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The Value of Different Electrocardiographic Patterns at Hospital Admission in Predicting Clinical Outcome in Pulmonary Embolism

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Abstract

Background: Literature reports the presence of several Electrocardiographic (ECG) patterns of Right Ventricular (RV) strain in acute Pulmonary Embolism (PE). These reports are inconsistent considering the prognostic value of these patterns. Aim: to evaluate the significance of ECG RV strain patterns, as well as the total number of these ECG patterns in predicting short-term (in-hospital) clinical outcome.

Methods: This retrospective study was consisted of 183 patients (107 male, age: 61±14 years) with acute PE. The 12-lead ECG done at hospital admission was analysed. ECG RV strain was diagnosed in presence of one or more of following 12 patterns: tachycardia, atrial fibrillation, low QRS voltage, S1Q3T3, Q in III, aVF, right axis deviation, right bundle branch block, Qr in V1, negative T wave in inferior, precordial leads, ST elevation in inferior leads, aVR, V1 and ST depression. The outcome was defined as experience of an adverse event (in-hospital complications and death all-cause). The association of ECG patterns with outcome was evaluated by multivariable Cox hazards regression analysis.

Results: During a median hospitalization time of 15 days, 41 (22.4%) adverse events occurred. Event rate was higher in patients with ≥5 ECG patterns than in <5 (63.4% vs. 0.7%; p<0.0001). Number of ECG RV strain patterns (Hazard Ratio (HR):1.7 per pattern; 95% Confidence Interval (CI): 1.1-2.6; p=0.009), ST elevation in inferior leads (HR: 8.4; 95% CI: 6.0-68.3; p=0.001) and ST depression (HR: 0.1; 95% CI: 0.03-0.6; p=0.01) were independently associated with adverse outcome.

Conclusion: Number of ECG RV strain patterns, ST elevation in inferior leads, ST depression has independent value in predicting in-hospital adverse outcome in acute PE.

Keywords: Acute pulmonary embolism; Electrocardiographic right ventricular strain pattern; Number of electrocardiographic right ventricular strain pattern; Ischemic patterns

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Introduction

Acute Pulmonary Embolism (PE) is a major cause of cardiovascular mortality with rate up to 24.5% in high-risk patients, despite evident progress in diagnosis and treatment. Early risk stratification for patients with acute PE remains essential in order to establish the appropriate treatment and management [1].

A basic 12 lead Electrocardiogram (ECG) is initial, most common non-invasive test that is quickly interpretable and performed in almost every patient with cardiac or respiratory symptoms in the emergency department. Numerous ECG abnormalities have been reported in PE. Certain constellations of ECG abnormalities (patterns) have been associated with Right Ventricular (RV) dysfunction in the context of PE. This is commonly known in the literature as a concept of ECG RV strain patterns. These ECG patterns are including changes in the rhythm, rate, conduction, axis of QRS complex and morphology of P wave, QRS complex, ST segment and T wave [1]. Many studies [3-13] that have been published are describing the association between various ECG RV strain patterns and: more extensive and complicated PE [2,3];

pulmonary arterial hypertension [4,5] and association with negative clinical outcome [6-13].

Current guidelines of the European Society of Cardiology (ESC) [1] are discussing ECG findings in PE, however the use of ECG as a prognostic tool is not listed in the recommended modalities. On the other side, there is growing evidence in the literature supporting the usefulness of ECG in predicting outcome in acute PE. Various ECG RV strain patterns related to clinical deterioration and mortality among patients with PE are shown in many clinical studies [6-13]. A recent meta-analysis [13] found several ECG patterns (atrial fibrillation, S1Q3T3 pattern, right bundle branch block, right axis deviation) and ischemic patterns (negative T waves, ST depression, ST elevation) to be significantly predictive of an adverse outcome in acute PE. As such, ECG could be an easily, widely available prognostic tool to help guide management in acute PE.

Furthermore, the reported results in previous studies vary greatly and are showing inconsistent data regarding the prognostic value of different ECG RV strain patterns in PE. Currently, there is a paucity of data about the prognostic significance of the number of ECG RV strain patterns.

We hypothesized that various ECG RV strain patterns at hospital admission, as well as the total number of these ECG patterns, could predict an adverse in-hospital outcome in patients with acute PE. Thus, the aim of this study was to evaluate and analyze various ECG RV strain patterns at hospital admission, their occurrence rate in patients with acute PE and their relation with in-hospital clinical outcome. In addition, we investigated the relationship between total number of ECG RV strain patterns and in-hospital clinical outcome in patients with acute PE.

Materials and Methods

This was a retrospective study, that evaluated data from medical charts of 183 consecutive patients diagnosed with acute pulmonary embolism, who were hospitalized in one university hospital in Skopje (Clinic of Anesthesiology, Reanimation and Intensive Care) during a 7 year period ((January 2013- September 2020). All patients included in the study had acute first time diagnosed PE, were hospitalized, had ECG done within the first 24 hours upon hospital admission and echocardiography within 72 h from admission. Patients whose medical documents were not complete, patients with recurrent PE, uninterpretable ECG (pacemaker leads, left bundle branch block) and those who were transferred to other centers for different reasons were excluded from the study.

Pulmonary embolism was diagnosed by multislice Computed Tomographic (CT) scan of the pulmonary arteries presented as partial or complete filling defect within the pulmonary arteries or by echocardiographic visualization of the thrombus in the right heart or pulmonary arteries. In all patients we analyzed demographic data, clinical data, risk stratifications, admission ECG, admission echocardiography, laboratory and CT findings, and treatment and patient outcomes.

Additionally all patients were stratified into one of the following 3 risk categories: high, intermediate and low risk group of patients, defined by the different levels of PE severity (according to latest ESC recommendations for the diagnosis and management of pulmonary embolism [1]. High-risk group of patients were defined as those haemodynamically unstable, suffering cardiac arrest or obstructive shock or persistent hypotension (systolic arterial blood pressure at presentation ≤ 90 mmHg or a pressure drops of ≥ 40 mmHg for more than 15 min (if not caused by hypovolaemia, sepsis or new onset arrhythmias). All those patients who were haemodynamically stable at admission were classified as not high risk patients. The criteria used to categorize not high risk patients into intermediate or low-risk groups were the presence or absence of RV dysfunction (strain) at echocardiography or presence or absence of myocardial injury as indicated by an elevated cardiac troponin level [1].

We analyzed the prevalence of different ECG patterns and patient outcomes in relation to these risk groups of patients with different severity of PE. The study received institutional review board approval.

Electrocardiographic analysis

Standard surface 12-lead ECG (recorded with a paper speed of 25 mm/s) was done during the first 24 hours of hospital admission. The first ECG recorded following presentation to hospital was analysed. Single research member cardiologist (M.K. Angjushev) unaware of the patients' clinical outcome, analysed 12 predefined ECG patterns of RV strain in all patients. The decision for analyses of these following patterns was due to the fact that they are the most frequently used in routine clinical practice [5,12]. The following 12 ECG patterns were regarded as suggestive of RV strain:

1. Sinus tachycardia (>100 beats/min) [3,5,12,13];
2. Recent onset of atrial arrhythmias (atrial fibrillation or flutter) [3,5,12,13];
3. S1Q3T3 pattern (S-waves in lead I combined with Q waves in lead III and negative T wave in lead III) [3,5,12-14];
4. Right axis deviation (QRS axis between +90° and +180°) [3,5,13];
5. Complete or incomplete Right Bundle Branch Block (RBBB) [3,5,12,13,15];
6. Low QRS voltage (low voltage in the QRS complex <5 mm in limb leads) [5,13,16];
7. Pseudo infarction pattern (prominent Q waves) in leads III and aVF (not in lead II) [13];
8. ST elevation in lead V1 and aVR [9-13,15];
9. ST elevation in inferior leads [17-19];
10. ST depression in lead I, II or right or left precordial leads [5,9,13];
11. Negative T-waves (more than one) in precordial leads [2,3,5,12,13,18,20] and/or (more than one negative T wave) in inferior leads [5,13,19];
12. Qr in lead V1 (presence of a prominent Q wave of ≥ 0.2 mV and a ventricular depolarization <120 ms) [13,17].

ST elevations, ST depressions and negative T waves were defined as either present or absent in each lead, without quantifying the magnitude of these deflections. Patients with one or more than one of these ECG patterns were considered to have RV strain (dysfunction) on ECG.

Right heart strain on echocardiography

RV function was assessed by transthoracic echocardiography, performed in the first 72 hours from hospital admission according to the recommendations of the American Society of Echocardiography [21]. Patients with one or more than one of the following findings were considered to have RV strain (dysfunction) on echocardiography [22]: (1) RV hypokinesia; (2) RV dilatation (RV/left ventricular (LV) ratio ≥ 1.0). The RV/LV ratio was calculated by measurement of the basal RV end-diastolic dimension and basal LV end-diastolic dimension on the apical 4-chamber view; (3) abnormal interventricular septum movement; (4) direct visualization of thrombus in the right heart or pulmonary arteries.

Study outcomes

In our study outcome was evaluated with the occurrence of an adverse clinical event during hospitalization, defined as in-hospital death (from any cause) and complicated in-hospital course (use of vasopressors for inotropic support, mechanical ventilation for respiratory support, treatment with systemic thrombolysis or cardiopulmonary resuscitation).

Statistical analysis

Data are expressed as mean ± SD for continuous variables and as number (%) for categorical variables. Continuous variables were compared by Student's t-test. Proportions were compared by chi-square statistics; the Fisher exact test was used when appropriate.

Continuous variables among groups of patients defined by different levels of PE severity were Analyzed by Analysis of Variance (ANOVA). If any interactions were significant, post hoc comparison was performed using unpaired Student's t-test with Bonferroni correction to detect differences between 2 groups. Categorical variables were compared using the chi-square test among groups.

Univariable analyses by Cox proportional hazards models were performed to assess the association between total number of ECG patterns and each ECG pattern with in-hospital clinical outcome. The primary endpoint was the time to-first-event analysis by a multivariable Cox proportional hazards model. Hazard ratios with the corresponding 95% confidence interval were estimated. Selection of ECG independent predictors was performed for proportional hazards model with a backward approach using a p value of 0.10 as threshold for inclusion in the model. Multivariable analysis was adjusted by age and gender.

A probability value of <0.05 was considered statistically significant. All statistical analyses were performed with Statistical Package for Social Science (SPSS) 25.0 for Windows.

Results

Demographic and basic clinical data

Over a 7 year period in one university hospital institution (Clinic of Anesthesiology, Reanimation and Intensive Care) retrospectively 218 patients with confirmed diagnosis of pulmonary embolism were reviewed. Total of 35 patients were excluded from further analysis since in seven patients ECG was not performed at hospital admission and in 28 patients documented previous episode of PE in their medical records was present.

The final study sample comprised 183 patients with acute pulmonary embolism (76 female and 107 male), aged between 21-89 years (mean age of 61.4 ± 14.2 years). There were 138 (75.4%) out patients presented to emergency department and 45 patients (24.6%) developed PE during their hospital stay. Acute PE was diagnosed mostly by computed tomography pulmonary angiography (CTPA) in 180 patients (98.3%) and by direct visualization by echocardiography in only 3 (1.7%) patients with cardiogenic shock.

Based on ESC risk stratification of acute PE, there were 26 (14.2%) high-risk patients, 126 (68.9%) intermediate-risk and 31 (16.9%) low-risk. Clinical characteristics are summarized in **Table 1.**

Prevalence of ECG RV strain patterns in the stratified groups of patients (defined by the different levels of PE severity)

The prevalence of at least one ECG pattern was 80.3% in total population. The most prevalent ECG pattern was sinus tachycardia (47%), followed by negative T wave in precordial leads (31%) and right axis deviation (19%).

The frequency of ECG patterns was continuously rising from low-risk to intermediate and to high risk group. The total number of ECG patterns was significantly lower in low risk group as compared to intermediate and high risk. Also the total number of ECG patterns differed significantly between the intermediate and high risk group (1.6 vs. 4.5; p<0.001). The prevalence of ECG RV strain patterns in these three groups of patients are presented in **Table 2.**

Outcome data

During the median hospitalization time of 15 days (interquartile range: 1 to 45 days) in 183 patients, 26 (14.2%) patients died, 37 (20.2%) had inotropic support, 30 (16.4%) were put on mechanical ventilation, 27 (14.8%) experienced cardiopulmonary resuscitation and 4 (2.2%) received systemic thrombolysis. The median time from presentation to in-hospital death was 6 days (range: 1 to 45 days) and to in-hospital complications was 12 days (range: 1 to 45 days).

The event rate was significantly lower in patients with low risk PE compared with patients with high and intermediate risk (p<0.0001). Also events were more frequent in patients with high risk PE than in intermediate risk (65.4 vs. 18.4%; p<0.0001) **(Table 3 and Figure 1).** Patients with adverse events had significantly higher total number of ECG patterns compared to those without events (4.67 (0-10) vs. 1.1 (0-5); p<0.0001) **(Figure 2).**

Table 1 Clinical characteristics of total population.

Variables	All patients (n=183)
Age, years	61.4 ± 14.2
Male sex	107 (58.5%)
Outpatient/inpatient	138/45 (75.4/ 24.6)
Hemodynamic classification	
High risk	26 (14.2%)
Intermediate risk	126 (68.9%)
Low risk	31 (16.9%)
Risk factors	
Cancer at hospitalization	27 (14.8%)
Congestive heart failure	71 (38.8%)
Infections	51 (27.9%)
Recent surgery	44 (24.0%)
Recent trauma	20 (10.9%)
Recent bedrest	48 (26.2%)
Comorbidities	
Diabetes mellitus	46 (25.1%)
Hypertension arterials	111 (61.0%)
Chronic renal disease	33 (18.1%)
COPD	20 (10.9%)
Coronary artery disease	18 (9.8%)
Clinical and laboratory findings	
Syncope	10 (5.5%)
Angina	20 (10.9%)
Pleurodynia	45 (24.6%)
Dyspnea	155 (84.7%)
HR (beats/min)	100± 25
Systolic BP (mm Hg)	132 ± 26
Elevated troponin I*	22 (13.8%)
D-dimers	8329 ± 7930
ECHO RV strain	134 (73.2%)
Thrombi in right heart	4 (2.2%)
Thrombi in pulmonary arteries	3 (1.6%)
Anatomic location of PE	
Central PE	139 (76%)
Peripheral PE	44 (24%)

Data are presented as median (interquartile range) or n (%).
COPD =Chronic Obstructive Pulmonary Disease; ECHO RV strain=Echocardiographic Right Ventricular strain; PE=Pulmonary Embolism; * Cutoff for Troponin elevated is blood level >34 ng/L;

Table 2 Prevalence of ECG RV strain patterns in groups of patients defined by different levels of PE severity.

ECG patterns	All patients (n=183)	High risk group (n=26)	Intermediate risk group (n=126)	Low risk group (n=31)	P value (high. vs. intermediate risk)
At least one RV strain pattern	147 (80.3%)	25 (96.2%)	112 (88.9%)	10 (32.3%)	0.257
Number of RV strain patterns	1.52 (0-10)	4.5 (0-10)	1.62 (0-10)	0.34 (0-1)	<0.0001
Tachycardia	87 (47.5%)	22 (84.6%)	61 (48.8%)	4 (12.5%)	0.001
AF at presentation	21 (11.5%)	2 (7.7%)	19 (15.1%)	0 (0%)	0.324
Right axis deviation	35 (19.1%)	15 (57.7%)	20 (15.9%)	0 (0%)	<0.0001
Qr in V1	13 (7.1%)	6 (23.1%)	7 (5.6%)	0 (0%)	0.003
S1Q3T3	23 (12.6%)	8 (30.8%)	15 (11.9%)	0 (0%)	0.014
Q in D3 and aVF	27 (14.8%)	10 (38.5%)	16 (12.7%)	1 (3.2%)	0.001
Negative T wave in inferior leads	29 (15.8%)	7 (26.9%)	20 (15.9%)	2 (6.5%)	0.182
Negative T wave in precordial leads	58 (31.7%)	11 (42.3%)	47 (37.3%)	0 (0%)	0.635
RBBB incomplete	19 (10.4%)	5 (19.2%)	14 (11.2%)	0 (0%)	0.1
RBBB complete	16 (8.7%)	10 (38.5%)	6 (4.8%)	0 (0%)	<0.0001

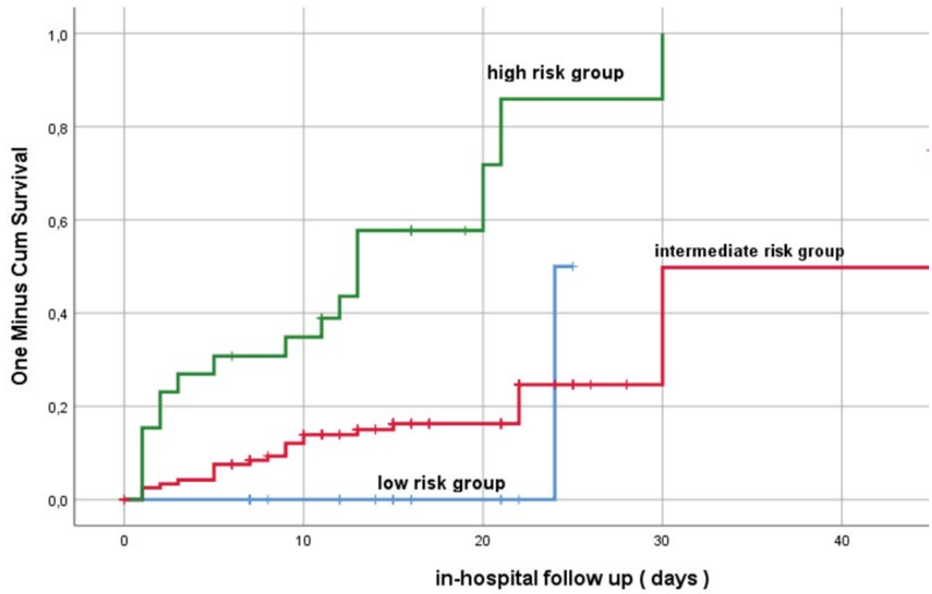
ECG patterns	All patients (n=183)	High risk group (n=26)	Intermediate risk group (n=126)	Low risk group (n=31)	P value (high. vs. intermediate risk)
ST depression in I,II or V2-V3 or V4-V6	18 (9.8%)	6 (23.1%)	12 (9.5%)	0 (0%)	0.05
ST elevation in inferior leads	10 (5.5%)	5 (19.2%)	5 (4.0%)	0 (0%)	0.004
ST elevation in aVR,V1	17 (9.3%)	7 (26.9%)	10 (7.9%)	0 (0%)	0.005
Low QRS voltage	4 (2.2%)	0 (0%)	4 (3.2%)	0 (0%)	0.359

Values are mean ± SD; median (range), or n (%).
AF=Atrial fibrillation; AV=Atrioventricular; ECG = Electrocardiography; RBBB = Right Bundle Branch Block; RV=Right Ventricle

Table 3 Adverse clinical outcome in total population and in groups defined by different levels of PE severity.

Adverse Outcomes	All	High risk group	Intermediate risk group	Low risk group	P value High vs intermediate
Length of hospital stay (days)	15.3 ±7.52	14.7 ±8.70	15.8 ±7.81	14 ± 4.90	0.49
Adverse clinical event (in-hospital death or complicated in-hospital course)	41 (22.4%)	17 (65.4%)	23 (18.4%)	1 (3.1%)	<0.0001
In-hospital death	26 (14.2%)	13 (50.0%)	13 (10.4%)	0 (0.0%)	<0.0001
Complicated in-hospital course	41 (22.4%)	17 (65.4%)	23 (18.4%)	1 (3.1%)	<0.0001
• Vasopressors	37 (20.2%)	17 (65.4%)	19 (15.2%)	1 (3.1%)	<0.0001
• Thrombolysis	4 (2.2%)	0 (0.0%)	4 (3.2%)	0 (0.0%)	0.032
• Respiratory support	30 (16.4%)	14 (53.8%)	15 (12.0%)	1 (3.1%)	<0.0001
• CPR	27 (14.8%)	13 (50.0%)	13 (10.4%)	1 (3.1%)	<0.0001

PE = Pulmonary Embolism; CPR= Cardiopulmonary Resuscitation



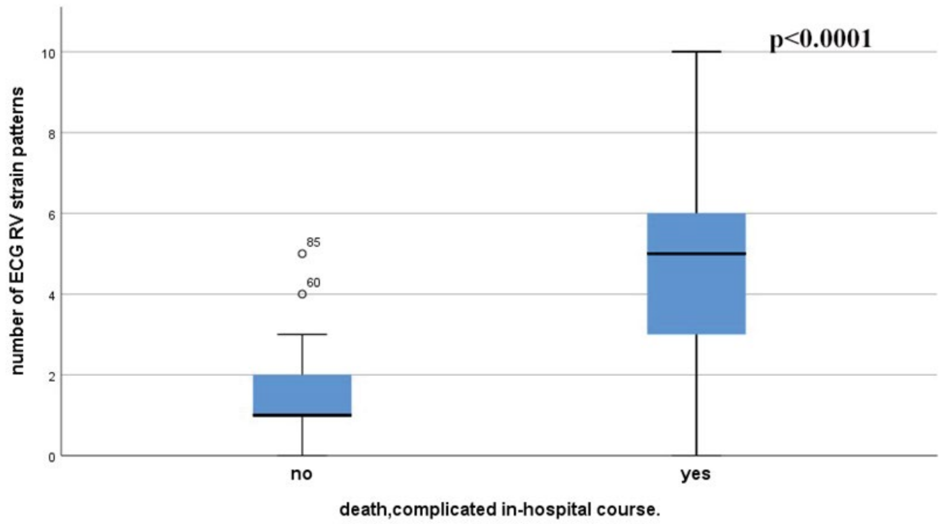
Event rate in patients with high risk PE (worse survival), intermediate risk PE (intermediate survival), and low risk PE (better survival).

Figure 1 Survival curves in patients stratified according to the level of PE severity.

The event rate was higher in patients with ≥ 5 ECG patterns than in those with less than 5 (63.4% vs. 0.7%; p<0.0001) **(Figure 3).** Specifically, compared to the patients with less than 5 ECG patterns, the patients with ≥ 5 ECG patterns had significantly higher rate of in-hospital mortality (51.9 vs. 7.7%; p<0.0001). Similarly, there were significantly higher rates of the administration of inotropic (88.9 vs.8.3%; p<0.0001) and respiratory support (59.3 vs. 9%; p<0.0001) and resuscitation (51.9 vs. 8.3%; p<0.0001 in patients with ≥ 5 ECG patterns. Rate of administration of thrombolysys was insignificant between both groups of patients (7.4 vs. 1.3; p=0.104). The survival curves based on the total number of ECG RV strain patterns are shown in **Figure 3.**

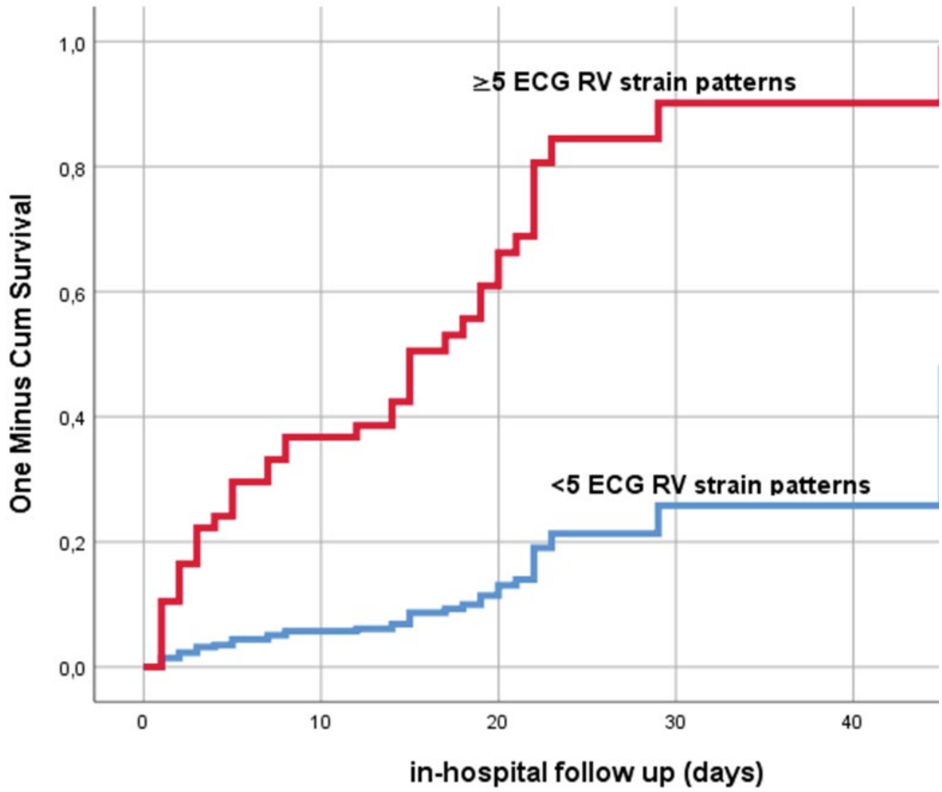
Predictors of adverse outcome

To identify predictors of adverse outcome, we performed a univariable Cox regression analysis. All ECG patterns that were significant predictors of adverse outcome in a univariable analysis, adjusted for age and gender were included in the



ECG = Electrocardiography; RV=Right Ventricle;

Figure 2 Number of ECG RV strain patterns at hospital admission in patients with adverse events and without adverse events. Patients with events had significantly higher total number of ECG patterns than patients without events (4.67 (0-10) vs 1.1 (0-5); p<0.0001).



ECG = Electrocardiography; RV=Right Ventricle

Figure 3 Survival curves based on number of ECG RV strain patterns at hospital admission. In-hospital event rate in patients stratified according to the presence of ≥ 5 ECG patterns (worse survival) and less than 5 patterns (better survival).

multivariable proportional hazards analysis. At this analysis, two patterns typical of myocardial ischaemia, known as ischemic patterns (ST elevation in inferior leads and ST depression) were independent predictor of events. The presence of ST elevation in inferior leads significantly elevated the hazard ratio of an adverse event. The presence of other ECG patterns was not associated

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with negative outcome. The total number of ECG patterns was significant predictor of events in a univariable analysis, and remained independent predictor of events (HR 1.8 per pattern; 95% confidence interval (CI):1.2-2.7; p=0.003) in multivariable analysis. The results of univariate and multivariate cox proportional-hazards age-adjusted analysis are shown on **Table 4.**

Discussion

The majority of clinically relevant acute PE have ECG abnormalities at admission in the emergency department [12,13]. Several ECG abnormalities (patterns) known as RV strain patterns were found to correlate with the degree of thrombus obstruction in the pulmonary arterial circulation [3] that subsequently increases the RV afterload. These changes are leading to RV dilatation, dysfunction and ischemia [23], which subsequently alters the ECG in a specific RV strain pattern. The total number of ECG patterns are closely related with the severity of PE [2,4,5].

The main finding of this study is that the total number of ECG RV strain patterns and occurrence of two patterns typical for myocardial ischaemia, represented as ischemic patterns (ST elevation in inferior leads and ST depression in I, II or left or right precordial leads) identified a subset of patients that are at higher risk for in-hospital adverse outcome in acute PE. Moreover, we found that higher number of ECG patterns more significantly altered the prognosis than the presence of specific ECG pattern. In particular, ≥ 5 ECG patterns were associated with worse in-hospital survival. Other examined ECG patterns showed no prognostic impact.

ECG patterns typical of myocardial ischaemia in the course of acute PE were recently introduced and are represented as ischemic ECG patterns (ST elevation, ST depression, negative T waves and specific combination of ST elevation and depression) [13,16,24-27]. ST depressions and/or negative T-waves are frequent findings in acute PE, in contrast to ST elevation which is a rare finding. Several patterns of ST elevation in terms of prognostic association with acute PE have been described. ST elevation in inferior leads as a sign of RV strain has been reported in clinical studies [18,24,27-29] and several case reports [30,31]. Appearance of ischemic pattern is due to sub-endocardial ischemia of the LV as well as transmural ischemia of the RV [32]. Transmural acute myocardial infarction of the RV as a consequence of massive PE has been revealed by autopsy [33]. Ischemic patterns are often associated with poor outcome in acute PE, often misdiagnosed and mistreated [18,19,24,27-31].

Comparison with previous studies. The results of the present study are consistent with a large body of evidence about the value of various ECG RV strain patterns in outcome prediction. Many previous studies [6-13,27,28] examined the prognostic value of ECG patterns in PE. They examined different types of ECG patterns and they used different clinical outcomes. Various ECG patterns have been shown to be predictors of adverse in-hospital outcome [6,8], hemodynamic instability [27], cardiogenic shock [12] and mortality [7-13].

Table 4 Predictors of in-hospital adverse events.

Predictors of in-hospital events				
ECG patterns	Univariable Regression Analysis		Multivariable Regression Analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age, yrs	1.027 (1.000-1.055)	0.05	1.031 (0.996-1.067)	0.086
Male gender	0.451 (0.219-0.931)	0.031	0.356 (0.115-1.095)	0.072
Number of ECG RV strain patterns	1.310 (1.206-1.423)	<0.0001	1.729 (1.149-2.604)	0.009
Tachycardia (yes/no)	0.134 (0.041-0.440)	0.001	0.321 (0.085-1.220)	0.095
AF at admission (yes/no)	0.322 (0.159-0.650)	0.002	0.157 (0.030-0.824)	0.069
Right axis deviation (yes/no)	0.175 (0.091-0.335)	<0.0001	0.490 (0.141-1.706)	0.263
Qr in V1 (yes/no)	0.304 (0.147-0.632)	0.001	0.607 (0.095-3.894)	0.599
S1Q3T3 (yes/no)	2.755 (1.458-5.206)	0.002	1.690 (0.387-7.382)	0.486
Q in III, aVF (yes/no)	0.204 (0.107-0.387)	<0.0001	1.181 (0.199-7.004)	0.855
Negative T wave in inferior leads (yes/no)	0.815 (0.385-1.725)	0.592		
Negative T wave in precordial leads (yes/no)	1.255 (0.656-2.399)	0.493		
RBBB incomplete (yes/no)	1.921 (0.800-4.611)	0.144		
RBBB complete (yes/no)	0.237 (0.121-0.462)	<0.0001	1.584 (0.445-5.630)	0.477
ST depression I,II or V2-V3 or V4-V6 (yes/no)	0.228 (0.117-0.441)	<0.0001	0.148 (0.034-0.635)	0.01
ST elevation in inferior leads (yes/no)	0.311 (0.142-0.683)	0.004	8.400 (6.038-68.398)	0.001
ST elevation in aVR,V1 (yes/no)	0.298 (0.147-0.606)	0.001	2.000 (0.351-11.411)	0.435
Low QRS voltage (yes/no)	0.466 (0.112-1.948)	0.296		

AF=Atrial Fibrillation; CI = Confidence Interval; ECG = Electrocardiography; ECHO RV strain=Echocardiographic Right Ventricular Strain; HR=Hazard Ratio; RV= Right Ventricular; RBBB = Right Bundle Branch Block

Data in literature on prognostic role of the number of ECG RV strain patterns in PE are scarce. Only few studies [4-6] have examined this topic. One study [6] examined the association of the number of ECG patterns with outcome and other two studies [4,5] its association with severity of PE. Bolt et al. [6] reported comparable results as our study. This author showed that increasing numbers of ECG patterns were related to increased adverse events in 390 patients with acute PE. The incidence of events was 5.7% for the presence of 0 patterns up to 18.6% for 4 patterns and more than 4. In adjusted analyses the number of ECG patterns was independently associated with adverse outcome (odds ratio 1.3 per pattern). In our study we reported an association between the total number of ECG patterns and in-hospital adverse events. We found that patients who had ≥ 5 ECG patterns had significantly higher event rate in comparison to patients with<5 (63.4% vs. 0.7%; p<0.0001). At multivariable analysis the number of ECG patterns remained significant independent predictor of adverse events (hazard ratio of 1.7 per pattern; 95% CI: 1.1-2.6; p=0.009).

In the present study, higher total number of ECG patterns indicated more severe PE. Importantly, patients with high and intermediate risk PE had higher total number of ECG patterns (4.5 vs. 1.6; p<0.0001). In contrast, low risk PE had below 1 pattern. Consequently, events were more prevalent in high and intermediate risk PE. These results correspond to previously reported data [4,5] for significant correlation between the total number of ECG patterns and the severity of acute PE. The number of ECG patterns increased along with increases in the degree of pulmonary hypertension, which is an often used measure of severity in PE. In particular, 5 or more patterns were noticed in pulmonary hypertension ≥ 45 mmHg [4].

Our findings are consistent with prior researches on the prognostic role of ischemic ECG patterns in acute PE. Many studies [2,7,10,13,18,24-27,34] found that ischemic patterns are predictive of worse clinical outcome in acute PE. ST segment changes (elevation or depression) were significantly more frequent in patients with a fatal outcome [25]. In a meta-analysis of 39 studies (over 9000 patients) of PE, Qaddoura et al. [13] showed that several ischemic patterns (ST elevation in III; ST depression in V4-V6; negative T waves in inferior or precordial leads) were significantly predictive for in-hospital mortality. Kukla [26] demonstrated worse in-hospital outcomes in patients with ischemic pattern. According to this author an ischemic ECG pattern on hospital admission when added to classic risk markers, remained an independent risk factor for negative in-hospital outcome. Absence of ischemic ECG pattern was associated with favorable in-hospital outcome [10,27,28]. In contrast, Casazza et al. [28] found no significant association between ischemic pattern (ST elevation in inferior leads) and outcome (odds ratio 2.18; p=0.13), but found that the pattern Qr in V1 was the only pattern significantly associated with in-hospital mortality (odds ratio 3.23; p= 0.01).

In our study, we found that ischemic patterns were strong independent predictors of adverse outcome in PE, similar to the results of previous studies [7,13,18,24-27,34]. We found that ST elevation in inferior leads (present in 5.5% of the study patients) was the strongest independent predictor for in-hospital adverse events (hazard ratio 8). This pattern more significantly increased the hazard ratio for events as compared to other ECG patterns. Negative T waves were not of any prognostic significance in our study.

Limitations

The number of study patients was relatively small. One of the main limitations of our study was its retrospective design. Thus, analyses were limited to information available in the medical records. Another limitation was that we did not had preceding ECG tracings, therefore we cannot exclude whether some ECG abnormalities were existing before the happening of acute PE. We did not exclude patients with comorbidities (chronic obstructive pulmonary disease, coronary artery disease) that are influencing the ECG pattern and have ability to mimic RV strain [3], in order to reflect the variety of patients met in real-world conditions.

Clinical Implications

Despite the limitations, our studies have potential clinical implications. Acute PE has a high mortality rate, thus risk-stratifying of the patients is essential. Since ischemic ECG patterns portend poor prognosis, a comprehensive ECG analysis should be considered in PE, in order to identify patterns with increased risk. Additionally, our study demonstrated that not only the presence of ischemic ECG patterns, but also the total number of ECG patterns bring important information concerning in-hospital prognosis of patients with acute PE. Therefore, quantitative assessment of the number of ECG patterns can be useful to risk stratify the patients with acute PE.

Ischemic patterns, especially ST elevation, are not common ECG manifestations of acute PE. However, when they are present, are clinically important as they could predict adverse clinical outcomes in acute PE. Besides its prognostic role in PE, ischemic pattern mimics acute coronary syndrome [35]. A delay in PE diagnosis is associated with worse outcomes. Prompt recognition of these ECG patterns in patients with acute PE may help in avoiding misdiagnosis leading to unnecessary medical investigations, treatments and poor outcome [36]. Recognition of these ECG patterns may aid in the rapid identification of high-risk patients who may benefit from thrombolytic therapy or mechanical intervention and pulmonary selective vasodilation [37].

Conclusion

In patients with acute PE, the number of ECG RV strain patterns on admission ECG is a strong independent predictor of in-hospital adverse clinical outcome. Less than 5 patterns identify the patients with more favorable outcome, whereas ≥ 5 patterns identify a group with much worse outcomes. Among various ECG RV strain patterns, two ischemic patterns (ST elevation in inferior leads and ST depression) are strong independent prognostic predictors for in-hospital adverse events. The current study adds the number of ECG patterns as a potential prognostic marker for predicting adverse outcomes. Along with these two ischemic patterns should be considered for more accurate early risk stratification in patients with acute PE. However in order to confirm these findings, more prospective studies with a larger study population of patients are required in the near future.

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References

1 Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, et al. (2020) 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J 41: 543-603.

2 Ferrari E, Imbert A, Chevalier T, Mihoubi A, Morand P, et al. (1997) The ECG in pulmonary embolism. Predictive value of negative T waves in precordial leads. Chest 111: 537-543.

3 Ullman E, Brady WJ, Perron AD, Chan T, Mattu A (2001) Electrocardiographic manifestations of pulmonary embolism. Am J Emerg Med 19: 514.

4 Yoshinaga T, Ikeda S, Shikuwa M, Miyahara Y, Kohno S (2003) Relationship between ECG findings and pulmonary artery pressure in patients with acute massive pulmonary thromboembolism. Circ J 67: 229-232.

5 Stein PD, Dalen JI, Mclntyre KM, Sasahara AA, Wenger NK, et al. (1975) The electrocardiogram in acute pulmonary embolism. Prog Cardiovasc Dis 17:247-257.

6 Bolt L, Lauber S, Limacher A (2019) Prognostic Value of Electrocardiography in Elderly Patients with Acute Pulmonary Embolism. Am J Med 132: 835-843.

7 Kukla P, Długopolski R, Krupa E (2011) The value of ECG parameters in estimating myocardial injury and establishing prognosis in patients with acute pulmonary embolism. Kardiol Pol 69: 933-938.

8 Vanni S, Polidori G, Vergara R, Pepe G, Nazerian P, et al. (2009) Prognostic value of ECG among patients with acute pulmonary embolism and normal blood pressure. Am J Med 122: 257-264.

9 Zhong-Qun Z, Chong-QuanW, Nikus KC, Sclarovsky S, Chao-Rong H (2013) A new electrocardiogram finding for massive pulmonary embolism: ST elevation in lead aVR with ST depression in leads I and V(4) to V(6). Am J Emerg Med 31: e5-8.

10 Kukla P, Długopolski R, Krupa E, Furtak R, Mirek-Bryniarska E, et al. (2011) The prognostic value of ST-segment elevation in the lead aVR in patients with acute pulmonary embolism. Kardiol Pol 69: 649-654.

11 Pourafkari L, Ghaffari S, Tajlil A, Akbarzadeh F, Jamali F, et al. (2017) Clinical Significance of ST Elevation in Lead aVR in Acute Pulmonary Embolism. Ann Noninvasive Electrocardiol 22: e12368.

12 Shopp JD, Stewart LK, Emmett TW, Kline JA (2015) Findings from 12-lead electrocardiography that predict circulatory shock from pulmonary embolism: systematic review and meta-analysis. Acad Emerg Med 22: 1127-1137.

13 Qaddoura A, Digby GC, Kabali C, Kukla P, Zhan ZQ, et al. (2017) The value of electrocardiography in prognosticating clinical deterioration and mortality in acute pulmonary embolism: a systematic review and meta-analysis. Clin Cardiol 40: 814-824.

14 McGinn S, White PD (1935) Acute cor pulmonale resulting from pulmonary embolism. JAMA 104: 1473.

15 Goldschlager N, Goldman M (1989) Principles of Clinical Electrocardiography. Appleton & Lange, San Mateo CA.

16 Kukla P, McIntyre WF, Fijorek K (2014) Electrocardiographic abnormalities in patients with acute pulmonary embolism complicated by cardiogenic shock. Am J Emerg Med 32: 507-510.

17 Kucher N, Walpoth N,Wustmann K, Noveanu M, Gertsch M (2003) QR in V1–an ECG sign associated with right ventricular strain and adverse clinical outcome in pulmonary embolism. Eur Heart J 24: 1113-1119.

18 Kukla P, Dlugopolski R, Krupa E (2011) Electrocardiography and prognosis of patients with acute pulmonary embolism. Cardiol J 18: 648-653.

19 Kahyaoğlu M, Alizade E, Naser A, İzgi A (2017) Pulmonary embolism presenting with ST segment elevation in inferior leads. International Journal of the Cardiovascular Academy 3: 41-44.

20 Kosuge M, Kimura K, Ishikawa T (2006) Prognostic significance of inverted T waves in patients with acute pulmonary embolism. Circ J 70: 750-755.

21 Rudski LG, Lai WW, Afilalo J (2010) Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorse by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 23: 685-713.

22 George E, Kumamaru KK, Ghosh N (2014) Computed tomography and echocardiography in patients with acute pulmonary embolism: Part 2: prognostic value. J Thorac Imaging 29: W7-W12.

23 Orde MM, Puranik R, Morrow PL, Duflou J (2011) Myocardial pathology in pulmonary thromboembolism. Heart 97: 1695-1699.

24 Zhan Z, Wang C, Nikus KC (2014) Electrocardiogram patterns during hemodynamic instability in patients with acute pulmonary embolism. Ann Noninvasive Electrocardiol 19: 543-551.

25 Geibel A, Zehender M, Kasper W (2005) Prognostic value of the ECG on admission in patients with acute major pulmonary embolism. Eur Respir J 25: 843-88.

26 Kukla P, McIntyre WF, Fijorek K (2014) Use of ischemic ECG patterns for risk stratification in intermediate-risk patients with acute PE. Am J Emerg Med 32: 1248-1252.

27 Zhan ZQ, Wang CQ, Wang ZX (2015) Significance of ST-segment deviation in patients with acute pulmonary embolism and negative T waves. Cardiol J 22: 583-589.

28 Casazza F, Pacchetti I, Rulli E (2018) Prognostic significance of electrocardiogram at presentation in patients with pulmonary embolism of different severity. Thromb Res 163: 123-127.

29 Pollack ML (2006) ECG manifestations of selected extracardiac diseases. EmergMed Clin North Am 24: 133-143.

30 Zhang F, Qian J, Dong L, Ge J (2012) Multiple ST-segment elevations in anterior and inferior leads: an unusual electrocardiographic manifestation in acute pulmonary embolism. Int J Cardiol 160: e18-20.

31 Villablanca PA, Vlismas PP, Aleksandrovich T (2019) Case report and systematic review of pulmonary embolism mimicking ST-elevation myocardial infarction. Vascular 27: 90-97.

32 Zhong-qun Z, Chong- quan W, Nikus KC (2013) A new electrocardiogram finding for massive pulmonary embolism: ST elevation in lead aVR with ST depression in leads I and V(4) to V(6). Am J Emerg Med 31: 456-458.

33 Coma- Canella I, Gamallo C, Martinez Onsurbe P (1988) Acute right ventricular infarction secondary to massive pulmonary embolism. Eur Heart J 9: 534–540.

34 Kaczyńska A, Bochowicz A, Kostrubiec M (2004) Electrocardiography and prediction of myocardial damage in patients with acute pulmonary embolism. Pol Arch Med Wew 112: 1039-1046.

35 Kukla P, Długopolski R, Krupa E (2011) How often pulmonary embolism mimics acute coronary syndrome?. Kardiol Pol 69: 235-240.

36 Aydogdu M, Dogan NO, Sinanoglu NT (2013) Delay in diagnosis of pulmonary thromboembolism in emergency department: is it still a problem? Clin Appl Thromb Hemost 19: 402-409.

37 Kline JA, Hernandez J, Garrett JS (2014) Pilot study of a protocol to administer inhaled nitric oxide to treat severe acute submassive pulmonary embolism. Emerg Med J 31: 459-462.