ORIGINAL ARTICLE

UDC: 616.12-073.7:616.24-005.6/.7
DOI: 10.2298/VSP150512011K

Association of different electrocardiographic patterns with shock index, right ventricle systolic pressure and diameter, and embolic burden score in pulmonary embolism

Povezanost različitih elektrokardiografskih znakova sa šok indeksom, veličinom i sistolnim pritiskom desne komore i skorom embolijskog opterećenja kod akutne plućne tromboembolije

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Abstract

Background/Aim. Some electrocardiographic (ECG) patterns are characteristic for pulmonary embolism but exact meaning of the different ECG signs are not well known. The aim of this study was to determine the association between four common ECG signs in pulmonary embolism [complete or incomplete right bundle branch block (RBBB), S-waves in the aVL lead, $S_1Q_3T_3$ sign and negative T-waves in the precordial leads] with shock index (SI), right ventricle diastolic diameter (RVDD) and peak systolic pressure (RVSP) and embolic burden score (EBS). **Methods.** The presence of complete or incomplete RBBB, S waves in aVL lead, $S_1Q_3T_3$ sign and negative T-waves in the precordial leads were determined at admission ECG in 130 consecutive patients admitted to the intensive care unit of a single tertiary medical center in a 5-year period. Echocardiography examination with measurement of RVDD and RVSP, multidetector computed tomography pulmonary angiography (MDCT-PA) with the calculation of EBS and SI was determined during the admission process. Multivariable regression models were calculated with ECG parameters as independent variables and the mentioned ultrasound, MDCT-PA parameters and SI as dependent variables. **Results.** The presence of S-waves in the aVL was the only independent predictor of RVDD ($F = 39.430$, $p < 0.001$; adjusted $R^2 = 0.231$) and systolic peak right ventricle pressure ($F = 29.903$, $p < 0.001$; adjusted $R^2 = 0.185$). Negative T-waves in precordial leads were the only independent predictor for EBS ($F = 24.177$, $p < 0.001$; $R^2 = 0.160$). Complete or incomplete RBBB was the independent predictor of SI ($F = 20.980$, $p < 0.001$; adjusted $R^2 = 0.134$). **Conclusion.** In patients with pulmonary embolism different ECG patterns at admission correlate with different clinical, ultrasound and MDCT-PA parameters. RBBB is associated with shock, S-wave in the aVL is associated with right ventricle pressure and negative T-waves with the thrombus burden in the pulmonary tree.

Key words:
pulmonary embolism; electrocardiography; diagnosis, differential; tomography; angiography; ventricular function, right; sensitivity and specificity.

Apstrakt

Uvod/Cilj. Pojava pojedinih elektrokardiografskih (EKG) znakova karakteristična je za akutnu plućnu tromboemboliju (APTE). U ovu grupu znakova spadaju kompletan ili nekompletan blok desne grane (BDG), prisustvo S-zupca u aVL odvodu, $S_1Q_3T_3$ znak i prisustvo negativnih T-talasa u prekordijalnim odvodima. Tačno značenje pojave ovih znakova i njihova povezanost sa kliničkim stanjem, ehokardiografskim i angiografskim karakteristikama još uvek nisu utvrđeni. Cilj ove studije bio je da se utvrdi povezanost karakterističnih EKG obrazaca na prijemu kod bolesnika sa APTE sa šok indeksom (ŠI), srednjim pritiskom i prečnikom desne komore (SPDK i DDK) i skorom embolijskog opterećenja (*embolic burden score*, EBS). **Metode.** Prisustvo BDG, S-zupca u aVL odvodu, $S_1Q_3T_3$ znaka i negativnih T-talasa u prekordijalnim odvodima zabeleženi su kod 130 bolesnika na prijemu u jedinicu intenzivne nege jedne tercijarne zdravstvene ustanove tokom pet godina. Ehokardiografsko ispitivanje sa merenjem SPDK i DDK, multidetektorska kompjuterizovana tomografska plućna angiografija (MDKT-PA) sa izračunavanjem EBS i utvrđivanje ŠI vršeni su tokom pri-

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jemne obrade bolesnika. Multivarijabilni regresioni modeli utvrđeni su na osnovu pomenutih EKG znakova kao nezavisnih promenljivih i ŠI, SPDK, DDK i EBS kao zavisnih promenljivih varijabli. **Rezultati.** Prisustvo S-zupca u aVL odvodu jedini je nezavisni prediktor visine SPDK (F = 29,903, $p <$ 0,001; usklađen R^2 = 0,185) i veličine DDK (F = 39,430, $p <$ 0,001; usklađen R^2 = 0.231). Negativni T-talasi u prekordijalnim odvodima jedini su nezavisni prediktori veličine EBS (F = 24,177, $p <$ 0,001; usklađeni R^2 = 0,160). Jedini nezavisan prediktor veličine ŠI je BDG (F = 20,980, $p <$ 0,001; usklađeni R^2 = 0,134). **Zaključak.** Kod bolesnika sa APTE karakteristični EKG obrasci povezani su sa kliničkim, ehokardiografskim i angiografskim statusom. Pojava BDG ukazuje na veći ŠI, a shodno tome na težu kliničku sliku. Prisutan S-zubac u aVL odvodu u vezi je sa visinom SPDK i veličinom DDK, pa se njegova pojava može shvatiti kao preteča disfunkcija desne komore. Prisustvo negativnih T-talasa u prekordijalnim odvodima ukazuje na veći EBS, samim tim, na zahvaćenost velikih krvnih sudova plućnog vaskularnog korita trombnim masama.

Ključne reči:
pluća, embolija; elektrokardiografija; dijagnoza, diferencijalna; tomografija; angiografija; srce, funkcija desne komore; osetljivost i specifičnost.

Introduction

Acute pulmonary thromboembolism (APE) is a common and potentially fatal disease caused by the migration of thrombi from the veins to the pulmonary arteries. Thrombi may be small and asymptomatic, may cause pulmonary infarction with secondary pneumonia and large thrombi may overload the weak right ventricle with the shock state and circulatory and respiratory failure [1]. The diagnosis of APE is remarkably improved after introduction of multidetector computed tomography pulmonary angiography (MDCT-PA) which is widely available and after clinical assessment of and D-dimer level determination it becomes the cornerstone for the APE diagnosis [2, 3]. Echocardiography is important for the assessment of right ventricle function which is important for the risk stratification of patients at admission. Urgent estimation of risk for death is extremely important in APE because the treatment modality is based on that [2]. Electrocardiography (ECG) is simple, inexpensive and repeatable diagnostic tool which is part of routine procedures in every acutely ill patient. In APE ECG changes are typical, but have low sensitivity and specificity for the diagnosis [4]. However, ECG changes in APE are extremely dynamic and may follow-up closely hemodynamic deterioration or successful reperfusion and be very useful for the direction of therapeutic measures. Several parameters, like shock index (SI), right ventricle diastolic diameter (RVDD) and systolic pressure (RVSP) measured by echocardiography and embolic burden score (EBS) on MDCT-PA are well-known markers of prognosis for APE.

The aim of this investigation was to examine the association of the most common ECG signs in APE at admission with hemodynamic status (presented by SI), function of the right ventricle (presented by echocardiographic measured RVSP and RVDD) and thrombus burden in the pulmonary arterial tree (presented by EBS).

Methods

This study included 130 consecutive patients with confirmed APE hospitalized at the Clinic of Emergency Internal Medicine in the Military Medical Academy, Belgrade, during a 5-year period, from January 2010 to December 2014. All patients were submitted to clinical, biochemical, electrocardiographic, echocardiographic, and radiological investigations at admission. The diagnosis of APE was confirmed radiologically with MDCT-PA which visualized a thromb in the pulmonary vascular tree.

The basic clinical assesment included the measurement of heart rate and arterial pressure at admission with calculation of shock index according the formula SI = heart rate/systolic blood pressure [5]. Electrocardiographic (ECG) recording was done in all the patients at admission by conventional 12-leads. Five classical ECG characteristics which are commonly used for the estimation of acute PTE were analysed: heart rate, $S_1Q_3T_3$ sign, S-wave in the aVL lead, negative T-waves in the precordial leads and the presence of incomplete or complete right bundle branch block (RBBB). The right ventricle (RV) dysfunction was measured by transthoracic echocardiography examination at admission. The RVD was measured in diastole 1 cm beyond the tricuspid anulus in apical 4-chamber view. Right ventricle systolic blood pressure was measured through the regurgitation blood velocity and adding 10 mmHg for the estimated right atrium pressure. Thrombus burden was measured by the admission MDCT-PA using EBS [6].

All the patients were scheduled for the follow-up visit at 1, 3 and 6 months after disharge. If a patient was not present at the scheduled visit he was contacted by phone.

Statistical analysis

SPSS software (Statistical Package for the Social Sciences, version 20.0, SSPS Inc, Chicago, IL, USA) was used for statistical analyses. Categorical variables were expressed as numbers and percentages, and continuous variables as means and standard deviations. The characteristics of study population (gender, age, risk factors, DDK, SPDK, EBS, heart rate, ECG signs, clinical parameters) were calculated by descriptive methods. Significant differences in shock index, echocardiographic and MDCT-PA parameters between the groups of patients with and without the presence of some ECG parameters were calculated by the Mann-Whitney U-test. Multivariable regression models were calculated with ECG parameters as independent variables and the mentioned RVDD, RVSP, EBS and SI as dependent variables. A p value less than 0.05 was considered statistically significant.

Results

Clinical characteristics

The study enrolled 130 patients (65 men and 65 women; mean age 60 ± 17 years) with APE. The basic patient characteristics are shown in Table 1. The history of the previous surgery in a few last months was present in 33 (25.4%) and active smoking in 25 (19.8%) of the patients. Malignancy was found in 12 (9.2%) and clinical signs of deep vein thrombosis (DVT) in 72 (55.4%) of the patients. Hypotension (systolic arterial blood pressure less than 90 mmHg) at admission was detected in 24 (18.5%) and RV dysfunction in 86 (68.3%) of the patients. The risk for APE was calculated in all the patients and 65 (50.0%) of them had intermediate risk. Pulmanary embolism severity index (PESI) score 0 was present in 41 (31.5%) of the patients. The mean values of SI, RVSP, RVDD and EBS are presented in Table 1.

ECG characteristics

The mean heart rate in the study group was 103 ± 22 (beats/min). Atrial fibrillation was present only in 15 (11.5%) patients. Frequencies of the basic ECG patterns at initial ECG recording are shown in Table 2.

Association of the most common ECG patterns with hemodynamic status, right ventricle function and thrombus burden in pulmonary tree

A multiple stepwise regression analysis with ECG parameters as independent variables and hemodynamic status, right ventricle function parameters and pulmonary thrombus burden score as dependent variables is shown in Table 3. RBBB at presentation was the independent predictor of SI ($F = 20.980$, $p < 0.001$; adjusted $R^2 = 0.134$). The patients

Table 1

Characteristics of 130 patients with pulmonary thromboembolism

Parameters	Values
Age (years), mean ± SD	60 ± 17
Male, n (%)	64 (49.2)
Female, n (%)	66 (50.8)
Spontaneous APE, n (%)	65 (50.0)
Provoked APE, n (%)	65 (50.0)
Active smoking, n (%)	25 (19.8)
Surgery in last few months, n (%)	33 (25.4)
Malignancy, n (%)	12 (9.2)
Clinical signs of DVT, n (%)	72 (55.4)
DVT or APE cases in family, n (%)	14 (10.8)
Hypotension (SP < 90 mmHg), n (%)	24 (18.5)
RV disfunction (RVMP > 40 mmHg), n (%)	86 (68,3)
Risk, n (%)	
high	23 (17.7)
intermediate	65 (50.0)
low	42 (32.3)
Wells score (Inter Quartal Range)	4.5 (IQR = 4)
PESI score, n (%)	
0	41 (31.5)
1	33 (25.4)
2	29 (22.3)
≥ 3	27 (20.8)
Shock index, $\bar{x}$ ± SD	0.95 ± 0.41
Right ventricle SP, $\bar{x}$ ± SD	50.70 ± 19.13
RV diameter at four chamber view, $\bar{x}$ ± SD	3.80 ± 0.80
Embolic burden score at MDCT-PA, $\bar{x}$ ± SD	11.76 ± 5.37

APE − pulmonary thromboembolism; DVT − deep vein thrombosis; RV − right ventricle; SP – systolic pressure; RVMP – right ventricle medial pressure; PESI – pulmonary embolism severity index; MDCT-PA – computed tomography pulmonary angiography.

Table 2

The electrocardiographic (ECG) parameters at admission

The ECG characteristics	Values
Heart rate (beat/min), mean ± SD	103 ± 22
Atrial fibrillation, n (%)	15 (11.5)
$S_1Q_3T_3$ sign, n (%)	37 (28.5)
RBBB or incomplete RBBB, n (%)	34 (26.2)
S wave in aVL, n (%)	62 (47.7)
Negative T waves in precordial leads, n (%)	60 (46.2)

RBBB – right bundle branch block.

Table 3

Independent electrocardiographic variables in regression models for the association with shock index (SI), right ventricle diastolic diameter (RVDD), right ventricle systolic pressure (RVSP) and embolic burden score (EBS)

Dependent variable	Indpendent variables	R square	Adjusted R square	Unstandardized coefficient	Standardized coefficient beta	*p*	95.0% CI for B Lower bound	95.0% CI for B Upper bound
SI	RBBB	0.375	0.141	0.351	0.375	< 0.001	0.200	0.503
RVDD	S wave in aVL	0.237	0.231	0.779	0.487	< 0.001	0.534	1.025
RVSP	S Wave in aVL	0.192	0.185	16.700	0.438	< 0.001	10.657	22.744
EBS	Negative T waves in precordial leads	0.167	0.160	4.382	0.408	< 0.001	2.617	6.146

RBBB – right bundle branch block; CI – confidence interval.

with RBBB had significantly higher SI than those without it [0.77 (0.61−1.02) *vs* 1.10 (0.70−1.54) respectively; $p = 0.002$] (Figure 1). S-wave in the aVL lead at admission was an independent predictor of RVSP (F = 29.903, $p < 0.001$; adjusted $R^2 = 0.185$) and RVDD (F = 39.430, $p < 0.001$; adjusted $R^2 = 0.231$). The patients with S-waves in the aVL lead had a significantly higher RVSP [41.00 mmHg (27.25−58.50 mmHg) *vs* 59.00 mmHg (45.00−68.50 mmHg), respectively; $p < 0.001$] and a larger RVDD [3.20 cm (3.00−4.00 cm) *vs* 4.2 cm (3.57−4.95 cm), respectively; $p < 0.001$] (Figures 2 and 3). Presentation of negative precordial T-waves was independent predictor of EBS (F = 24.177, $p < 0.001$; $R^2 = 0.160$). The patients with negative T waves in precordial leads had significantly higher EBS than the patients without them [9.00 (5.00−13.00) *vs* 14.50 (12.00−18.00), respectively; $p < 0.001$] (Figure 4).

Discussion

The intention of this investigation was to find individual ECG patterns whose occurrence could predict unstable hemodynamic status, massive thrombus burden and

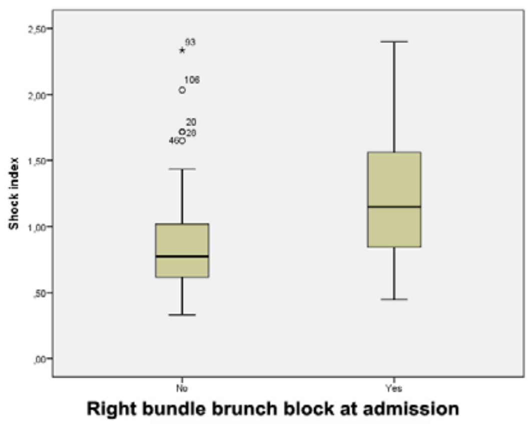

Fig. 1 − Shock index according to the presence of right bundle branch block at admission electrocardiography.

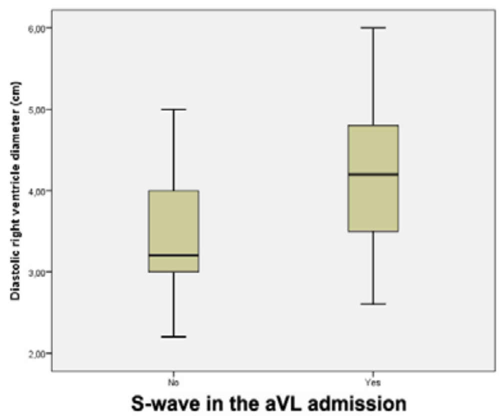

Fig. 2 − Diastolic right ventricle diameter according to the presence of S-waves at admission electrocardiography.

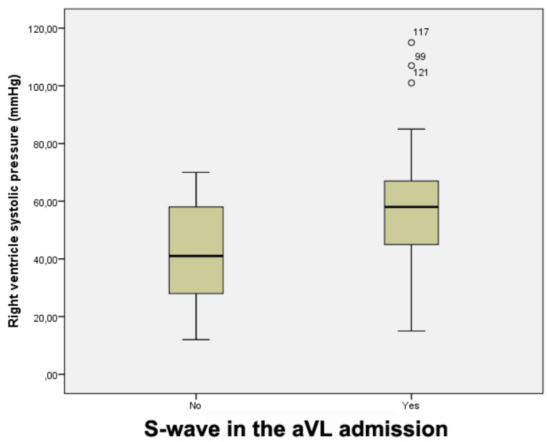

Fig. 3 − Right ventricle systolic pressure according to the presence of S-waves at admission electrocardiography.

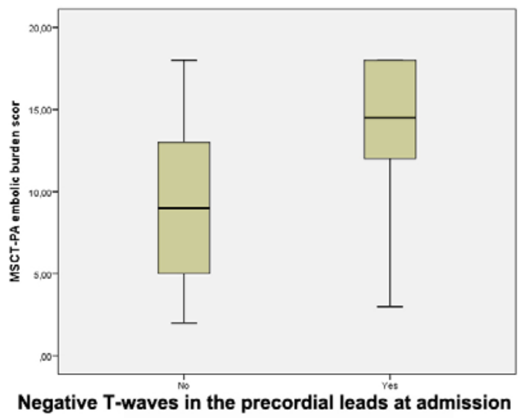

Fig. 4 − Embolic burden score according to the negative T-waves in the precordial leads at admission electrocardiography. MSCT-PA – multislice computed tomography pulmonary angiography.

dysfunction of the right ventricle. Several previous studies have suggested that ECG may be useful for predicting right ventricular dysfunction and the severity of APE.

We concluded that the presence of RBBB on admission, among all other ECG signs, was the only independent predictor of shock index, which was an indication of hemodynamic instability and shock. The presence of RBBB is an indicator of acute right ventricular overload. In our study the RBBB was found in 34 (26.2%) of the patients. Petrov et al. [7] found that patients with autopsy proven trunk pulmonary embolism had the newly emerged RBBB in 80% of cases and in none of the cases with peripheral embolism.The author of this study believes that the appearance of RBBB is a marker of significant obstruction of the main pulmonary artery. However, we did not found a significant correlation between RBBB and EBS which is the more precise method of the measure of central thrombus pulmonary obstruction. Sreeram et al. [8] observed RBBB in 33 (69%) patients. Kukla et al. [9] found RBBB in 20 (22.2%) cases of APE complicated by cardiogenic shock and in 10.2% without shock. They showed the association of low QRS voltage, RBBB, and ST-segment elevation in the lead V1 with cardiogenic shock. According to the current European Society of Cardiology (ESC) guidelines, patients with APE and shock are considered at high risk of death. RBBB is the independent predictor of mortality [10]. All this suggests that RBBB is present when the obstruction is massive, which directly causes saturation decrease, acute right ventricular dysfunction and, consequently, a reduction in left ventricle preload, which leads to shock. RBBB means desinchronization of the ventricles. This situation leads to left ventricle filling reduction and, consequently, to hypotension and higher SI [11].

The presence of S-wave in the aVL lead is associated with the right ventricle diastolic diameter and right ventricle systolic pressure. We found the mentioned pattern in 62 (47.7%) of the patients. Sreeram et al. [8] found this ECG sign in 36 (73%) patients. Presumably, the reason for this discrepancy may have been the presence of high right ventricle peak systolic pressure and the increased right ventricular end-diastolic diameter in all 49 patients included in their study. In the present study the RVSP was 55 ± 13 mmHg (ranged from 33 to 84 mmHg) and the diameter was 40 ± 7 mm (range 28−60 mm). RVSP in our study group ranged from 12 to 115 mmHg (mean 50.7 ± 19.13 mmHg) and RVDD ranged from 2.2 to 6.5 (mean 3.8 ± 0.8) mm. After all, they did not notice the difference in RVSP and RVDD between patients with and without abnormal ECG. Ryu et al. [12] used ECG score proposed by Daniel et al. [13] with tachycardia, T-wave inversion, RBBB $S_1Q_3T_3$. They found that the ECG score was the independent predictor of RVSP. Stein et al. [14] showed sensitivity, positive predictive value, and negative predictive value that were insufficient for the diagnosis or exclusion of RV enlargement in patients without cardiopulmonary disease. Sukhija et al. [15] found similar results. Both groups of authors did not have data about S wave presentation in the aVL lead. Hariharan et al. [16] found the association between right heart strain and tachycardia, T-wave inversion in the leads V1-V3, and S-wave in the lead I. They used that pattern to create TwiST score which can identify patients likely or not likely to have right heart strain with > 80% specificity and sensitivity. In experimental studies, Love et al. [17] show that ECG changes emerge after echocardiography visible right ventricular dilatation that leads to the conclusion that the appearance of ECG changes takes time. Considering that ECG is more accessible and preceding echocardiography in the diagnostic algorithm, based on our results, the S-wave presence in the aVL lead has a great value in identifying the right ventricle enlargement and overload.

Negative T-waves in the precordial leads (electrocardiographic pattern of subepicardial ischemia) are independent predictors of EBS in our study. This means that a patient with APE will have massive thrombus burden if this pattern is present in his/her ECG at admission. We found the mentioned pattern in 60 (46.2%) patients. Sreeram et al. [8] found negative T-waves in the leads V1 to V4 in 13 (27%) patients and in 9 of them symptoms lasted longer than 7 days. Petrov [7] observed T-wave inversion in the V1–V4 in 4 of 20 cases of massive trunk embolism. Geibel et al. [18] found T-wave inversion in the leads V2−V3 in 45%, and in the leads V4−V6 in 35% of patients. Punukollu et al. [19] observed T-wave inversion in the leads V1−V3 in 43% patients. Ferrari et al. [20] reported T-wave inversion in the precordial leads in 68% of patients and concluded that mentioned sign was the independent predictor of severity of APE. Choi and Park [21] observed T-wave inversion in the precordial leads in 35% of patients and showed that this pattern was the independent predictor of right ventricular dysfunction. This conclusion is supported by our results, because right ventricular dysfunction is the result of massive thrombus burden and depends on the sum of occluded pulmonary arteries. According to McIntyre et al. [22] electrocardiographic patterns suggestive of right ventricular overload were present only with angiographic obstruction of ≥ 47%. This percentage is equivalent to the value of EBS about 9. EBS in our group ranged from 2 to 18 (mean 11.76 ± 5.37). Kukla et al. [23] concluded that patients having ≥ 5 leads with T-wave inversion in comparison to patients having < 5 leads with the mentioned sign had a higher mortality rate and developed more complications throughout hospitalization period. The group of patients with T-wave inversion in ≥ 5 leads entailed higher rates of thrombolytic therapy and inotrope support. These authors showed that T-wave inversion in the leads V1−V4 is a common pattern in patients with elevated troponin levels [24]. A higher number of leads with T-wave inversion is connected with higher troponin levels, too. On the bases of the mentioned results it is certain that a higher number of occluded arteries (presented by EBS) implies myocardial injury.

Conclusion

In patients with pulmonary embolism different ECG patterns at admission correlate with different clinical, ultrasound and MDCT-PA parameters. Right bundle branch block is associated with shock, S-wave in the aVL is associated with right ventricle pressure and negative T-waves with the thrombus burden in the pulmonary tree.

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Received on May 12, 2015.
Revised on July 6, 2015.
Accepted on July 27, 2015.
Online First January, 2016.