed no effect.[9,10] In these studies, RVD were evaluated by echocardiographic examination. However, echocardiographic signs of PE have not been universally validated. Additionally, the determination of RVD by echocardiography is examiner dependent, and echocardiography facilities may not be available at all the time.[11] However, there are also recent studies indicating that some echocardiographic findings of PE such as pulmonary

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hypertension, diameters of RV or LV, and shape of interventricular septum may also be detected by computed tomography (CT) examination.[12-15]

Electrocardiography (ECG) is a simple, cheap, and very fast tool to evaluate the patients with PE, and it is feasible at almost all health centers. Numerous findings that are generally nonspecific and reflect the extent and hemodynamic consequences of PE event may be seen in acute phase of PE.[16-18] Recently, an ECG scoring system was developed by Daniel et al.[16] The scores obtained in this system were shown to correlate with the degree of pulmonary hypertension and could predict the patients with the greater percentage of perfusion defects in a ventilation/perfusion (V/Q) scan,[19] as well as predict the patients with RVD by echocardiography.[20] Because of the low specificity of ECG findings to predict severity of PE, noninvasive additional testing is required to identify the patients with severe PE. In literature, there are multiple studies some of which use a clinical model to diagnose PE[21-23] and some of which use ECG to predict the degree of perfusion defect[19,24]; however, there exist no study using a clinical scoring system that aimed to predict severity of PE evaluated by spiral CT pulmonary vascular obstruction index (PVOI). Because both shock and alteration in arterial blood gases (ABGs) are usually seen in severe PE, we hypothesized that adding scores obtained from shock index (heart rate/systolic blood pressure; SI) and arterial blood gas analyses to ECG score (sECG) may increase its ability to predict patients with severe PE. Therefore, this study aimed to analyze the role of sECG alone or in combination with the SI and ABG score in predicting severe PE defined by PVOI and the RVD that were assessed by spiral CT.

Methods

Participants

This prospective study was conducted at Suleyman Demirel University Faculty of Medicine, Research and Practice Hospital in Isparta, Turkey. All adult patients >18 years of age diagnosed as acute PE between the dates of June 2005 and December 2008 were included in the study. If the patient had contrast agent allergy or had renal function impairment, the spiral CT was not used as a diagnostic test. Patients who had a negative spiral CT for PE or who experienced technical insufficiency while performing CT were not enrolled in the study group. Patients were also excluded if the ECGs were not performed within the first 24 hours of detection of PE, if atrial fibrillation was detected on ECG records, or if supplemental oxygen therapy was given while the patient had been evaluated for PE at emergency department or relevant clinics. All participants gave informed consent for spiral CT examination.

None of the patients gave history of a previous PE attack. Diagnosis of PE was confirmed with intermediate–high probability V/Q lung scintigraphy (n = 25). All the remaining patients had either a high clinical suspicion with a high serum D-dimer level result or a positive sign for deep venous thrombosis on a lower extremity venous Doppler ultrasonography. The demographic features of all patients as well as their predisposing factors (permanent or transient risk factors) for PE were recorded. The presence of an underlying cardiopulmonary disease (CPD) was also questioned. Cardiopulmonary disease was defined as the presence of valvular heart or coronary artery disease, history of a myocardial infarction, and left- or right-hand side heart failure. Pulmonary disease comprised chronic obstructive pulmonary disease (COPD), asthma, pneumonia, and any other acute or chronic lung diseases coexistent with PE.

Therapeutic anticoagulation or thrombolytic therapy was administered in accordance with the current guidelines.[25]

Spiral CT Technique

Computed tomography scans were obtained with a single-detector spiral CT (SDSCT) scanner (Tomoscan AV-E1; Philips Medical Systems, Best, the Netherlands). The examination included the volume between the diaphragm and the top of the aortic arch, with a caudocranial direction in suspended respiration. Data were acquired with a 5-mm/s table feed and collimation of 3 mm with reconstruction of overlapping images at 2-mm intervals (1 sec scanning time, 12 kV, 200 mA). The patients received an injection of 90 to 120 mL of a nonionic contrast agent at a rate of 3 mL/s. An automatic injector (Medrad, Pittsburgh, Pennsylvania) was used in every case. Imaging started 15 to 20 seconds after the initiation of contrast material injection. In elder patients or those with signs of right heart failure, we selected a longer delay 20 to 25 seconds. The images were viewed directly on a workstation and displayed in 2 different gray scales, at pulmonary vascular (window width 400 HU; window level 50 HU) and at lung parenchyma (window width 1250 HU; window level −500 HU) settings.

Image Analysis

The CT scans were interpreted by 2 radiologists who were unaware of the clinical signs and symptoms of the patient and the decisions were made by consensus. It was the slightly modified angiographic scoring system of Qanadli et al[26] that had been previously used in a study by Collomb et al.[12] The embolic scores were defined as follows on CT images: (1) each positive peripheral zone had a score equal to the number of segmental branches in a given lobe (upper lobe score = 3, middle lobe score and lingula scores = 2, lower lobe score = 5); (2) the presence of a filling defect at the level of a proximal artery resulted in a score equal to the number of branches that arise distally (lower lobe artery score = 5, middle lobe [lingular] artery score = 2, interlobar artery score = 7, truncus anterior [left upper lobe trunk] score = 3, main pulmonary artery score = 10, pulmonary artery trunk score = 20). When a proximal artery was involved, more peripheral emboli were not scored. A weighting factor is used for the degree of obstruction scored as partial occlusion (value of 1) or complete obstruction (value of 2). The maximum possible score is 40 (thrombus

Table 1. Electrocardiography (ECG) Scoring Method Used in the Study

Findings	Score
Tachycardia (>100 beats/min)	2
Incomplete right bundle-branch block[a]	2
Complete right bundle-branch block[b]	3
S wave in lead I[c]	0
Q wave in lead III[d]	1
Inverted T wave in lead III	1
If all of S1Q3T3 is present, add	2
T-wave inversion in lead V_1 through V_4	4
T-wave inversion in lead V_1, mm	
<1	0
1-2	1
>2	2
T-wave inversion in lead V_2, mm	
<1	1
1-2	2
>2	3
T-wave inversion in lead V_3, mm	
<1	1
1-2	2
>2	3
Total ECG score, maximum 21 points	

[a] QRS complex of 0.10 to 0.11 seconds and an S wave in lead I and terminal R wave in V1 > 1.5 mm.
[b] QRS >0.11 seconds and S wave in lead I and terminal R wave in V_1 > 1.5 mm.
[c] First negative deflection after an R wave > 1.5 mm.
[d] First negative deflection after the P wave and before any R wave > 1.5 mm.

completely obstructing the pulmonary trunk), which corresponds to a 100% obstructing index. The percentage of involvement of arterial circulation by thrombi was found in every patient by dividing the calculated score by the maximum possible score. Thereafter, the severity of the thromboembolic event was defined in 2 categories as nonsevere (<50%) and severe (≥50%). The analysis of parenchymal abnormalities due to PE was not included in this study.

Computed Tomography Signs of Pulmonary Hypertension

We measured maximum minor axes of the RV and LV of the heart according to predefined criteria.[12] The RV/LV minor axis ratio was calculated and was interpreted as RVD if it was >1. Right ventricular dysfunction was considered modest if the ratio was >1 but ≤1.5 and severe if the ratio was >1.5.

Clinical Markers of High Mortality Risk

The ratio of heart rate to systolic arterial blood pressure (SI) was calculated in each patient. If the ratio was ≥1 (SI was positive), 1 point was added to new generated total score and the patient was accepted as having a high mortality risk.[11,20,27]

Arterial Blood Gas Analysis

All ABG analyses were done before supplementary oxygen administration. Arterial oxygen and carbon dioxide tensions were analyzed with a blood gas analyzer (Roche OMNI C; Roche Diagnostics, Mannheim, Germany). In this study, the levels of hypoxemia and hypocapnia and their relevant scores were used as described in the original Geneva scoring system.[27] Briefly, <48.8 mm Hg = 4 points; 48.8 to 59.9 mm Hg = 3 points; 60 to 71.2 mm Hg = 2 points; 71.3 to 82.4 mm Hg = 1 point for partial arterial oxygen tension and <36 mm Hg = 2 points; 36 to 38 mm Hg = 1 point for partial arterial carbon dioxide tension. These points were added to new generated total score.

Electrocardiographic Evaluation

The ECG scoring system used in this study has been previously described by Daniel et al.[19] Briefly, it was based on 4 abnormalities that were previously shown to be associated with massive PE; sinus tachycardia, incomplete or complete right bundle branch block, T-wave inversion, and S1Q3T3 pattern (Table 1). As seen in Table 1, atrial fibrillation is not a component of ECG scoring system. Therefore, these patients were excluded from our study as well as in the study of Kanbay et al.[24] All ECGs were interpreted by one of the cardiologists (E.V. or M.O.) who were unaware of the clinical and radiological findings of the patient. Electrocardiography score were stratified in 3 groups as 0 to 2 points, 3 to 6 points, and ≥7 points. Lastly, a final total score was generated by adding SI and ABG scores to the sECG.

Statistical Analysis

The statistical analysis was performed with Statistical Package for Social Sciences (SPSS; Version 15.0 for Windows, Chicago, Illinois). The mean and SD are given for continuous variables. Pearson correlation test was used for variables that were normally distributed although Spearman correlation test was used for categorical variables. Mann-Whitney *U* test were used to compare mean sECG of patients with PE grouped according to severity by spiral CT (sPVO or RVD groups). Chi-square or Fisher exact *t* tests were used to compare the frequencies of ECG findings in 2 groups of patients. The diagnostic accuracy of the sECG and its combinations with the SI and ABG analysis in predicting the patients with severe PE were represented as a receiver operator characteristic (ROC) curve. Sensitivities and specificities of the sECG and its combinations with the SI and ABG analysis for each variable were calculated. A P value <.05 was considered significant.

This study was approved by the local ethics committee.

Results

Ninety-six patients were diagnosed as acute PE in the study period. Twenty-five patients were excluded from the study due

Table 2. Baseline Characteristics of the Patients Included in the Study

Age, years, mean ± SD, range	62.6 ± 13.4 (23-82)
Male/female	30/23
Hypotension/shock	5 (9.4)
Tachycardia (>100 beats/min)	35 (66)
Shock index, mean ± SD, range	0.95 ± 0.26 (0.50-1.51)
Positive shock index	22 (41.5%)
Pa_{O_2}, mm Hg	57 ± 13.5
Pa_{CO_2}, mm Hg	31.2 ± 8.4
Deep vein thrombosis	27/41 (65.9)
Cardiopulmonary risk factor	20 (37.7)
Comorbidity[a]	40 (75.5)
Hypertension	14 (26.4)
COPD	7 (13.2)
Malignancy	5 (9.4)
Cerebrovascular accident	6 (11.3)
Cardiac failure	5 (9.4)

NOTE: COPD = chronic obstructive pulmonary disease.
[a] Some patients had multiple comorbidities. Unless otherwise indicated, the values are the numbers of patients with percentages in parentheses.

Table 3. Risk Factors Detected in 53 Patients With PE

Risk factors[a]	n (%)
Immobility	44 (83.01)
Advance age (>65 years)	31 (58.43)
Surgery/trauma	24 (45.28)
Smoking cigarette	16 (30.18)
Obesity (BMI ≥ 30)	15 (28.30)
Cardiac failure	8 (15.09)
Malignancy/chemotherapy	7 (13.20)
Previous venous thrombosis	4 (7.54)
Chronic venous insufficiency	4 (7.54)
Hyperviscosity	4 (7.54)
Cerebrovascular accident	3 (5.66)
Genetic disorders (mutations of FV leiden, protrombin G20210A, MTHFR and antithrombin III, deficiency of protein C and S)	3 (5.66)
Oral contraceptive usage	1 (1.88)

NOTES: BMI = body mass index; MTHFR = methylene tetra hydro folate reductase; PE = pulmonary embolism.
[a] Multiple risk factors may be present in 1 patient.

to problems in performing spiral CT. Ten patients met exclusion criteria for ECG records (7 had no ECG record within the first 24 hours of detection of PE and 3 had atrial fibrillation on ECG records). Eight patients who received supplemental oxygen therapy while being evaluated for PE were also excluded from the study. Data of the remaining 53 patients were analyzed.

The mean age of patients (30 M/23 F) was 62.6 ± 13.4 years and ranged between 23 and 82 years. Some clinical features of the patients are presented in Table 2. As seen in Table 3, immobility, advanced age, and surgery/trauma were the most common predisposing factors in our study group found in 83.01%, 58.43%, and 45.28% of the patients, respectively.

On CT examination, thrombi in the pulmonary vasculature were localized bilaterally (including involvement of truncus pulmonalis in 3 patients) in 33 (62.3%) patients, on the right-hand side in 13 (24.5%) patients and on the left-hand side in 7 (13.2%) patients. The mean CT PVOI was found as 42.3 ± 18.7%, and it was classified as ≥ 50% (severe PE) in 27 (50.9%) patients and <50% (nonsevere PE) in 26 (49.1%) patients. Distribution of the index values is shown in Figure 1. The mean diameter of RV was 42.5 ± 7.3 mm (ranged between 26.4 and 59.7 mm). The RV/LV ratio was found as normal in 19 (35.8%) patients, but it was increased in other patients as modest or severe in 18 (34%) and 16 (30.2%) cases, respectively. There was a significant correlation between PVOI and RV/LV ratio ($r = .366$, $P = .007$). The RVD was more frequently seen in severe PE group than those in nonsevere group 24 of 27 (88.9%) and 10 of 26 (38.5%), respectively ($P = .0001$).

At presentation, at least 1 comorbid disease and CPD was found in 40 (75.5%) and 20 (37.7%) of 53 patients, respectively (Table 2). No significant differences in the mean sECG and CT PVOI were found between the groups with and without CPD; 6 ± 4.9 and 41.5% ± 19.5%; 5.9 ± 5.2 and

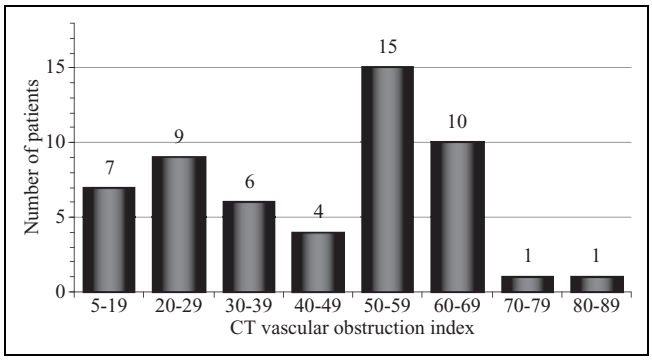

Figure 1. Distribution of computed tomography (CT) pulmonary vascular obstruction indices in the patients.

42.7% ± 18.6%, respectively. The frequency of each ECG abnormalities was also similar. The mean cigarette consumption (pack-years) was the only difference between these 2 groups.

Electrocardiography was found as normal in only 3 (5.7%) patients. Distribution of ECG abnormalities according to the severity of PE and the presence of RVD is shown in Table 4. The most common findings were tachycardia, inverted T wave in lead III, inverted T wave in lead V_1, and Q wave in lead III with the frequency of 66%, 56.4%, 53.7%, and 41.5%, respectively. All abnormalities were seen more frequent in patients with severe PE or in patients with RVD than the other relevant groups. However, statistical significant levels were reached only for negative T in V_2 and in V_1 to V_4 (Table 4).

The mean sECG was found as 5.9 ± 5.1, and it showed a good positive correlation with CT PVOIs, RV diameters, and RV/LV ratio ($r = .385$, $P = .004$; $r = .415$, $P = .002$; and $r = .329$, $P = .016$, respectively). Additionally, mean sECG was also different in the severe PE and nonsevere PE groups;

Table 4. Distribution of Electrocardiography (ECG) Abnormalities in Patients According to the Severity of PE and the Presence of RVD[a]

	Patients					
Findings	Non-severe PE (n = 26)	Severe PE (n = 27)	*P*	RVD (−) (n = 19)	RVD (+) (n = 34)	*P*
Tachycardia (>100 beats/min)	18 (51.4)	17 (48.6)	ns	11 (31.4)	24 (68.6)	ns
Complete RBBB	0 (0)	0 (0)	–	0 (0)	0 (0)	–
Incomplete RBBB	5 (41.7)	7 (58.3)	ns	3 (25)	9 (75)	ns
S in lead I	3 (42.9)	4 (57.1)	ns	2 (28.6)	5 (71.4)	ns
Q wave in lead III	9 (40.9)	13 (59.1)	ns	7 (31.8)	15 (68.2)	ns
Negative T in lead III	15 (48.4)	16 (51.6)	ns	10 (32.3)	21 (67.7)	ns
S1Q3T3	2 (22.2)	7 (77.8)	ns	1 (11.1)	8 (88.9)	ns
Negative T in V_1	11 (37.9)	18 (62.1)	ns	9 (31)	20 (69)	ns
Negative T in V_2	5 (27.8)	13 (72.2)	.042	4 (22.2)	14 (77.8)	ns
Negative T in V_3	6 (33.3)	12 (66.7)	ns	4 (22.2)	17 (77.8)	ns
Negative T in V_1-V_4	2 (18.2)	9 (81.8)	.039	2 (18.2)	9 (81.8)	ns

NOTES: PE = pulmonary embolism; ns = not significant; RBBB = right bundle-branch block; RVD = right ventricular dysfunction.
[a] Values presented as numbers and percentages.

Table 5. The Distribution of ECG, ECG + SI, ECG + ABG, and ECG + SI + ABG Scores in Patients With PE According to Severity of Disease or Presence of RVD

	Score	Nonsevere PE (n = 26)	Severe PE (n = 27)	*P*	RVD (−) (n = 19)	RVD (+) (n = 34)	*P*
ECG	0-2	11 (61.1)	7 (38.9)	.029	10 (55.6)	8 (44.4)	.042
	3-6	12 (60)	8 (40)		7 (35)	13 (65)	
	7+	3 (20)	12 (80)		2 (13.3)	13 (86.7)	
ECG + SI	0-3	12 (63.2)	7 (36.8)	.028	10 (52.6)	9 (47.4)	.060
	4-7	11 (57.9)	8 (42.1)		7 (36.8)	12 (63.2)	
	8+	3 (20)	12 (80)		2 (13.3)	13 (86.7)	
ECG + ABG	0-8	16 (64)	9 (36)	.009	13 (52)	12 (48)	.050
	9-12	8 (57.1)	6 (42.9)		4 (28.6)	10 (71.4)	
	13+	2 (14.3)	12 (85.7)		2 (14.3)	12 (85.7)	
ECG + SI + ABG	0-9	18 (64.3)	10 (35.7)	.022	14 (50)	14 (50)	.016
	10-13	5 (50)	5 (50)		3 (30)	7 (70)	
	14+	3 (20)	12 (80)		2 (13.3)	13 (86.7)	

NOTES: ABG = arterial blood gas; ECG = electrocardiography; PE = pulmonary embolism; RVD = right ventricular dysfunction; SI = shock index.

4.2 ± 3.4 versus 7.6 ± 5.8, respectively ($P = .014$). The sECG were grouped as 0 to 2 points, 3 to 6 points, and >7 points in 18 (34%), in 20 (37.7%), and in 15 (28.3%) patients, respectively. Severe PE and RVD were more frequently detected in patients having higher sECG group in comparison with those having lower sECG ($P = .029$ and $P = .042$, respectively; Table 5).

The mean SI was 0.95 ± 0.26 and ranged between 0.5 and 1.51 in the whole group. We found that mean SI was similar in the severe and nonsevere PE groups, but it was statistically different in patients with and without RVD, 1.01 ± 0.24 and 0.85 ± 0.27, respectively ($P = .027$). All ECG abnormalities were more frequent in SI positive (n = 17) than negative ones (n = 17) in the subgroup analysis of RVD (+) cases without statistically significance. Positive SI (≥ 1) was present in 22 (41.5%) of 53 patients, but only 5 (9.4%) of them was accepted as massive PE. In massive PE group, the median 25th to 75th percentiles of the RV and RV/LV were found to be higher than those in nonmassive PE cases; 44.8 to 58.1 and 1.4 to 2.0 versus 36.2 to 46.4 and 0.8 to 1.5, respectively ($P = .007$ and $P = .003$).

In the ABG, hypoxemia was found in 50 (94.3%) of the 53 patients. The mean Pao_2 was 57 ± 13.5 mm Hg. Mild, moderate, severe, and very severe hypoxemia were detected in 4 (7.5%), 12 (22.6%), 17 (32.1%), and 17 (32.1%) of all patients, respectively. The hypoxemia score was correlated with the mean diameter of RV, the RV/LV ratio ($r = .348$, $P = .011$ and $r = .313$, $P = .023$, respectively) but not with mean CT PVOI. Hypocapnia was found in 46 (86.8%) of the 53 patients. The mean $PaCO_2$ level was 31.2 + 8.4 mm Hg (ranged 17 to 63 mm Hg). $Paco_2$ level was negatively correlated with RV/LV ratio and CT PVOI ($r = -.300$, $P = .029$ and $r = -.392$, $P = .004$, respectively).

The mean total score obtained from SI, ABG analyses, and ECG was 10.9 ± 5.5 (ranged between 2 and 26) and positively correlated with CT PVOI, right ventricular diameter, and RV/LV ratio ($r = .394$, $P = .004$; $r = .483$, $P = .0001$; and $r = .393$, $P = .004$, respectively). Although statistically significance levels were not reached, the mean scores of ECG, ECG + SI, ECG + ABG, ECG + ABG + SI were found as 6.2 ± 4.7 versus 7.8 ± 5.8, 6.2 ± 4.7 versus 8.8 ± 5.8, 10.8 ± 4.7 versus

Table 6. The Area Under the Curve for Each Scores in the ROC Analyses for Predicting Patients With Severe PE

Scores	Area	SE	*P*	95% CI
ECG	0.667	0.076	.037	0.519-0.815
ECG + SI	0.664	0.076	.041	0.515-0.813
ECG + ABG	0.711	0.072	.008	0.570-0.851
ECG + SI + ABG	0.707	0.072	.010	0.566-0.849

NOTES: ABG = arterial blood gas; ECG = electrocardiography; PE = pulmonary embolism; ROC = receiver operator characteristic; SI = shock index.

Table 7. The Area Under the Curve for Each Scores in the ROC Analyses for Predicting RVD (+) PE

Scores	Area	SE	*P*	95% CI
ECG	0.681	0.077	.030	0.530-0.832
ECG + SI	0.687	0.077	.025	0.537-0.838
ECG + ABG	0.738	0.073	.004	0.595-0.882
ECG + SI + ABG	0.735	0.073	.005	0.593-0.878

NOTES: ABG = arterial blood gas; PE = pulmonary embolism; ROC = receiver operator characteristic; RVD = right ventricular dysfunction; SI = shock index.

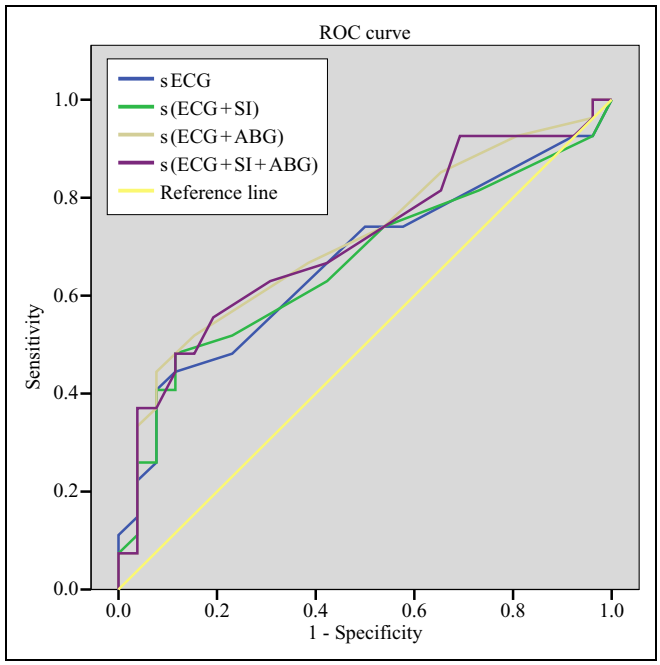

Figure 2. Receiver operator characteristic (ROC) curve analyses for predicting severe pulmonary embolism (PE) patients.

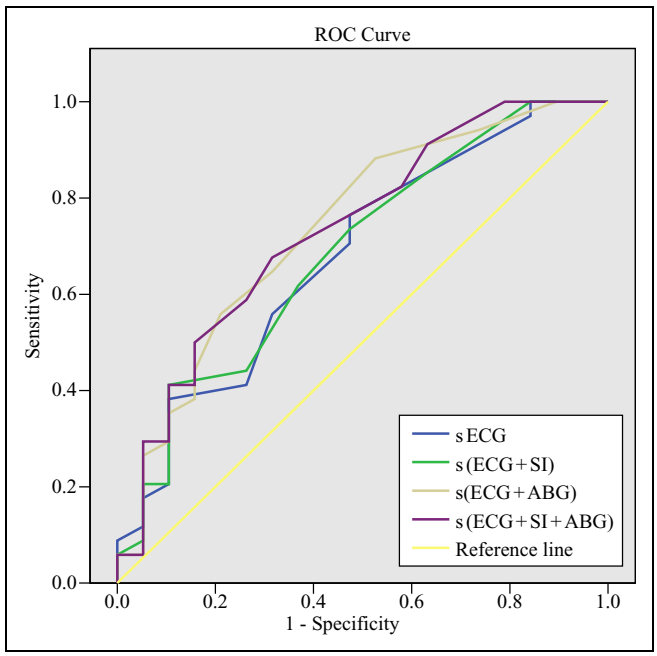

Figure 3. Receiver operator characteristic (ROC) curve analyses for predicting RVD (+) patients with PE.PE indicates pulmonary embolism; RVD = right ventricular dysfunction.

12.7 ± 6.2, and 10.9 ± 4.6 versus 13.9 ± 6.1 in the groups with SI-positive and SI-negative PE patients with RVD, respectively.

To assess the ability of the mean sECG and other newly generated scores, namely (ECG + SI), (ECG + ABG), and (ECG + SI + ABG), and to predict those with severe PE and RVD (+) PE, a ROC curve was constructed. The ROC curve analyses revealed that sECG ≥ 3.5, s (ECG + SI) ≥ 4.5, s (ECG + ABG) ≥ 8.5, and s (ECG + SI + ABG) ≥ 9.5 can predict severe PE patients with 74.1%, 63%, 66.7%, and 63% sensitivities and 50%, 57.7%, 61.5%, and 69.2% specificities, respectively (Table 6, Figure 2). Receiver operator characteristic curve analyses also revealed that sECG ≥ 3.5, s (ECG + SI) ≥ 4.5, s (ECG + ABG) ≥ 8.5, and s (ECG + SI + ABG) ≥ 9.5 can predict PE patients with RVD with 70.6%, 61.8%, 64.7%, and 58.8% sensitivities and 52.6%, 63.2%, 68.4%, and 73.7% specificities, respectively (Table 7, Figure 3).

In a period of 30 days, 9 patients died in hospital due to PE (1 recurrent PE and 1 major bleeding due to thrombolytic treatment) or other underlying diseases (3 malignant processes, 1 decompensated cardiac failure, and 3 cerebrovascular accidents).

Discussion

In the current study, we have found that the newly generated scores obtained by adding SI and ABG scores was more valuable than the sECG alone for predicting severe PE defined according to the CT PVOI.

For defining PE severity, a number of interpretations can be used such as presence of symptoms like syncope, shock, or SI, and more objectively presence of RVD determined by ECG, echocardiography, or CT. Pulmonary embolism severity can also be assessed by determining the burden of embolic occlusion of pulmonary arterial bed by means of pulmonary angiography,[28,29] lung scintigraphy,[30] or spiral CT.[26] Spiral CT is now routinely used as the first-line diagnostic modality for acute PE in many centers due to high sensitivity and specificity values.[14,31-34] The reported sensitivity and specificity of SDSCT for the diagnosis of PE has ranged between 53% and 100% and 81% and 100%, respectively.[31,32,35,36] A number of methods have been proposed to quantify the extension of

perfusion defect using a spiral CT scan[10,12,26]; the most accepted one is the PVOI, as used in our study, referred by Qanadli et al.[26] In this study, SDSCT was used for both diagnosing and assessing severity of the patients with acute symptomatic PE. Almost half of our patients (50.9%) had severe PE and almost two thirds of them (64.2%) had also RVD on admission. In previous studies, it was also shown that some of the well-described echocardiographic morphologic cardiac parameters of severe PE such as abnormalities of the size of RV, LV, pulmonary artery, and RVD might also be detected using spiral CT.[14,34,37]

Although life-threatening PE traditionally has been equated with anatomically massive PE (defined as a >50% obstruction of the pulmonary vasculature or the occlusion of 2 or more lobar arteries), the consequences of thromboembolism in the lung also depend on the cardiopulmonary reserve of the patient. Patients with preexisting CPD often have diminished pulmonary vascular reserve, and even a relatively minor embolus may result in significant hemodynamic instability.[38] In the Urokinase Embolic Pulmonary Massive PE trial, 90% of the patients who presented in shock had prior CPD and 56% of the patients with prior CPD presented in shock compared to 2% of patients without CPD.[39] In our study, prior CPD was detected in 20 patients and 40% of them had a positive SI. Positive SI was detected in 22 patients and 36.4% of them had prior CPD. In our study, no significant difference was found in mean sECG and other newly generated scores between the groups with or without CPD.

There are several studies evaluating the 12-lead ECG for its potential use in the diagnosis of PE and in determining the severity and prognosis of the disease.[16-18] In a study done by Sinha et al,[18] sinus tachycardia (39% vs 24%), an S1Q3T3 pattern (12% vs 3%), atrial tachyarrhythmias (15% vs 4%), a Q wave in lead III (40% vs 26%), and a Q3T3 pattern (8% vs 1%) were the findings significantly associated with PE. These findings are generally nonspecific and often change over time, with worsening or resolution of the embolic event. Even the classical S1Q3T3 pattern that was described by McGinn and White[40] in 1935 in 7 patients with acute cor pulmonale lacks specificity. However, once the diagnosis of PE has been established, the ECG could have a role in differentiating 2 forms, massive and nonmassive PE, of the disease. Yoshinaga et al[41] reported that S1Q3T3 pattern is the most frequently seen ECG abnormality in massive PE diagnosed with pulmonary arteriography and at least 5 ECG abnormalities were noted in patients with mean pulmonary artery pressure (PAP) >45 mm Hg. In a prospective study, it has been found that T-wave inversion in the precordial leads is the most common abnormality (68%) and represents the ECG sign best correlated to the severity of PE. Among those patients with anterior T-wave inversion, 90% had a Miller index >50% (mean, 60% $\pm$ 8%), 81% had a mean PAP >30 mm Hg (mean, 37% $\pm$ 8%).[42] In a recent study, Abecasis et al[43] report that anterior and inferior T-wave inversion is the most frequently associated ECG finding in the case of massive and submassive PE. In accordance with the literature, normal ECG findings were found in only 3 (5.7%) patients in current study. Tachycardia, inverted T wave in lead III, and in lead V_1, and Q wave in lead III were the most common findings with a frequency of 66%, 56.4%, 53.7%, and 41.5%, respectively. Almost all ECG abnormalities were more frequent in patients with RVD or severe PE. T-wave inversions in at least 1 precordial derivation were found in 31 (58.5%) of 53 patients, more frequent in patients with severe PE and represent the ECG sign best reflecting the severity of the PE (Table 4). Among patients with diffuse anterior T-wave inversion, 81.8% of patients had RVD with mean right ventricular diameter of 45.8 $\pm$ 5.6 mm.

In a prospective study by Iles et al,[19] 229 acute PE patients with high-probability V/Q scan were investigated and ECG was found to predict those with the greatest amount of perfusion defects. In their study, mean sECG was found as 2.6 $\pm$ 2.8 in patients with <30% perfusion defect, 3.2 $\pm$ 2.9 in patients with 30% to 50% perfusion defect, and 5.3 $\pm$ 3.7 in patients with >50% perfusion defect. A sECG of $\geq$3 predicted those with severe PE with a sensitivity of 70% (95% confidence interval [CI], 59-81%) and a specificity of 59% (95% CI, 51-67%). In contrast to our study and previous studies, the mean sECG, Wells scores, and combined scores were not different in severe and nonsevere patients with PE according to Kanbay et al.[24] In their study, an ECG score of 6.5 predicts severe disease, with a sensitivity of 41.7% and a specificity of 82%, and no beneficial effect of combined scores over ECG scoring system was found in predicting anatomic severity of PE evaluated by scintigraphically.[24] In our study, good positive correlations were found between both the mean sECG and the newly generated total scores and severity of disease assessed by RV/LV ratio and CT PVOI. In contrast to study done by Kanbay et al,[24] the mean ECG score was also different in severe and nonsevere patients with PE, but as similar with their findings, an ECG score $\geq$3.5 predicts severe PE patients with a sensitivity of 74.1% and specificity of 50%. If 7 points were chosen as a cutoff point of the sECG, severe disease was predicted with a 44.5% and 88.5% sensitivity and specificity, respectively.

However, the main issue is to differentiate massive and submassive forms of PE with high mortality that need to be treated with thrombolytics or surgery. In our study, subgroup analysis of ECG findings was not helpful to differentiate RVD (+) PE patients with SI-positive or -negative ones, although all ECG abnormalities were more frequent and newly generated scores were higher in SI-positive cases. Stein et al[44] studied ECGs of 90 patients with arteriographically documented acute submassive or massive PE and showed that the ECG was normal in 6% and 23% of patients, respectively. Larger defects on the lung scan or pulmonary arteriogram had been detected in patients with various abnormalities on the ECG than in patients with normal ECGs.

In patients with PE, one of the clinical risk factors for adverse outcome is the clinical signs on admission. The reported incidence of the initial presence of shock ranges between 4.2% and 9% of all patients.[3,45,46] In the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study, 10% of all patients (38 of 383 patients) presented with circulatory collapse, as defined by the presence of shock or

syncope.[30] In the MAPPET (Management and Prognosis in Pulmonary Embolism Trial) study,[47] it was reported that 59% of 1001 patients had hemodynamic instability on presentation (cardiac arrest, 18%; shock requiring vasopressor therapy support, 10%; and arterial hypotension of <90 mm Hg not requiring vasopressor therapy, 31%). The PE patients with syncope have a higher risk of death within 30 days than the patients without syncope, 14.4% versus 7.3%, respectively.[47] In our study, the rates of 9.4% (5 of 53 patients) of unstable severe PE and 41.5% (22 of 53 patients) of arterial hypotension and/or tachycardia that resulted in positive SI were found quite similar to the previous results. Of the 5 patients who had syncope, all had massive PE and were treated with thrombolytics; only one of them died due to postoperative major hemorrhage.

Some degree of arterial hypoxemia usually develops in patients with PE as a result of widening of the arteriovenous oxygen gradient caused by right ventricular failure, V/Q mismatch, or loss of pulmonary surfactant. Although the diagnostic utility of hypoxemia is very low, blood gas analysis is often performed in the initial diagnosis of acute PE and the presence of hypoxemia strengthen the suspicion of PE. In our study, hypoxemia was found in almost all (94.3%) the patients and associated with the right ventricular diameter, RV/LV ratio, and RVD but not with the CT PVOI. However, hypocapnia level was negatively correlated with the right ventricular diameter, RV/LV ratio, and CT PVOI. Hypoxemia level was more profound in RVD (+) PE group ($P = .041$). In contrast to our study, Metafratzi et al[48] have observed a good correlation between the degree of angiographic obstruction and the blood gas values in patients with PE without CPD. They stated that a $Paco_2$ value of 30 mm Hg or less is highly suggestive of an obstruction index of more than 50% of the arterial bed. In a recent study, it has been shown that the measurement of alveolar-arterial oxygen pressure gradient is a simple and a highly useful method for predicting short-term prognosis in patients with acute PE.[49]

Finally, we generated newly combined scores via adding the scores obtained from SI and ABG analysis to sECG to predict the patients with severe PE. The mean total score was found to be positively correlated with CT PVOI, right ventricular diameter of RV, and the RV/LV ratio. We found that the likelihood of a patient having severe PE or RVD (+) PE group increase with increasing points of each score. According to ROC analyses, patients with $\geq$50% CT PVOI could be predicted accurately by our newly generated scores. In conclusion, a sECG of ≥ 3.5 has a relatively low sensitivity and specificity in predicting the patients with RVD or severe PE. The specificity of ECG may be increased by adding the scores obtained from SI and ABG to the sECG. Our promising results about predicting the patients with severe PE who needs thrombolytics without an angiographic or echocardiographic examination should be further evaluated by future studies comprising larger number of patients.

Declaration of Conflicting Interest

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