Is it possible to use standard electrocardiography for risk assessment of patients with pulmonary embolism?

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Abstract

Background: Risk stratification of patients with acute pulmonary embolism (APE) is crucial for appropriate treatment selection. Shock and hypotonia are known indications for aggressive management. However, in the haemodynamically stable group the best prognosis strategy is still being sought. Acute pulmonary embolism often provokes changes in electrocardiography recordings (ECG). **Aim:** To assess whether ECG features recorded on admission can be useful for risk stratification during hospitalisation.

Methods: We analysed 12-lead ECG and echocardiography of 56 patients (22 males, age: 64.3 ± 17.9 years) with diagnosed APE. The diagnosis of APE was confirmed by spiral computer tomography. The ECG analysis was based on the 21-point ECG score including: the presence of tachycardia (> 100 beats/min), right bundle branch block, negative S waves in lead I, negative Q or T waves in lead III, S1Q3T3 complex and depth of negative T waves in leads V_1-V_4 . ECG features were scored from 0 to 21 points. Complicated in-hospital course was defined as need for vasopressor, thrombolysis, embolectomy or resuscitation and the presence of shock index > 1 (heart rate/systolic blood pressure).

Results: Four (7.1%) patients died during hospitalisation and in 8 (14.3%) others complications occurred. Patients with complications had higher mean sum of 21-ECG score compared to subjects with uneventful course [8 (1-17) vs. 3 (0-18); p = 0.04]. Right ventricular contractility dysfunction (RVD) in echocardiography was found in 13 (23.2%) patients, who had higher ECG score compared to patients without RVD [8 (3-17) vs. 2 (0-18); p = 0.004]. The area under the ROC curve to assess the usefulness of 21-ECG score to predict RVD was 0.794 (95% CI 0.665-0.891) and for PPH 0.727 (95% CI 0.591-0.837). The sensitivity and specificity, positive and negative predictive value for the value > 3 points in 21-ECG score to predict RVD were: 92, 65, 44, 97% and for PPH: 75, 46, 19, 92%, respectively.

Conclusions: 21-ECG score is a simple and cheap method which can be used to predict RVD and serious complications in patients with APE. A value \leq 3 points in the 21-ECG score can exclude RVD with high probability and limit the need of echocardiography to 23% of haemodynamically stable patients.

Key words: pulmonary embolism, risk stratification, electrocardiogram

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Introduction

Patients with acute pulmonary embolism (APE) form an inhomogeneous population in which the choice of the best management is often difficult. According to the current guidelines, therapy should be tailored to the estimated risk of death due to APE [1]. Currently, risk assessment in this group is based on clinical examination, evaluation of right ventricular (RV) volume overload, most commonly using echocardiographic study, and the markers of myocardial injury [1]. Patients with shock and hypotonia have the worst prognosis – the risk of death in this group exceeds 15%. The demonstration of RV function abnormalities in the echocardiographic study even in stable

haemodynamic patients indicates an intermediate risk [2, 3]. As an alternative for echocardiographic study RV measurements by computed tomography or natriuretic peptides analysis can be utilised [4, 5]. There are reports indicating that a standard electrocardiographic (ECG) study can be useful in risk stratification in this population [6]. It is worth mentioning that echocardiography is not available 24 h a day in all centres whereas ECG is performed routinely in all patients with chest pain and dyspnoea – the most common symptoms of APE.

The ECG in APE can be completely normal. However, changes in ECG can often be observed, including arrhythmias (sinus tachycardia, atrial fibrillation or atrial flutter), changes of the P wave and QRS axis or

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morphology, non-specific ST segment changes and negative T waves in the RV leads, S1Q3T3 complex (S wave in the I lead, Q wave in lead III and negative T wave in lead III), and complete or incomplete right bundle branch block [7]. Electrocardiographic changes have been described in 77% of patients with submassive APE and in 94% of patients with the massive type [8]. The presence of negative T waves in lead III was observed in 88% of patients with APE [9]. Ferrari et al. demonstrated that the most common change in the ECG was the presence of negative T waves in the precordial leads. This sign showed the closest correlation with disease severity, and T wave normalisation within 6 days after thrombolytic therapy is regarded as a good prognostic marker [10]. Negative T waves in precordial leads and in the inferior leads, which can be found in ECG of patients with APE, often mimic changes occurring in acute coronary syndromes without ST segment elevation [11]. Moreover, ST segment depression in this group of patients may indicate myocardial injury, which in turn probably results in poorer outcome [12]. Daniel et al. proposed a 21-point ECG scale to evaluate the association between the severity of pulmonary hypertension and ECG in patients with APE [13] (Table I).

The aim of the study was to evaluate the usefulness of ECG in predicting RV function abnormalities and outcome in patients with confirmed APE using the 21-point ECG scale.

Methods

The study population included 56 consecutive patients (22 male - 39.3% and 34 female - 60.7%, mean age 64.3 ± 17.9 years) hospitalised due to APE in years 2006-2007. The diagnosis of APE was confirmed in all patients using spiral computed tomography. In each patient we performed a retrospective analysis of the standard 12-lead ECG on admission and the first available echocardiographic study performed within 24 h after diagnosis. The 21-point scale previously described by Daniel et al. [13] was used to evaluate ECG. The scale includes: tachycardia (heart rate > 100 beats per minute), right bundle branch block, the presence of S wave in the first lead, Q wave or negative T wave in lead III, S1Q3T3 complex, and the amplitude of negative T waves in V_1-V_4 . Thereafter points for the presence and severity of each criterion of the ECG scale are summed up. A precise description of the ECG scale in presented in Table I. The total score ranged from 0 to 21.

The following parameters were assessed in the echocardiographic study: left ventricle (LV) and RV dimensions, pulmonary acceleration time and the peak gradient of tricuspid insufficiency. The RV overload was defined as an RV/LV ratio > 0.6, peak gradient of tricuspid regurgitation exceeding 30 mmHg and shortened pulmonary acceleration time \leq 90 ms. In addition to these parameters, qualitative RV function abnormalities, defined as hypo- or

Table I. 21-point scale of ECG changes developed by Daniel et al. [13]

Sign	Points
Tachycardia (> 100/min)	2
Incomplete right bundle branch block	2
Complete right bundle branch block	3
Negative T wave in leads V ₁ –V ₄	4
Negative T wave in lead V ₁ [mm]	
< 1	0
1-2	1
> 2	2
Negative T wave in lead V ₂ [mm]	
< 1	1
1-2	2
> 2	3
Negative T wave in lead V ₃ [mm]	
< 1	1
1-2	2
> 2	5
S wave in lead I	0
Q wave (> 1.5 mm) in lead III	1
Negative T wave in lead III	1
S1Q3T3 complex	2

akinesia of the RV free wall or RV apex in four-chamber view, were analysed. The pre-specified endpoints included: death and complications during hospitalisation. Complications during hospitalisation were defined as the occurrence of at least one of the following events: the need of infusion of ≥ 1 vasopressor agent, need for thrombolysis, embolectomy or cardiopulmonary resuscitation, shock index > 1 (heart rate divided by systolic blood pressure) [14].

Statistical analysis

Normally distributed variables are presented as means with standard deviations. Data without normal distribution are presented as medians with range. T-test was used for comparisons between normally distributed variables and Mann-Whitney test (for comparisons between two groups) or Kruskal-Wallis test (for more than two groups) were used for not normally distributed variables. Categorical variables were compared using the chi-square test. Receiver operator curves (ROC) were used to assess the usefulness of measurements, identify the cut-off value, and to determine sensitivity and specificity of the test. A p value < 0.05 was considered statistically significant. The statistical analysis was performed with MedCalc software.

Results

There were 4 (7.1%) in-hospital deaths among 56 studied patients. An additional 8 (14.3%) patients experienced complications during hospitalisation. The baseline characteristics of the study group are presented in Table II.

746 Maciej Kostrubiec et al.

Table II. Clinical characteristics of 56 patients with acute pulmonary embolism divided according to the outcome: a) composite end point (complications during hospitalisation with the need to use ≥ 1 vasopressor agent, the need for thrombolysis, embolectomy or cardiopulmonary resuscitation), b) in-hospital death

	Complications during hospitalisation			Death during hospitalisation		
	yes n = 8	no n = 48	р	yes no n = 4 n = 52	р	
Male gender, n (%)	6 (75)	16 (33.3)	0.04	2 (50) 20 (38.5)	NS	
Age [years]	66 ± 21.1	64 ± 17.6	NS	80.3 ± 9.6 46.1 ± 23.8	NS	
sBP [mmHg]	121.9 ± 20.3	130.6 ± 22.7	0.02	121.3 ± 29.5 130±22.1	NS	
dBP [mmHg]	73.8 ± 19.2	79.5 ± 14.1	0.02	72.5 ± 27.5 79.1 ± 13.8	NS	
HR [1/min]	120.3 ± 27.8	85.9 ± 19.9	< 0.001	110.5 ± 38.5 89.3 ± 22.6	NS	
Smoking, n (%)	3 (37.5)	20 (41.7)	NS	3 (75) 20 (38.5)	NS	
Immobilisation > 3 days, n (%)	1 (12.5)	4 (8.3)	NS	0 (0) 5 (9.6)	NS	
Venous thromboembolic disease, n (%)	4 (50)	25 (56.3)	NS	1 (25) 30 (57.7)	NS	
Malignant neoplasm, n (%)	1 (12.5)	13 (27.1)	NS	1 (25) 13 (25)	NS	
Oral contraceptives, n (%)	0 (0)	2 (4.2)	NS	0 (0) 2 (3.8)	NS	
HRT, n (%)	0 (0)	1 (2.1)	NS	0 (0) 1 (1.9)	NS	
Hypertension, n (%)	2 (25)	24 (50)	NS	2 (50) 25 (48.1)	NS	
Injury in the history, n (%)	2 (25)	9 (18.8)	NS	0 (0) 11 (21.2)	NS	
Surgery in the history, n (%)	3 (37.5)	32 (66.7)	NS	1 (25) 34 (65.4)	NS	
CAD/HF, n (%)	3 (37.5)	17 (35.4)	NS	2 (50) 18 (34.6)	NS	
RV systolic function abnormalities, n (%)	2 (25)	11 (22.9)	NS	0 (0) 13 (25)	NS	
RV overload, n (%)	4 (50)	26 (54.2)	NS	3 (75) 27 (51.9)	NS	

 $Abbreviations: sBP-systolic\ blood\ pressure,\ dBP-diastolic\ blood\ pressure,\ HR-heart\ rate,\ HRT-hormone\ replacement\ the rapy,\ CAD-coronary\ artery\ disease,\ HF-heart\ failure,\ RV-right\ ventricle$

Table III. Electrocardiographic data in the study group

	Complications during hospitalisation			Death during hospitalisation		
	yes n = 8	no n = 48	р	yes n = 4	no n = 52	р
Tachycardia (HR > 100/min), n (%)	7 (87.5)	9 (18.8)	0.0003	3 (75)	0 (0)	NS
Incomplete RBBB, n (%)	0 (0)	5 (10.4)	NS	0 (0)	5 (9.6)	NS
RBBB, n (%)	4 (50)	14 (29.2)	NS	2 (50)	16 (30.8)	NS
S wave in lead I, n (%)	5 (62.5)	20 (41.2)	NS	2 (50)	23 (44.2)	NS
Q wave in lead III, n (%)	4 (50)	19 (39.6)	NS	1 (25)	22 (42.3)	NS
Negative T wave in lead III, n (%)	3 (37.5)	22 (45.8)	NS	1 (25)	24 (46.2)	NS
S1Q3T3, n (%)	3 (37.5)	8 (16.7)	0.04	1 (25)	10 (19.2)	NS
T wave in leads V ₁ –V ₄ , n (%)	1 (12.5)	7 (14.6)	NS	1 (25)	7 (13.5)	NS
T wave in lead V ₁						
< 1 mm, n (%)	8 (100)	34 (70.8)	NS	4 (100)	37 (71.2)	NS
1-2 mm, n (%)	0 (0)	10 (20.8)	NS	0 (0)	10 (19.2)	NS
> 2 mm, n (%)	0 (0)	4 (8.3)	NS	0 (0)	5 (9.6)	NS
T wave in lead V ₂						
< 1 mm, n (%)	7 (87.5)	42 (87.5)	NS	4 (100)	45 (86.5)	NS
1-2 mm, n (%)	0 (0)	2 (4.2)	NS	0 (0)	2 (3.8)	NS
> 2 mm, n (%)	1 (12.5)	4 (8.3)	NS	0 (0)	5 (9.6)	NS
T wave in lead V ₃						
< 1 mm, n (%)	7 (87.5)	41 (85.4)	NS	4 (100)	44 (84.6)	NS
1-2 mm, n (%)	1 (12.5)	3 (6.3)	NS	0 (0)	4 (7.7)	NS
> 2 mm, n (%)	0 (0)	4 (8.3)	NS	0 (0)	4 (7.7)	NS
Total score (median and range)	8 (1-17)	3 (0-18)	0.04	3.5 (0-15)	3 (0-18)	NS

Abbreviations: HR – heart rate, RBBB – right bundle branch block

In patients with in-hospital complications more points on the ECG scale were noted, when compared to the group with uneventful course. In patients who died during hospitalisation a non-significant trend toward higher total score in the ECG scale was observed when compared to the rest of patients. Tachycardia and S1Q3T3 sign were more often observed in patients with complications. On the other hand, the presence of negative T-waves did not differ between studied groups (Table III).

In 30 (53.6%) patients RV overload as assessed with echocardiography was observed and systolic function abnormalities were observed in 13 (23.2%) individuals. The total number of points on the ECG scale was higher in patients with the presence of RV overload in the echocardiographic study, when compared to patients without RV overload, but the difference did not reach statistical significance [5.5 (0-18) vs. 2 (0-15); NS]. On the other hand, patients with RV systolic dysfunction present in the echocardiographic study were characterised by significantly higher total score on the ECG scale when compared to patients without RV hypokinesia [8 (3-17) vs. 2 (0-18); p = 0.0004]. Area under the ROC curve evaluating the usefulness of the ECG scale in predicting RV systolic dysfunction was 0.794 (95% CI 0.665-0.891) (Figure 1). Area under the curve assessing the usefulness of the ECG scale in predicting complicated course of APE was 0.727 (95% CI 0.591-0.837) (Figure 2), and for prediction of in-hospital mortality 0.520 (95% CI 0.366--0.639). Sensitivity and specificity, positive and negative predictive values with a cut-off value of > 3 points for predicting RV systolic dysfunction were: 92, 65, 44, 97%; for RV overload: 60, 65, 67, 59%; for complications: 75, 46, 19, 92% and for death: 50, 54, 7, 94%, respectively.

There was a significant correlation between total points on the ECG scale and the presence of RV dysfunction in the echocardiographic study (r=0.433; p=0.001). We also observed a weak but significant correlation between ECG scale and the occurrence of complications (r=0.276; p=0.04). The presence of tachycardia correlated with complications (r=0.420; p=0.002) and with total mortality (r=0.285; p=0.03). No other significant correlations for electrocardiographic changes were observed. Total score on the ECG scale correlated neither with mortality, nor with RV overload. No correlation between the presence of tachycardia in the ECG and RV dysfunction was observed.

Discussion

The risk of death in patients with APE should be evaluated on the basis of clinical signs such as the presence of shock and hypotonia [15]. Further evaluation should be based on RV dysfunction and biochemical markers of myocardial injury [16, 17]. Risk stratification in patients with APE is of crucial importance in tailoring the most suitable therapy [18]. Patients with

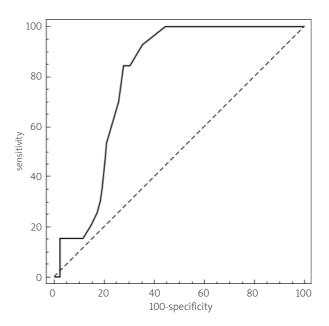


Figure 1. ROC curve for prediction of right ventricular dysfunction in the echocardiographic study on the basis of the total points on the ECG scale

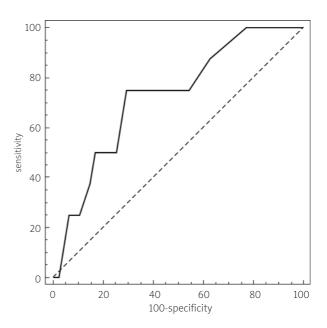


Figure 2. ROC curve for prediction of complications during hospitalisation on the basis of the total points on the ECG scale

shock and hypotonia should receive thrombolytic therapy [1]. Moreover, it seems that a group of normotensive patients but with RV overload and markers of RV injury can benefit from aggressive treatment [19, 20].

An association between RV dysfunction and mortality in patients with APE has been demonstrated in previous studies

748 Maciej Kostrubiec et al.

[21, 22]. However, in some patients visualisation in echocardiographic study is insufficient for reliable RV function assessment. It is also hard to introduce repeated echocardiographic evaluation into everyday clinical practice in order to monitor the severity of RV dysfunction [23]. It seems justified to search for a simple, readily-available test which could serve as an initial evaluation, and which could limit the number of patients requiring ultrasound study. The role of the ECG scale, developed by Daniel et al. [13] for in-hospital risk stratification in patients with APE, is not yet clearly defined. The previous studies indicated that it can be useful in the identification of cases of high pulmonary hypertension. With the total score \geq 10 points, a pressure value exceeding 50 mmHg in the angiographic measurements was observed, and the mortality was over 50% [13].

The ECG point scale was evaluated in a cohort study by Iles et al. in a group of 229 patients with high probability of APE on the basis of ventilation-perfusion scintigraphy according to PIOPED criteria [24]. Total score ≥ 3 indicated patients with perfusion abnormalities exceeding 50% with sensitivity of 70% and specificity of 95%. The authors of this study have suggested that the ECG point scale could be used for an initial evaluation of patients with suspected APE. However, the scale was less useful for differentiating between patients with APE with < 30% or 30-50% pulmonary perfusion abnormalities [24]. In the study by Toosi et al. the results with ≥ 3 on the ECG scale correlated significantly with RV dysfunction. However, the predictive value of the scale in prognosis of in-hospital complications was relatively low. Interestingly, for the total score ≤ 3 an association with better prognosis was observed [6].

In our study the total score on the ECG scale was significantly higher in patients with complications during hospitalisation when compared to the group without complications. It should be underlined that a result \leq 3 points on the ECG scale represented a high negative predictive value and was associated with 90% probability of uncomplicated clinical course. It indicates that on the basis of a simple, cheap and readily available test represented by ECG the risk of in-hospital complications can be estimated even at the first evaluation of a patient with APE.

Wall motion abnormalities of the RV in patients with APE are associated with higher risk of death in short-term observation [25]. In our study a value \geq 3 on the 21-point ECG scale predicted with high sensitivity and specificity abnormal systolic function of the RV in the echocardiographic study and was associated with a higher rate of complications during hospitalisation. Interestingly, of all the ECG signs, only tachycardia correlated with complications during hospitalisation and overall mortality.

In the study by Escobar et al. the presence of sinus tachycardia was the only parameter in the ECG which was associated with higher risk of death during 30 days. On the other hand, the presence of any other atrial arrhythmia was associated with 2.2 higher risk of in-hospital death

among 15 stable patients with APE [26]. Iles et al. have suggested that a precise analysis of ECG changes could allow assessment of the severity of RV dysfunction and the severity of pulmonary hypertension [24]. Because 3 or fewer points on the ECG scale had a high negative predictive value (97%), it seems that ECG analysis could lead to a decrease of the number of echocardiographic studies. The number of patients in this group (\leq 3 points) in our study was 13 (23.2%).

Limitations of the study

The main limitations of our study include its retrospective character and the fact that the study population was relatively small. Moreover, the score was based mainly on the amplitude of the negative T wave, which can be secondary to right bundle branch block or other cardiovascular diseases, or can even be present in the healthy population. On the other hand, it should be stressed that there is a high probability of confirmation in a larger population of such a close association between RV contraction abnormalities with ECG changes observed in the current study in this relatively small group of patients with APE. It should also be underlined that in our study the majority of patients represented the non-high risk population and therefore the results should be restricted mainly to this group.

Conclusions

The ECG scale is a simple, cheap and rapid method enabling the prediction of RV systolic dysfunction and negative course of hospitalisation in patients with APE. Considering the high negative predictive value, 3 points or less on the ECG scale enables exclusion of RV dysfunction with high probability in about 23% of stable patients with APE. It is worth noting that even 7-11% of high-risk patients with APE may have no changes in the ECG.

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Czy na podstawie standardowego badania elektrokardiograficznego możliwa jest ocena rokowania u chorych z zatorowością płucną?

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Streszczenie

Wstęp: Stratyfikacja ryzyka u chorych z ostrą zatorowością płucną (OZP) ma decydujące znaczenie w doborze odpowiedniej terapii. Uznanym wskazaniem do agresywnego leczenia jest wstrząs lub hipotonia. Wśród chorych początkowo stabilnych hemodynamicznie znajdują się osoby, których stan może ulec pogorszeniu mimo leczenia przeciwzakrzepowego. W związku z tym poszukuje się najlepszych metod oceny rokowania tej grupy chorych. W przebiegu OZP występują różnorodne zmiany w standardowym elektrokardiogramie (EKG).

Cel: Ustalenie, czy zmiany w EKG wykonanym przy przyjęciu są pomocne w ocenie rokowania podczas hospitalizacji.

Metody: Dokonano retrospektywnej analizy wykonanych przy przyjęciu zapisów 12-odprowadzeniowego EKG oraz badań echokardiograficznych u 56 pacjentów (22 mężczyzn, wiek 64,3 \pm 17,9 roku) z OZP potwierdzoną w spiralnej tomografii komputerowej. W analizie EKG uwzględniono występowanie: tachykardii (> 100/min), bloku prawej odnogi pęczka Hisa, obecności załamków S w odprowadzeniu I, załamków Q lub ujemnych T w odprowadzeniu III, zespołu S1Q3T3 oraz głębokości ujemnych załamków T w odprowadzeniach V_1 – V_4 . Suma powyższych objawów w EKG i stopień ich nasilenia były następnie oceniane w skali od 0 do 21. Powikłany przebieg hospitalizacji (PPH) zdefiniowano jako konieczność zastosowania wlewu leku wazopresyjnego, trombolizy, embolektomii lub resuscytacji krążeniowo-oddechowej oraz wystąpienie wskaźnika wstrząsowego > 1 (częstotliwość rytmu serca//skurczowe ciśnienie krwi).

Wyniki: W czasie hospitalizacji zmarło 4 (7,1%) pacjentów, a u 8 (14,3%) innych wystąpił PPH. U chorych z PPH stwierdzano wyższą średnią sumę punktów skali EKG w porównaniu z pacjentami, u których PPH nie wystąpił [8 (1–17) vs 3 (0–18); p = 0,04]. U 13 (23,2%) osób rozpoznano dysfunkcję skurczową prawej komory (PK) w badaniu echokardiograficznym. Wśród nich obserwowano wyższą średnią sumę punktów skali EKG w porównaniu z chorymi bez dysfunkcji PK [8 (3–17) vs 2 (0–18); p = 0,004]. Pole powierzchni pod krzywą ROC oceniającą przydatność skali EKG do przewidywania dysfunkcji skurczowej PK wynosiło 0,794 (95% CI 0,665–0,891), a do predykcji wystąpienia PPH 0,727 (95% CI 0,591–0,837). Czułość i swoistość, pozytywna oraz negatywna wartość predykcyjna dla wartości > 3 punktów w skali EKG dla przewidywania dysfunkcji skurczowej PK wynosiły odpowiednio: 92, 65, 44, 97%, a dla PPH odpowiednio: 75, 46, 19, 92%.

Wnioski: Zastosowanie skali EKG jest prostą, tanią, a zarazem szybką metodą pozwalającą przewidzieć dysfunkcję skurczową PK oraz niekorzystny przebieg hospitalizacji u pacjentów z OZP. Z uwagi na wysoką ujemną wartość predykcyjną wynik 3 lub mniej w skali EKG pozwala z dużym prawdopodobieństwem wykluczyć dysfunkcję PK i ograniczyć częstość wykonywania badań echokardiograficznych u ok. 23% stabilnych hemodynamicznie chorych z OZP.

Słowa kluczowe: zatorowość płucna, stratyfikacja ryzyka, elektrokardiogram

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