Electrocardiographic Differentiation between Acute Pulmonary Embolism and Non-ST Elevation Acute Coronary Syndromes at the Bedside

Krzysztof Jankowski, M.D., Ph.D., Maciej Kostrubiec, M.D., Ph.D., Patrycja Ozdowska, M.D., Blanka Milanowska-Puncewicz, M.D., Szymon Pacho, M.D., Justyna Pedowska-Włoszek, M.D., Anna Kaczyńska, M.D., Ph.D., Andrzej Łabyk, M.D., Anna Hrynkiewicz, M.D., and Piotr Pruszczyk, M.D., Ph.D.

From the Department of Internal Medicine and Cardiology of Warsaw Medical University, Warsaw, Poland

Background: Clinical picture of acute pulmonary embolism (APE), with wide range of electrocardiographic (ECG) abnormalities can mimic acute coronary syndromes.

Objectives: Assessment of standard 12-lead ECG usefulness in differentiation at the bedside between APE and non-ST elevation acute coronary syndrome (NSTE-ACS).

Methods: Retrospective analysis of 143 patients: 98 consecutive patients (mean age 63.4 ± 19.4 year, 45 M) with APE and 45 consecutive patients (mean age 72.8 ± 10.8 year, 44 M) with NSTE-ACS. Standard ECGs recorded on admission were compared in separated groups.

Results: Right bundle branch block (RBBB) and $S_1S_2S_3$ or $S_1Q_3T_3$ pattern were found in similar frequency in both groups (10 [11%] APE patients vs 6 [14%] NSTE-ACS patients, 27 [28%] patients vs 7 [16%] patients, respectively, NS). Negative T waves in leads V_{1-3} together with negative T waves in inferior wall leads II, III, aVF (OR 1.3 [1.14–1.68]) significantly indicated APE with a positive predictive value of 85% and specificity of 87%. However, counterclockwise axis rotation (OR 4.57 [2.74–7.61]), ventricular premature beats (OR 2.60 [1.60–4.19]), ST depression in leads V_{1-3} (OR 2.25 [1.43–3.56]), and negative T waves in leads V_{5-6} (OR 2.08 [1.31–3.29]) significantly predicted NSTE-ACS.

Conclusions: RBBB, $S_1S_2S_3$, or $S_1Q_3T_3$ pattern described as characteristic for APE were not helpful in the differentiation between APE and NSTE-ACS in studied group. Coexistence of negative T waves in precordial leads V_{1-3} and inferior wall leads may suggest APE diagnosis.

Ann Noninvasive Electrocardiol 2010;15(2):145–150

electrocardiogram; pulmonary embolism; NSTE-ACS

Clinical picture of acute pulmonary embolism (APE), especially chest pain, syncope, together with electrocardiographic (ECG) abnormalities and elevated plasma troponin levels can mimic acute coronary syndromes and even may lead to an unnecessary urgent coronary angiography.[1]

A wide range of ECG abnormalities have been reported in patients with APE. The most frequent ECG signs of APE include $S_1Q_3T_3$ pattern, sinus tachycardia, inverted T waves in the precordial leads, ST displacement, right bundle branch block (RBBB), P pulmonale, S-wave notch in lead V_1.[2–7] However, none of them is unequivocally diagnostic of APE. Moreover, negative T waves in the precordial leads and ST depression can lead to diagnostic mistakes, suggesting ongoing ischemia of the left ventricular anterior wall.

Therefore, we assessed if standard 12-lead ECG can be useful in differentiation between APE and non-ST elevation acute coronary syndrome (NSTE-ACS), at the bedside.

Address for correspondence: Andrzej Łabyk, M.D., Department of Internal Medicine and Cardiology, Lindley'a str. 4, 02-005 Warsaw, Poland. Fax: +48 22 502 13 63; E-mail: endrjulab@tlen.pl

Conflict of Interest: The authors of this manuscript do not report any conflict of interest in connection with submitted article.

METHODS

We performed a retrospective analysis of 143 patients: 98 consecutive patients (mean age 63.4 ± 19.4 year, 45 M) with APE confirmed by spiral contrast-enhanced computed tomography (group APE) and 45 consecutive patients (mean age 72.8 ± 10.8 year, 44 M) with NSTE-ACS diagnosed according to European Society of Cardiology (at least two of three symptoms: chest pain, signs of myocardial ischemia on ECG, elevated troponin levels (group NSTE-ACS).[8]

Patients with chronic obstructive pulmonary disease, primary pulmonary hypertension, dilated cardiomyopathy, severe heart failure (NYHA class III or IV), significant electrolyte abnormalities on admission were not included into the study.

Left bundle branch block was found in 3 patients in APE group and in 2 patients in group NSTE-ACS, and they were also excluded from further analysis. The analysis of ECG tracings was performed in 95 patients with APE and 43 subjects with NSTE-ACS.

Standard 12-lead ECGs recorded on the admission day were reviewed by three physicians blinded to the final diagnosis. Axis deviation, signs of myocardial ischemia (T-wave inversion defined by the presence of pointed and symmetrical inverted T waves, ST depression at least 0.1 mV, at least in two continuous leads), the prevalence of supra- and ventricular arrhythmias, RBBB (QRS > 0.11 sec and S wave in lead I and terminal R wave in V_1 with amplitude > 0.15 mV), $S_1S_2S_3$ or $S_1Q_3T_3$ pattern (S wave in lead I and Q wave in lead III with amplitude > 0.15 mV, associated with T-wave inversion in lead III), P pulmonale, S-wave notch in lead V_1 were compared in both groups.

ECG tracings were also compared in patients with high, medium, and low risk of APE, defined according to European Society of Cardiology Guidelines, based on systemic systolic blood pressure on admission and the presence of right ventricular dysfunction at echocardiography and elevated plasma troponin levels.

Statistical Analysis

Data characterized by a normal distribution are expressed as mean followed by standard deviation. Parameters without such a distribution are expressed as median with range. Student's or Mann–Whitney's tests were used for comparisons between two groups, while comparisons between more than two groups were performed by ANOVA or Kruskal–Wallis tests. The chi-square test was used to compare discrete variables. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated for the chosen parameters. Univariable logistic regression analysis was used to assess, which ECG abnormalities were significant predictors of APE or NSTE-ACS. All tests were 2-sided. Data were considered significant at $P < 0.05$. STATISTICA software (StatSoft 8.0, StatSoft Polska, Krakow, Poland) was used for statistical calculations.

RESULTS

Clinical characteristic of both groups are presented in Table 1.

The ECG abnormalities are described in Table 2.

Table 1. Clinical Characteristic of Patients with APE (Group APE, n = 95) and Patients with NSTE-ACS (Group NSTE-ACS, n = 43)

Parameter	Group APE n (%)	Group NSTE-ACS n (%)	P
Age (year ± SD)	63.4 ± 19.4	72.8 ± 10.8	<000.1
Sex (male)	43 (45)	19 (44)	NS
History of ischemic heart disease	30 (32)	32 (74)	<0.0001
History of myocardial infarction	0	0	-
History of pulmonary embolism	0	0	-
Symptoms—Onset of Incidence			
Chest pain	40 (42)	30 (70)	<0.01
Dyspnea	81 (85)	19 (44)	<0.001
Syncope	24 (25)	7 (16)	NS

APE = acute pulmonary embolism; NSTE-ACS = non-ST elevation acute coronary syndrome.

Table 2. Electrocardiographic Abnormalities in Patients with APE (Group APE, n = 95) and in Patients with NSTE-ACS (Group NSTE-ACS, n = 43)

ECG abnormalities	Group APE n (%)	Group NSTE-ACS N (%)	P
Clockwise axis rotation	30 (32)	26 (61)	<0.01
ST depression* in leads II, III, aVF	32 (34)	12 (28)	NS
ST depression in leads V_{1-3}	19 (20)	21 (49)	<0.001
ST depression in leads V_{5-6}	38 (40)	21 (49)	NS
Negative T waves in leads II, III, aVF	24 (25)	7 (16)	NS
Negative T waves in leads II, III, aVF with ST depression	16 (17)	6 (14)	NS
Negative T waves in leads V_{1-3}	46 (48)	10 (23)	<0.01
Negative T waves in leads V_{1-3} with ST depression	17 (18)	11 (26)	NS
Negative T waves in leads V_{5-6}	4 (4)	5 (12)	NS
Negative T waves in leads V_{5-6} with ST depression	13 (14)	13 (30)	<0.05
Supraventricular premature beats	17 (18)	9 (21)	NS
Ventricular premature beats	2 (2)	6 (14)	<0.05
Right bundle branch block	10 (11)	6 (14)	NS
$S_1S_2S_3$ or $S_1Q_3T_3$ pattern	27 (28)	7 (16)	NS
P pulmonale	1 (1)	0	NS
S-wave notch in lead V_1	9 (9)	4 (9)	NS
Atrial fibrillation	12 (13)	7 (16)	NS

*ST depression equal/more than 1 mm.
APE = acute pulmonary embolism; NSTE-ACS = non-ST elevation acute coronary syndrome.

Axis Deviation

Counterclockwise axis rotation in the horizontal axis (shift in the transition zone to V_5 or beyond) was recorded in 26 (61%) patients with NSTE-ACS and in 30 (32%) patients with APE ($P < 0.01$).

Signs of Myocardial Ischemia

The incidence of ST depression in leads II, III, aVF, and in leads V_5–V_6 were similar in both groups and the differences were not statistically significant. However, ST depression in leads V_1–V_3 was more frequent in patients with NSTE-ACS than in patients with APE (21 [49%] patients vs 19 [20%] patients, $P < 0.001$).

There were no significant differences between both groups in the simultaneous presence of negative T waves with or without ST depression in leads II, III, aVF (16 [17%] patients in group APE vs 6 [14%] patients in group NSTE-ACS, 24 [25%] patients vs 7 [16%] patients, respectively, NS). Moreover, negative T waves in leads V_5–V_6 with coexisting ST depression were significantly more frequent in group NSTE-ACS (13 [14%] patients in group APE vs 13 [30%] patients in group NSTE-ACS, $P < 0.05$).

RBBB and $S_1S_2S_3$ or $S_1Q_3T_3$ pattern was recorded in similar frequency in both groups (10 [11%] APE patients vs 6 [14%] NSTE-ACS patients, 27 [28%] patients vs 7 [16%] patients, respectively, NS). Similarly, presence of S-wave notch in lead V_1 did not differentiate both groups (9 [9%] patients in group APE versus 4 [9%] patients in group NSTE-ACS, NS).

Arrhythmias

The prevalence of supraventricular premature beats was similar in APE and NSTE-ACS patients (17 [18%] patients vs 9 [21%] patients, NS), ventricular premature beats was recorded in 2 (2%) patients in group APE, and in 6 (14%) patients in group NSTE-ACS ($P < 0.05$). There was no case of complex arrhythmias in both groups.

P pulmonale was found only in one patient in group with APE.

Sensitivity, specificity, NPV, and PPV were evaluated for the chosen parameters. The negative T waves in leads V_1–V_3 occurred simultaneously with negative T waves in leads II, III, aVF were high specific (87%) with a high PPV (85%) for APE. The occurrence of ventricular premature beats, ST depression in leads V_1–V_3, negative T waves in leads V_{5-6}, negative T waves in leads V_5–V_6 with ST depression, counterclockwise axis rotation were specific for NSTE-ACS (specificity 69–98%) (see Table 3).

Table 3. Sensitivity, Specificity, and Predictive Values of Chosen Electrocardiographic Parameters in Studied Groups of Patients with APE (Group APE, n = 95) and in Patients with NSTE-ACS (Group NSTE-ACS, n = 43)

Predictor	Number of Patients with Positive Test		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
	APE n (%)	NSTE-ACS n (%)				
Negative T waves in leads V_{1-3} for APE	63 (64)	21 (47)	64	53	75	41
Negative T waves in leads V_{1-3} and in leads II, III, aVF for APE	33 (34)	6 (13)	34	87	85	38
Counterclockwise rotation for NSTE-ACS	30 (31)	26 (58)	58	69	46	78
Ventricular premature beats for NSTE-ACS	2 (2)	6 (13)	13	98	75	69
ST depression in leads V_{1-3} for NSTE-ACS	19 (19)	21 (47)	47	81	53	77
Negative T waves in leads V_{5-6} for NSTE-ACS	17 (17)	18 (40)	40	83	51	75
Negative T waves in leads V_{5-6} with ST depression for NSTE-ACS	13 (13)	13 (29)	29	87	50	73

PPV = positive predictive value; NPV = negative predictive value; APE = acute pulmonary embolism; NSTE-ACS = non-ST elevation acute coronary syndrome.

Univariate Analysis

Logistic regression analysis revealed that negative T waves in leads V_1–V_3 (OR 1.26 [0.99–1.61]) and negative T waves in leads V_1–V_3 coexisting with negative T waves in leads II, III, aVF (OR 1.3 [1.14–1.68]) are significant predictors of APE. Whereas, counterclockwise axis rotation (OR 4.57 [2.74–7.61]), ventricular premature beats (OR 2.60 [1.60–4.19]), ST depression in leads V_1–V_3 (OR 2.25 [1.43–3.56]), and negative T waves in leads V_5–V_6 (OR 2.08 [1.31–3.29]) indicate NSTE-ACS (Table 4).

Relationship between severity of APE and ECG changes is presented in Table 5.

Table 4. Odds Ratio for APE (Group APE) and NSTE-ACS (Group NSTE-ACS), Depending on the Presence of Selected Electrocardiographic Abnormalities

ECG Abnormalities	OR (95% CI)	P
ECG abnormalities predicting APE		
Negative T waves in leads V_{1-3}	1.26 (0.99–1.61)	0.06
Negative T waves in leads V_{1-3}, II, III, aVF	1.3 (1.14–1.68)	<0.01
ECG abnormalities predicting NSTE-ACS		
Counterclockwise axis rotation	4.57 (2.74–7.61)	<0.01
Ventricular premature beats	2.60 (1.60–4.19)	<0.01
ST depression* in leads V_{1-3}	2.25 (1.43–3.56)	<0.01
negative T waves in leads V_{5-6}	2.08 (1.31–3.29)	<0.01
Negative T waves in leads V_{5-6} with ST depression*	1.83 (1.13–2.97)	<0.01

*ST depression equal/more than 1 mm.
APE = acute pulmonary embolism; NSTE-ACS = non-ST elevation acute coronary syndrome.

DISCUSSION

Although pulmonary embolism is one of the most common life-threatening cardiovascular conditions, it is often not properly diagnosed. Importantly, the prognosis in APE depends on prompt and adequate treatment. Unfortunately, the APE symptoms, such as dyspnea, chest pain, syncope, are not specific and can often mimic other acute cardiopulmonary pathologies including acute coronary syndromes. Unnecessary coronary angiographies were reported in patient with APE when initially ACS was diagnosed.[9] Because all patients hospitalized with acute chest pain or after syncope undergo standard 12-lead electrocardiogram, it seems justified to assess differences in ECG recording between APE and NSTE-ACS. Several studies reported that ECG abnormalities typical for APE are useful for discrimination from acute coronary syndromes. These are: clockwise axis rotation, RBBB, $S_1S_2S_3$ or $S_1Q_3T_3$ pattern, S-wave notch in lead V_1.[10–12] It was even suggested that when all above abnormalities are present in a patient with a suggestive clinical presentation and risk factors of venous thromboembolic disease,

Table 5. Electrocardiographic Abnormalities in Patients with Low, Intermediate, and High Risk of APE. Risk Groups Defined According to European Society of Cardiology Guidelines

	Low-Risk APE (n = 36)	Intermediate Risk APE (n = 57)	High-Risk APE (n = 5)	P
Clockwise axis rotation	9	18	3	0.76
ST depression* in leads II, III, aVF	9	21	2	0.91
ST depression in leads V_{1-3}	7	10	2	0.92
ST depression in leads V_{5-6}	11	24	3	0.82
Negative T waves in leads II, III, aVF without ST depression	6	16	2	0.82
Negative T waves in leads II, III, aVF with ST depression	3	12	1	0.75
Negative T waves in leads V_{1-3} without ST depression	13	31	2	0.69
Negative T waves in leads V_{1-3} with ST depression	7	8	2	0.80
Negative T waves in leads V_{5-6} without ST depression	0	4	0	0.93
Negative T waves in leads V_{5-6} with ST depression	1	12	0	0.26
Supra- and ventricular premature beats	3	13	2	0.45
Supraventricular premature beats	3	12	2	0.45
Ventricular premature beats	0	1	1	0.15
Right bundle branch block	3	5	2	0.40
$S_1S_2S_3$ or $S_1Q_3T_3$ pattern	8	12	5	0.04
$S_1S_2S_3$ pattern	2	3	2	0.13
$S_1Q_3T_3$ pattern	6	9	5	0.005
P pulmonale	0	1	0	0.99
S-wave notch in lead V_1	1	8	0	0.63
Atrial fibrillation	3	8	1	0.97
Left bundle branch block	1	2	0	0.99

*ST depression equal/more than 1 mm.
APE = acute pulmonary embolism.

they could be regarded for diagnostic procedure.[13] Our study found that RBBB, $S_1S_2S_3$ or $S_1Q_3T_3$ pattern could not differentiate APE from ACS. Moreover, it was found that these abnormalities occurred rather rarely in patient with APE, and the reported frequency of $S_1Q_3T_3$ pattern is 15%, while RBBB only 12%.[14] We found that counterclockwise axis rotation significantly predicted ACS (OR 4.57 [95% CI 2.74–7.61]).

Interestingly, negative T waves in precordial leads are often seen in patients with acute coronary syndrome, but may also occur in acute pulmonary embolism. Some authors regard T-wave inversion in the precordial lead for the most common abnormality in patients with APE. Moreover, negative T waves were reported to correlate with the severity of the PE.[15–17] Recently, standard ECG recordings of 127 patients (40 patients with APE and 87 patients with ACS patients) with negative T waves in the precordial leads were analyzed. It was found that pulmonary negative T waves in present simultaneously in both III and V_1 leads allow to differentiate APE from ACS with sensitivity, specificity, PPV, and NPV of 88%, 99%, 97%, and 95%, respectively, in studied groups.[10] Our data support these observations. Although isolated negative T wave in V_1–V_3 were only of borderline significance for APE ($P = 0.06$), their coexistence with negative T waves in inferior wall leads significantly predicted APE. Negative T waves in V_5–V_6 indicated ACS, especially when ST depression was present. Also premature ventricular beats instead of supraventricular beats in studied group indicated NSTE-ACS with a very high specificity.

In conclusion, RBBB, $S_1S_2S_3$ or $S_1Q_3T_3$ pattern commonly reported to be characteristic for APE, in studied group of patients did not differentiate APE from NSTE-ACS. However, coexistence of negative T waves in precordial leads and inferior wall leads should suggest APE, while negative T waves in V_5–V_6 especially with ST segment depression indicate ACS.

Acknowledgments: *The authors have certified that the manuscript conforms to the guidelines in "Uniform Requirements for Manuscripts Submitted to Biomedical Journals," 5th edition, published in New England Journal of Medicine 1997; 336: 309–315.*

REFERENCES

1. Pruszczyk P, Szulc M, Horszczaruk G, et al. Right ventricular infarction in a patient with acute pulmonary embolism and normal coronary arteries. Arch Intern Med 2003;163:1110–1111.
2. McGinn S, White PD. Acute cor pulmonale resulting from pulmonary embolism. JAMA 1935;104:1473–1480.
3. Rodger M, Makropoulos D, Turek M, et al. Diagnostic value of the electrocardiogram in suspected pulmonary embolism. Am J Cardiol 2000;86:807–809.
4. Ferrari E, Imbert A, Chevalier T, et al. The electrocardiogram in pulmonary embolism: Predictive value of negative T-waves in precordial leads −80 case report. Chest 1997;11:537–543.
5. Stein PD, Dalen JE, McIntyre KM, et al. The electrocardiogram in acute pulmonary embolism. Prog Cardiovasc Dis 1975;17:247–257.
6. Stein PD, Terrin ML, Hales CA, et al. Clinical, laboratory, roentgenographic, and electrocardiographic findings in patients with acute pulmonary embolism and no pre-existing cardiac or pulmonary disease. Chest 1991;100:598–603.
7. Mirvis DM, Goldberger AL. Electrocardiography. In: Zipes DP, Braunwald E (eds.): Braunwald's Heart Disease: A Textbook of Cardivascular Medicine, 7th Edition. Philadelphia: Elsevier Saunders, 2005.
8. Bassand JP, Hamm CW, Ardissino D, et al. Task Force for diagnosis and treatment of non-ST-segment elevation acute coronary syndromes of European Society of Cardiology, Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. Eur Heart J 2007;28:1598–1660.
9. Widimsky P, Stellova B, Groch L, et al. PRAGUE Study Group Investigators: Prevalance of normal coronary angiography in the acute phase of suspected ST-elevation myocardial infarction: Experience from the PRAGUE studies. Can J Cardiol 2006;22:1147–1152.
10. Kosuge M, Kimura K, Ishikawa T, et al. Electrocardiographic differentiation between acute pulmonary embolism and acute coronary syndromes on the basis of negative T-waves. Am J Cardiol 2007;99:817–821.
11. Sreeram N, Cheriex EC, Smeets JL, et al. Value of the 12-lead electrocardiogram at hospital admission in the diagnosis of pulmonary embolism. Am J Cardiol 1994;73:298–303.
12. Wilson GT, Schaller FA. Pulmonary embolism mimicking anteroseptal acute myocardial infarction. JAOA 2008;108:344–349.
13. Perrier A, Bounameaux H. Pulmonary thromboembolism and pulmonary vascular tumors. Diagnosis. In: Peacock AJ, Rubin LJ (eds.): Pulmonary Circulation. Diseases and Their Treatment, 2nd Edition. London: Edward Arnold (Publishers) Ltd, 2004.
14. Golbin JM, Prakash UBS. Pulmonary embolism. In: Murphy JG, Lloyd MA (eds.): Mayo Clinic Cardiology. Concise Textbook, 3rd Edition. Rochester, MN: Mayo Foundation for Medical Education and Research, 2007.
15. Yoshinaga T, Ikeda S, Nishimura E, et al. Serial changes in negative T-wave on electrocardiogram in acute pulmonary thromboembolism. Int J Cardiol 1999;72:65–72.
16. Punukollu G, Gowda RM, Khan IA, et al. QT interval prolongation with global T-wave inversion: A novel ECG finding in acute pulmonary embolism. Ann Noninvasive Electrocardiol 2004;9:94–98.
17. Ciurzynski M, Kurzyna M, Ficygowski W, et al. Pulmonary embolism hemodynamically significant. Electrocardiographic findings. Kardiol Pol 2000;52:458–460.