The Diagnostic Predictive Value of R wave peak time in Patients with Acute Pulmonary Embolism

Akut Pulmoner Embolili Hastalarda R Dalga Pik Zamanının Tanısal Öngörücü Değeri

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Abstract: This study aimed to investigate the diagnostic predictive value of R wave peak time (RWPT) in patients admitted to the emergency department with a preliminary diagnosis of acute pulmonary embolism (APE).
Computerized tomographic pulmonary angiography (CTPA) was performed in 74 consecutive patients with suspected APE, and of these 66 patients with appropriate electrocardiogram (ECG) and CTPA images composed the study population.By using CTPA, APE was confirmed in 27 patients. While the atrial arrhythmia, right axis deviation, complete or incomplete right bundle branch block, prominent S wave in the lead DI, S1Q3T3 pattern, and RWPT in the lead DIII (40±11 vs. 31±13 ms) were statistically different in patients with APE compared to those without APE ($p<0.05$, for all), the other ECG findings were similar. Multivariate analysis revealed that RWPT in the lead DIII (odds ratio: 14.959, 95% confidence interval: 1.811–123.582, p=0.012) was found to be an independent predictor of APE. A receiver operating characteristic analysis was drawn to show the best cut-off value of the RWPT in the lead DIII to predict APE was ≥40 ms with 48.1% sensitivity and 87.2 % specificity (area under curve (AUC): 0.718; 95% CI: 0.593–0.843; p=0.003).The present study demonstrated that the RWPT in the lead DIII may have diagnostic predictive value for APE. In addition, it may be useful in electrocardiographic signs for the diagnosis of APE.
Key Words: R wave peak time in the lead DIII, pulmonary embolism, electrocardiography

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Özet: Bu çalışmada, akut pulmoner emboli (APE) ön tanısı ile acil servise başvuran hastalarda R dalga pik zamanın (RDPZ) tanısal değerini araştırmayı amaçladık. APE şüphesi ile ardışık 74 hastaya bilgisayarlı tomografik pulmoner anjiyografi (BTPA) uygulandı ve bu hastalardan uygun elektrokardiyografi (EKG) ve BTPA görüntüleri olan 66 hasta çalışma nüfusunu oluşturdu. BTPA kullanılarak 27 hastada APE doğrulandı. Atrial aritmi, sağ aks deviyasyonu, komple ve in komple sağ dal bloğu, DI derivasyonunda belirgin S dalgası, S1Q3T3 bulgusu ve DIII derivasyonunda RDPZ (40±11 vs. 31±13 ms) APE hastalarında istatistiksel olarak farklı iken ($p<0.05$, hepsi), diğer EKG bulguları benzerdi. Çoklu değişken analizi, DIII derivasyonunda ki RDPZ APE'nin bağımsız öngörücü olarak bulundu (Odd oranı: 14.959, 95% Güven Aralığı: 1.811–123.582, p=0.012). Karar vericinin etkinliği (KVE) eğrisi çizilerek RDPZ değerinin APE'nin en iyi öngörücü değeri %87,2'lük duyarlılık ve %48,1'lük bir özgüllük ile >=40 ms olarak saptandı (Eğri altında kalan alan (EAK): 0.718, 95% CI: 0.593-0.843; p=0.003). Bu çalışma DIII derivasyonunda RDPZ'nın tanısal değeri olabileceğini göstermiştir. Bunun yanında, RDPZ'ı APE'nin tanısı için yararlı bir elektrografik bulgu olabilir.
Anahtar Kelimeler: DIII derivasyonunda R dalga pik zamanı, akut pulmoner emboli, elektrokardiyografi

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1. Introduction

Acute pulmonary embolism (APE) is a clinical entity that is associated with significant morbidity and mortality. The overall incidence of APE is about 1–2 per 1000 persons among the population of the United States (1). Based on clinical presentation, the mortality rate is variable and may reach as high as 60% in patients with massive APE. The clinical presentation of APE may range from mild complaints to shock, making the diagnosis challenging (2). Therefore, new diagnostic modalities to identify patients that will benefit from immediate treatment are needed for prompt and appropriate diagnosis of APE.

The role of electrocardiography (ECG) is mainly for diagnosing acute coronary syndromes and other clinical entities in acute settings. It has been reported that multiple ECG changes might be found in patients with APE. The ECG findings may include atrial arrhythmia, right axis deviation, complete or incomplete right bundle branch block, sinus tachycardia with secondary ST–T changes, S1Q3T3 pattern, T inversions and ST depressions in the right to mid-precordial leads (3, 4). However, the ECG changes are not in the desired range of sensitivity and specificity for the diagnosis of APE (5-7). The R wave peak time (RWPT) has been described as the duration from the isoelectric line to its first deflection, whether it is R or r' wave, also referred to as ventricular activation time or intrinsicoid deflection time (8). Several previous reports have demonstrated that the delay of RWPT is associated with multiple clinical conditions (9, 10). On the other hand, to the best of our knowledge, no data has been available for the diagnostic predictive value of the delay of RWPT in patients with APE. Hence, in the present study, we aimed to test the hypothesis that the delay of RWPT in the lead DIII may have diagnostic predictive value in patients with APE confirmed by computerized tomographic pulmonary angiography (CTPA).

2. Materials and Methods

Patients

A total of 74 patients who underwent CPTA with a preliminary diagnosis of APE at the emergency department from January 2015 to January 2016 were respectively analyzed. Five patients with poor ECG image quality were excluded from the study. In addition, three patients whose CTPA was not performed in accordance with standard protocol were also excluded. Therefore, the data for 66 patients were eligible for analysis. The baseline demographic characteristics, signs and symptoms of the patients, risk factors and hemodynamic parameters were noted on admission. The pulmonary emboli severity index (PESI), revised Geneva and Wells risk score were also calculated. In accordance with current guidelines, all patients were treated with the standard therapy (1). The study protocol was approved by our local ethics committee and was performed according to Declaration of Helsinki.

Electrocardiographic Interpretation

On admission to the emergency department, all patient ECGs were recorded with a low pass filter (0.5–25 Hz), 25 mm/sec paper speed, and 10 mm/mV voltage calibration. The ECG recordings were scanned and analyzed using digital image processing software (imagej.nih.gov/ij/). Two experienced cardiologists, blinded to the patient data, analyzed the ECG findings. In cases of disagreement, the two cardiologists reviewed the ECGs and jointly came to an agreement. The ECG was assessed for heart rate, S1Q3T3 pattern, incomplete or complete right bundle branch block, and ST-segment elevations or depressions. The S1Q3T3 was defined as the presence of any S wave in lead I, Q wave (>1.5 mm deep) in lead III and T wave inversion in the lead DIII. A complete right bundle branch block was defined as QRS duration >120 ms with a terminal R wave in lead V1 and terminal S wave in lead I and V6. An incomplete right bundle branch block was defined as a QRS duration 100 to 120 ms and

morphology otherwise similar to a right bundle branch block. The RWPT, defined as the interval from the start of the QRS complex until the peak of the R or r' wave, was analyzed in the leads DIII, V1 and V4-V6 (Figure 1). All durations were calculated in milliseconds (ms). *Echocardiography and Contrast Tomographic Pulmonary Angiography*

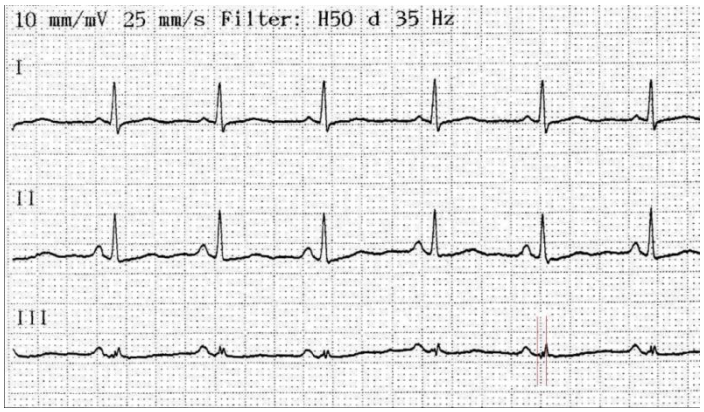

Figure 1. *The evaluation of RWPT, defined as the interval from the start of the QRS complex until the peak of the R or r' wave, in the lead DIII.*

The transthoracic echocardiographic assessment was performed using a Vivid 7 system (GE Vingmed Ultrasound AS, Horten, Norway) to study the patients. According to the Simpson method, the left ventricular ejection fraction was calculated. The calculation of pulmonary systolic pressure was determined primarily by calculating the systolic pressure gradient peak from the right ventricle to the right atrium, assessed through the simplified Bernoulli equation (4x squared V, where V= peak systolic velocity of tricuspid regurgitation measured using continuous Doppler, and the right atrium pressure was added according to the collapse of the inferior venous cava during inspiration) (11). Using the PE protocol, multi-slice spiral 64-slice CTPA (SOMATOM Sensation 64; Siemens, Erlangen, Germany) was performed. All CTPA images were evaluated by an experienced radiologist. The diagnosis of APE was determined in cases of a complete or partial luminal filling defect in the main pulmonary artery or its branches.

Statistical Analysis

Statistical analyses were performed using SPSS version 22.0 (IBM, Chicago, Illinois). Normality of the data was analyzed using the Kolmogorov–Smirnov test. The numerical variables with a normal distribution are presented as mean ± standard deviation, whereas those without a normal distribution are presented as median and interquartile range. A frequency distribution was calculated for the categorical variables (numbers and percentages [%]). The continuous variables of the two groups were compared using a t-test or the Mann-Whitney U test. Categorical data were compared using the chi-square test or the Fisher exact test. Statistical significance was defined as a p value <0.05. Multivariate logistic regression analyses were performed to identify the independent predictors of APE using variables that showed marginal association with APE in the univariate analyses. The RWPT value that predicted the best specificity and sensitivity was calculated using receiver operating characteristic (ROC) curve analysis. The effect size (Cohen's d) and power value (1–β) for RWPT in the lead DIII, compared between patients with and without PE, were calculated using G*Power software. The alpha level used for this analysis was <0.05. The effect size and power value were 0.74 and 0.90, respectively.

Table 1.
The baseline demographic characteristics and laboratory findings of all patients and patients with and without APE and with P value

	All patients, n:66	Patients without APE, n:39	Patients with APE, n:27	p
Age, years	59±17	60±16	59±20	0.848
Female sex, n %	34 (51.5%)	18 (46.2%)	16 (59.3%)	0.295
Risk factors				
Diabetes, n %	13 (19.7%)	7 (17.9%)	6 (22.2%)	0.668
Hypertension, n %	21 (31.8%)	8 (20.5%)	13 (48.1%)	0.018
Smoking, n %	28 (42.4%)	16 (41.0%)	12 (44.4%)	0.782
Pulmonary disease, n %	11 (16.7%)	5 (12.8%)	6 (22.2%)	0.314
Coronary artery disease, n %	11 (16.7%)	6 (15.4%)	5 (18.5%)	0.737
Heart failure, n %	6 (9.1%)	5 (12.8%)	1 (3.7%)	0.205
Pulmonary embolism, n %	4 (6.1%)	2 (5.1%)	2 (7.4%)	0.703
Deep vein thrombosis, n %	2 (3.0%)	1 (2.6%)	1 (3.7%)	0.791
Malignancy, n %	2 (3.0%)	1 (2.6%)	1 (3.7%)	0.791
Surgery or immobilization within past four weeks, n %	14 (21.2%)	5 (12.8%)	9 (33.3%)	0.045
Hemoptysis, n %	3 (4.5%)	1 (2.6%)	2 (7.4%)	0.353
Unilateral leg pain and/or swelling, n %	13 (19.7%)	5 (12.8%)	8 (29.6%)	0.091
On admission				
Systolic blood pressure; mmHg	128±25	133±25	121±24	0.054
Temperature; °C	36.6±0.6	36.6±0.5	36,5±0.7	0.79
Respiratory rate; /min	20 (18-24)	20 (18-22)	20 (18-28)	0.144
Oxygen saturation; %	93 (85-96)	94 (90-96)	90 (82-94)	0.026
Laboratory findings				
Glucose; mg/dl	137±55	138±63	134±41	0.781
Creatinine; mg/dl	0.89±0.23	0.88±0.24	0.89±0.22	0.872
Blood urea nitrogen	41±16	41±16	41±17	0.96
Alanine transaminase	26±18	26±19	25±18	0.872
Aspartate transaminase	30±18	31±17	29±19	0.756
Potassium	4.3±0.5	4.4±0.6	4.3±0.5	0.462
Sodium	138±4	137±5	140±4	0.026
Calcium	8.8±0.6	8.9±0.7	8.7±0.6	0.168
White blood cell;	9.6±4.0	9.6±4.3	9.6±3.5	0.994
Hemoglobin; g/dl	13.8±2.2	14.1±1.9	13,4±2.5	0,216
Platelet count;	232±78	231±79	234±79	0,889
D-dimer;	1378 (820-2224)	1230 (654-1921)	1560 (1123-3120)	0,005
Positive D-dimer test, n %	58 (87.9%)	32 (82.1%)	26 (96.3%)	0,081
Troponin	0.03 (0.01-0.15)	0.02 (0.00-0.20)	0.06 (0.01-0.27)	0,076

Positive troponin test, n %	29 (43.9%)	15 (38.5%)	14 (51.9%)	0,281
Wells score	3 (3-5)	3 (3-5)	3 (3.6)	0,091
Revised Geneva Score	5 (1-8)	3 (1-6)	5 (3-10)	0,031
Pulmonary embolism severity index	86±31	81±28	93±35	0,134

Acronym and their meaning are; *APE; Acute Pulmonary Embolism. Continuous variables are presented as mean±SD or median; nominal variables presented as frequency*

3. Results

A total of 66 consecutive patients were enrolled in the study. The study population was divided into two groups, patients with APE and without APE. APE was confirmed in 27 patients with CTPA. The final diagnosis of the patients without APE (n:39) were acute exacerbation of asthma (n:2), chronic obstructive pulmonary disease (n:5), pneumonia (n:2), acute decompensated heart failure (n:4) and acute coronary syndrome (n:2). No organic pathology was detected in the remaining 24 patients. The baseline demographic characteristics and laboratory findings of all patients with and without APE is shown in Table 1. The mean age of the study population was 59±17. Of the patients, 34 were female and the others were male. The frequency of hypertension was higher in patients with APE compared to those without APE (p=0.018). Whereas, the frequency of diabetes mellitus, smoking, pulmonary disease, coronary artery disease, heart failure, history of PE, deep vein thrombosis and malignancy were similar between the groups (p>0.05 for all). Surgery or immobilization within the past four weeks was more common in patients with APE (p=0.045). The patients with APE had lower oxygen saturation on admission compared to those without APE (p=0.026). The other hemodynamic parameters were similar between the two groups (p>0.05 for all). In terms of laboratory parameters, only D-dimer and sodium levels were different between the two groups (p=0.005 and p=0.026, respectively). The median value of the Wells score and revised Geneva score were 3 (3–6) and 5 (3–10) in patients with APE, respectively. Only the revised Geneva score was statistically different in patients with APE compared to those without APE (p=0.031), the Wells score was similar between the two groups (p>0.05 for all).

The echocardiographic parameters and ECG findings of all patients with and without APE are demonstrated in Table 2. The patients with APE had higher tricuspid regurgitation, pulmonary artery systolic pressure, and right ventricular dilatation compared to those without APE (p<0.05 for all). In terms of ECG findings, heart rate, fragmentation, T wave inversion, ST segment depression or elevation, ST segment elevation in the leads V1 or AVR, Q wave and T wave inversion in the lead DIII, QRS duration, and RWPT in the leads V1 and V4-6 were similar between the two groups (p>0.05 for all). Atrial arrhythmia, right axis deviation, complete or incomplete right bundle branch block, prominent S wave in the lead DI, S1Q3T3 pattern, and RWPT in the lead DIII (40±11 vs. 31±13 ms) were statistically different in patients with APE compared to those without APE (p<0.05 for all).

Table 2 The echocardiographic parameters and ECG findings of all patients and patients with and without APE with P value.

	All patients (n:66)		Patients without APE (n:39)		Patients with APE (n:27)		P value
Echocardiographic parameters							
Left ventricular ejection fraction; %	63	(57-65)	63	(58-65)	61	(55-65)	0.891
Tricuspid regurgitation more than mild degree, n %	24	(36.4%)	9	(23.1%)	15	(55.6%)	0.007
Pulmonary artery systolic pressure; mmHg	37	±11	30	±6	47	±10	<0.001
Right ventricular dilatation, n %	23	(34.8%)	8	(20.5%)	15	(55.6%)	0.003
Electrocardiographic findings							
Heart rate; /min	93	±26	89	±27	98	±25	0.219
Atrial arrhythmias, n %	12	(18.2%)	4	(10.3%)	8	(29.6%)	0.045
Right axis deviation, n %	10	(15.2%)	3	(7.7%)	7	(25.9%)	0,042
Complete or incomplete right bundle branch block, n %	15	(22.7%)	5	(12.8%)	10	(37.0%)	0.021
Fragmentation, n %	16	(24.2%)	7	(17.9%)	9	(33.3%)	0.152
Fragmentation in inferior leads, n %	11	(16.7%)	4	(10.3%)	7	(25.9%)	0.093
T wave inversion, n %	24	(36.4%)	13	(33.3%)	11	(40.7%)	0.539
ST segment depression, n %	17	(25.8%)	9	(23.1%)	8	(29.6%)	0.549
ST segment elevation, n %	25	(37.9%)	14	(35.9%)	11	(40.7%)	0.69
ST segment elevation in V1 lead, n %	15	(22.7%)	9	(23.1%)	6	(22.2%)	0.935
ST segment elevation in AVR lead, n %	18	(27.3%)	9	(23.1%)	9	(33.3%)	0.358
Prominent S wave in D1 lead, n %	22	(33.3%)	7	(17.9%)	15	(55.6%)	0.001
Q wave in D3 lead, n %	16	(24.2%)	7	(17.9%)	9	(33.3%)	0.152
T wave inversion in D3 lead, n %	19	(28.8%)	10	(25.6%)	9	(33.3%)	0.497
S1Q3T3 pattern, n %	4	(6.1%)	0	(0.0%)	4	(14.8%)	0.013
QRS duration; msc	98	±21	96	±25	101	±14	0.33
R wave peak time in V1 lead, msc	21	(17-27)	20	(16-26)	22	(20-64)	0.204
R wave peak time in V4-6 lead, msc	34	(28-41)	34	(27-37)	38	(34-44)	0.695
R wave peak time in D3 lead, msc	34	±13	31	±13	40	±11	0.004

Acronyms and their meanings are; APE; Acute Pulmonary Embolism, ECG; Electrocardiography. Continuous variables are presented as mean±SD; nominal variables presented as frequency

The univariate predictors of APE were oxygen saturation, complete or incomplete right bundle branch block, prominent S wave in the lead DI and RWPT in the lead DIII, as shown in Table 3. In multivariate logistic regression analysis, surgery or immobilization within the past four weeks (odds ratio [OR]: 5.01, 95% confidence interval [CI]: 1.13–22.14, p=0.033), prominent S wave in the lead DI (OR: 4.99, 95% CI: 1.22–20.33, p=0.025), and RWPT in the lead DIII (OR: 14.95, 95% CI: 1.81–123.5, p=0.012) were found to be independent predictors of APE. The Pearson correlation analysis demonstrated that RWPT in the lead DIII was moderately correlated with right ventricular dilation and pulmonary artery systolic pressure (r: 0.436, p<0.001 and r: 0.283, p=0.022, respectively) (Table 4). A ROC analysis was drawn and showed the best cut-off value of the RWPT in the lead DIII to predict APE was ≥40 ms with 48.1% sensitivity and 87.2 % specificity (area under curve (AUC): 0.718; 95% CI: 0.593–0.843; p=0.003) (Figure 2).

Table 3. Univariate and multivariate analyses for the predictor of APE

Univariate analysis	P value	OR (95% CI)	Multivariate analysis	P value	OR (95% CI)
Surgery or immobilization within four weeks	0.052	3.40(0.99 -11.63)	Surgery or immobilization within four weeks	0.033	5.01 (1.13- 22.14)
Oxygen saturation	0.048	0.94(0.88 –0.99)	-	-	-
Atrial arrhythmia	0.054	3.68 (0.98 –13.84)	-	-	-
Right axis deviation	0.054	4.20 (0.97 –18.06)	-	-	-
Complete or incomplete right bundle branch block	0.026	4.00 (1.17 –13.56)	-	-	-
Prominent S wave in lead I	0.002	5.71 (1.87 –17.44)	Prominent S wave in lead I	0.025	4.99 (1.22–20.33)
S1Q3T3 pattern	0.112	6.25 (0.98 –20.32)	-	-	-
RWPT in lead DIII	0.007	12.32 (1.97-76.87)	RWPT in lead DIII	0.012	14.95 (1.81-123.5)

All clinically relevant parameters were included in the model. ***Acronyms and their meanings are****: RWPT; R Wave Peak Time, OR; Odds Ratio, CI; Confidence Interval.*

Table 4 Pearson Correlation Analysis between RWPT and right ventricular dilation and pulmonary systolic artery pressure in all study population.

N: 66		Right ventricular dilation	Pulmonary systolic artery pressure
R Wave Peak Time	r	r=0.436	r=0.283
	p	p<0.001	p=0.022

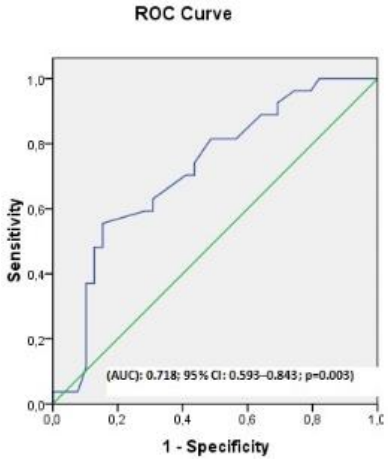

Figure 2. *The receiver operating characteristic (ROC) curve of the RWPT. The RWPT had an area under the curve value of (AUC): 0.718; 95% CI: 0.593–0.843; p=0.003) on the ROC curve. The best cut-off value of the RWPT in the lead DIII to predict acute pulmonary embolism was ≥40 ms with 48.1% sensitivity and 87.2 % specificity.*

3. Discussion

In this study, we have shown that the RWPT in the lead DIII is associated with the diagnosis of APE in unselected patients evaluated in the emergency department. Furthermore, this is the first study to demonstrate that the RWPT in the lead DIII may have an independent diagnostic predictive value in patients with APE.

APE is a deadly event that results from obstruction of the pulmonary artery or one of its branches by a thrombus. APE may remain asymptomatic and its diagnosis may be an incidental finding, or the first presentation may be sudden death (12). As clinical assessment alone cannot confirm or exclude APE, increasing data supports the use of clinical prediction models such as Wells and revised Geneva scores to guide the diagnostic approach (13, 14). According to current guidelines, patients with a preliminary diagnosis of APE should be classified as low, intermediate, or high risk by Wells or revised Geneva scores (1). In the present study, even though the patients' Wells scores did not differ between the two groups, patients with APE confirmed by CTPA had a higher revised Geneva score compared to those without. In addition, all patients were classified as low, intermediate or high risk in accordance with their Wells and revised Geneva scores. CTPA is the recommended imaging in patients with a high clinical probability of APE, and also for patients with intermediate or low clinical probability with D-dimer positivity (15). In the current study, 40.9% of patients with a preliminary diagnosis of APE were confirmed by CTPA.

In addition to being one of the first tests performed on patients presenting with chest pain, shortness of breath, and instability, the ECG may aid in the diagnosis of APE when applied to the entire clinical picture. Previous studies have reported that different ECG findings, including atrial arrhythmia, right axis deviation, complete or incomplete right bundle branch block, sinus tachycardia with secondary ST–T changes, S1Q3T3 pattern, T inversions and ST depressions in the right to mid-precordial leads, might be found in patients with APE (3). It was hypothesized that most of the ECG findings related to APE are a consequence of right ventricular dilatation and strain pattern as well as myocardial ischemia at the cellular level (16). It is thought that diminished blood flow to the lung due to embolus may cause the release of vasoconstrictive mediators such as serotonin and catecholamines (16, 17). Both vasoconstriction and mechanical obstruction from thrombus cause the increase of pulmonary artery pressure. As a result, this increase is transmitted to the right heart, causing the increase of right myocardial wall tension and dilatation of the right ventricle and atrium as well as hypoxia of the His–Purkinje system, eventually resulting in deceleration on the conduction pathway of the right side of the heart. In the acute setting, patients with right ventricular injury pattern may easily be misdiagnosed as an acute myocardial infarction. As shown in the literature (18), some APE patients may have a ST elevation in the inferior leads, mimicking ST segment elevation myocardial infarction. It was speculated that right ventricular strain may cause trans-mural ischemia, resulting in ST elevation in the inferior leads. In the present study, the right bundle branch block, fragmentation in the inferior leads, and Q wave in the lead DIII were more commonly found in patients with APE compared to those without APE, even though these ECG findings did not reach statistical significance. The S1Q3T3 pattern has been considered the pathognomonic ECG finding for APE. The reported incidence of S1Q3T3 pattern in patients with APE has been quite varied, from

10% to as high as 50% (16). A consistent finding in our cohort was the statistically different S1Q3T3 pattern between the groups (14.8% vs. 0%).

The characteristic that may be helpful to distinguish APE from acute myocardial infarction is the rightward deviation of the terminal component of the QRS vector. The right ventricle conduction is delayed and the final portion of the QRS vector represents the right ventricle in patients with right ventricle injury pattern. Hence, the terminal portion of the QRS vector generally has an axis between +90 degrees and -150 degrees that yields a S wave in the lead DI and R wave in the lead DIII (19). This feature is not commonly seen in patients with acute myocardial infarction except when there is an underlying right bundle branch block. Praveen et al. reported that the prominent S1 wave in the lead DI was independently associated with APE in their cohort (20). This feature was also confirmed in our cohort as the S wave in the lead DI was found to be independently associated with APE. The RWPT, also referred to as the intrinsicoid deflection time, is measured from the beginning of the QRS complex to the peak of the R or r' wave. The RWPT reflects the depolarization vector from the endocardium to epicardium. Holland et al. demonstrated that the RWPT may prolong myocardial ischemia because of the conduction delay in the Purkinje fibers and the myocytes (21). Furthermore, the delay of RWPT has also been shown in multiple clinical conditions including right or left ventricular hypertrophy or dilatation, coronary artery disease, acute coronary syndrome, and wide QRS complex tachycardia (**7**). To the best of our knowledge, no data has been available on the relationship between RWPT in the lead DIII and APE. The present study demonstrated that the delay of RWPT in the lead DIII was more common in patients with APE. In fact, our study results revealed that the delay of RWPT $\geq$ 40 ms in the lead DIII is an independent predictor of APE. Therefore, it may have a diagnostic predictive value in patients with APE.

Limitations of the Study

Certain limitations need to be acknowledged while interpreting the results of this study. Firstly, it was a retrospective study and the sample size was small, however consecutive patients were included in the study and statistical power analysis was performed. Secondly, even though the CTPA has a high sensitivity and specificity for the diagnosis of APE, some patients might be undiagnosed in the study. Finally, the prognostic data could not be obtained due to low event rates and the small sample size.

5. Conclusion

The present study revealed that the delay of RWPT $\geq$ 40 ms in the lead DIII is independently associated with the diagnosis of APE in unselected patients evaluated in the emergency department. Therefore, the delay of RWPT $\geq$ 40 ms in the lead DIII may have a diagnostic predictive value for APE.

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REFERENCES

1. Torbicki A. (Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology) Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). Eur Heart J. 2008;29:2276-315.
2. Stein PD, Terrin ML, Hales CA, Palevsky HI, Saltzman HA, Thompson BT, 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(3):598-603.
3. Van Mieghem C, Sabbe M, Knockaert D. The clinical value of the ECG in noncardiac conditions. Chest. 2004;125(4):1561-76.
4. Can MM, Ozveren O, Biteker M, Sengul C, Uz O, Isilak Z, et al. Role of electrocardiographic changes in discriminating acute or chronic right ventricular pressure overload. Anadolu kardiyoloji dergisi : AKD = the Anatolian journal of cardiology. 2013;13(4):344-9.
5. Sreeram N, Cheriex EC, Smeets JL, Gorgels AP, Wellens HJ. Value of the 12-lead electrocardiogram at hospital admission in the diagnosis of pulmonary embolism. American Journal of Cardiology. 1994;73(4):298-303.
6. Sinha N, Yalamanchili K, Sukhija R, Aronow WS, Fleisher AG, Maguire GP, et al. Role of the 12-lead electrocardiogram in diagnosing pulmonary embolism. Cardiology in review. 2005;13(1):46-9.
7. Sadeghpour A, Alizadeasl A. Can isolated ST elevation in aVR lead be a sign of acute pulmonary embolism? Anadolu kardiyoloji dergisi : AKD = the Anatolian journal of cardiology. 2013;13(3):288-9.
8. Macleod A, Wilson FN, Barker PS. The form of the electrocardiogram. I. Intrinsicoid electrocardiographic deflections in animals and man. Proceedings of the Society for Experimental Biology and Medicine. 1930;27(6):586-7.
9. Pérez-Riera AR, Abreu LC, Barbosa-Barros R, Nikus KC, Baranchuk A. R-Peak Time: An Electrocardiographic Parameter with Multiple Clinical Applications. Annals of Noninvasive Electrocardiology. 2016;21(1):10-9.
10. Rencüzoğulları İ, Çağdaş M, Karakoyun S, Karabağ Y, Yesin M, Artaç İ, et al. The association between electrocardiographic R wave peak time and coronary artery disease severity in patients with non-ST segment elevation myocardial infarction and unstable angina pectoris. Journal of electrocardiology. 2017.
11. Oh JK SJ, Tajik AJ., editor. The Echo Manual. 3rd ed. Philadelphia, PA: WWW; 2009.
12. Stein PD, Henry JW. Prevalence of acute pulmonary embolism among patients in a general hospital and at autopsy. Chest. 1995;108(4):978-81.
13. Wells PS, Anderson DR, Rodger M, Ginsberg JS, Kearon C, Gent M, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. Thrombosis and haemostasis. 2000;83(03):416-20.
14. Le Gal G, Righini M, Roy P-M, Sanchez O, Aujesky D, Bounameaux H, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. Annals of internal medicine. 2006;144(3):165-71.
15. Patel S, Kazerooni EA, Cascade PN. Pulmonary embolism: optimization of small pulmonary artery visualization at multi–detector row CT. Radiology. 2003;227(2):455-60.
16. Ullman E, Brady WJ, Perron AD, Chan T, Mattu A. Electrocardiographic manifestations of pulmonary embolism. The American journal of emergency medicine. 2001;19(6):514-9.
17. Rodger M, Makropoulos D, Turek M, Quevillon J, Raymond F, Rasuli P, et al. Diagnostic value of the electrocardiogram in suspected pulmonary embolism. The American journal of cardiology. 2000;86(7):807-9.
18. Zhan Z-Q, Wang C-Q, Wang Z-X. Diagnosing acute pulmonary embolism masquerading as inferior myocardial infarction. The American journal of emergency medicine. 2015;33(8):1114. e5-. e6.
19. Kosuge M, Ebina T, Hibi K, Tsukahara K, Iwahashi N, Umemura S, et al. Differences in negative T waves between acute pulmonary embolism and acute coronary syndrome. Circulation Journal. 2014;78(2):483-9.
20. Hariharan P, Dudzinski DM, Okechukwu I, Takayesu JK, Chang Y, Kabrhel C. Association Between Electrocardiographic Findings, Right Heart Strain, and Short-Term Adverse Clinical Events in Patients With Acute Pulmonary Embolism. Clinical cardiology. 2015;38(4):236-42.

21. Holland R, Brooks H. The QRS complex during myocardial ischemia. An experimental analysis in the porcine heart. The Journal of clinical investigation. 1976;57(3):541-50.

22. Dąbrowski R, Szwed H. Antiarrhythmic potential of aldosterone antagonists in atrial fibrillation. Cardiology Journal 2012; 19(3): 223-9.

23. Daubert JC, Pavin D, Jauvert G, Mabo P. Intra- and interatrial conduction delay: Implications for cardiac pacing. PACE 2004; 27: 507–25.