



Original article

Characteristics of synthesized right-sided chest electrocardiograms in patients with acute pulmonary embolism



Takashi Kusayama (MD, PhD)^a, Hiroshi Furusho (MD, PhD)^{a,*}, Masaki Kinoshita (MD)^b, Shuichi Kaneko (MD, PhD)^a, Kazuo Usuda (MD, PhD, FJCC)^b, Masayuki Takamura (MD, PhD)^a

^a Department of System Biology, Kanazawa University Graduate School of Advanced Preventive Medical Sciences, Ishikawa, Japan

^b Division of Cardiology, Department of Internal Medicine, Toyama Prefectural Central Hospital, Toyama, Japan

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ABSTRACT

Background: The significance of right-sided chest lead electrocardiogram (ECG) abnormalities in acute pulmonary embolism (APE) is unclear. This study evaluated the characteristics of such abnormalities in APE patients.

Methods: This retrospective study included consecutive patients who were diagnosed with APE by contrast-enhanced computed tomography or pulmonary artery angiography. A standard 12-lead ECG and a synthesized right-sided chest ECG were obtained from these patients. Waveform differences were noted between the acute and post-treatment phases.

Results: In total, 56 APE patients (18 men and 38 women, mean age 66.7 ± 13.3 years) were included. Traditional ECG findings, such as right-axis deviation, the $S_1Q_3T_3$ pattern, and clockwise rotation, were found in relatively few patients (14.3%, 32.1%, and 21.4%, respectively). In some cases, a negative T wave in standard 12-lead ECGs was observed in leads III, V1, and V2 (46.4%, 60.7%, and 39.9%, respectively). Syn-V3R ECG showed a higher frequency of negative T waves (66.1%) at the onset and significantly ($p < 0.01$) decreased at the follow-up. Multiple logistic regression analyses for differentiating APE revealed that the negative T waves only in lead syn-V3R were significantly related (odds ratio: 6.95, 95% confidence interval: 2.50–19.32, $p < 0.001$).

Conclusions: The presence of a negative T wave in a synthesized right-sided chest ECG, particularly in the V3R lead, is a new and distinctive finding denoting pulmonary embolism. To confirm the utility of this characteristic using synthesized right-sided chest ECGs for the diagnosis of APE, further studies with larger populations will be required.

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Introduction

Acute pulmonary embolism (APE) is a common and potentially fatal disease requiring urgent management [1]. A history of cancer is the most common risk factor of thromboembolism that results from the complex interaction of various factors [2,3]. The diagnosis of APE is often difficult in the

emergency department and the necessary treatment can be delayed. Echocardiography, contrast-enhanced computed tomography (CT), pulmonary angiography, and pulmonary blood flow scintigraphy are usually performed to diagnose APE. However, the 12-lead electrocardiogram (ECG) remains a useful method, as it is simple and noninvasive. Although ECG findings such as P pulmonale, right-axis deviation, and the $S_1Q_3T_3$ pattern have been reported in APE patients, these features are infrequently observed [4,5]. A synthesized ECG based on right-sided chest leads (syn-V3R, -V4R, and -V5R) can be derived mathematically from the data of a standard 12-lead ECG, as reported previously [6,7]. This method may provide useful information on patients with APE.

* Corresponding author at: Department of System Biology, Kanazawa University Graduate School of Advanced Preventive Medical Sciences, 13-1 Takaramachi, Kanazawa, Ishikawa 920-8641, Japan.

E-mail address: hfurusho@m-kanazawa.jp (H. Furusho).

This study evaluated the acute electrocardiographic findings of synthesized right-sided chest ECGs in patients with APE.

Methods

Study population

This was a retrospective chart review of consecutive patients who were diagnosed with APE and hospitalized at Toyama Prefectural Central Hospital between March 2007 and July 2015. In total, 56 patients (18 men and 38 women, mean age 66.7 ± 13.3 years) were enrolled. The exclusion criteria were as follows: left ventricular dysfunction, complete or incomplete left and right bundle branch block, primary pulmonary disease (i.e. pulmonary emphysema or pneumonitis), chronic thromboembolic pulmonary hypertension, receiving drugs with potential effects on the ST-T segment, and non-availability of relevant information in electronic medical charts. Diagnosis of APE was confirmed by contrast-enhanced CT and/or pulmonary angiography. Complete disappearance of the pulmonary thromboemboli was confirmed in all study patients by contrast-enhanced CT before discharge. We defined obesity as body mass index $>25 \text{ kg/m}^2$ and immobilization as bedrest >3 days.

The severity of pulmonary embolism (PE) severity was categorized by physicians in the acute phase based on the presence of hemodynamics and right ventricular (RV) dysfunction. Severity was defined as: (1) massive (systolic blood pressure <90 mmHg, or systolic blood pressure at rest decreased by ≥ 40 mmHg with RV dysfunction), (2) submassive (stable hemodynamics with RV dysfunction); and (3) non-massive (stable hemodynamics without RV dysfunction). On echocardiographic test, RV dysfunction included RV dilation >30 mm and/or an increased end-diastolic RV/left ventricular diameter ratio >0.9 or 1.0 ; hypokinesia of the free RV wall; increased velocity of the tricuspid regurgitation jet; or combinations of the above. On CT test, RV dysfunction was defined as an increased RV/left ventricular diameter ratio >0.9 or 1.0 [8].

This study was approved by our local institutional review board and ethics committee and was performed in accordance with institutional policies, national legal requirements, and the revised Declaration of Helsinki. Written informed consent was obtained from each patient.

Electrocardiographic recordings and data processing to obtain a synthesized ECG

A resting 12-lead ECG was obtained in all patients in the supine position using an electrocardiographic recorder (ECG-1500 or ECG-2500; Nihon Kohden, Inc., Tokyo, Japan) at a paper speed of 25 mm/s and an amplification of 10 mm/mV. All digital data from standard 12-lead ECG signals were instantaneously processed at a sampling rate of 1 kHz. Electrocardiographic data were subsequently transferred to an ECG diagnostic information system (PRM-3200; Nihon Kohden, Inc.) for analyses. Synthesized right-sided ECG (syn-V3R, -V4R, and -V5R) waveforms were rapidly synthesized using computer software [6,7]. The principle is that the heart vector (V) is estimated using the standard 12 leads (j) and then projected onto the additional leads (i). In the actual calculation, each additional lead (i) is derived with a matrix calculation of each coefficient (α) for the standard 12 leads (j). The coefficients (α) are obtained from approximately 150 recordings of each right-sided ECG lead with the least-squares method.

$$V_i = \sum_j a_{i,j} V_j$$

There are some previous papers reporting a good correlation between synthesized and actual right-sided leads [9–12]. Correlation

coefficients in ECG morphologies between synthesized and actual right-sided chest leads were 0.88–0.97 ($p < 0.001$) [10].

Evaluation and comparison of ECG findings

All ECGs were examined by a single cardiologist who was blinded to the clinical data. The following ECG findings, which have previously been shown to be associated with APE, were evaluated: tachycardia (greater than 100 beats per minute); atrial arrhythmia; P pulmonale (P waves with amplitudes ≥ 2.5 mm in limb leads or >1.5 mm in lead V1); right-axis deviation (QRS electrical axis $>90^\circ$); left-axis deviation (QRS electrical axis $\leq -30^\circ$); the $S_1S_2S_3$ pattern (presence of S waves with amplitudes ≥ 1.5 mm in leads I–III); the $S_1Q_3T_3$ pattern (presence of S waves in lead I and Q waves in lead III, each having amplitudes >1.5 mm; in association with a negative T wave in lead III); low voltage (overall deflection of QRS complex ≤ 5.0 mm in all limb leads); clockwise rotation (shift in the transition zone [R = S] in the precordial leads to V5 or beyond); ST segment elevation ≥ 1.0 mm in any lead except lead aVR; and ST segment depression (depression of horizontal or down-sloping ST segments ≥ 0.5 mm in any lead in the absence of complete bundle branch block or ventricular hypertrophy). ST segment deviation was measured manually to the nearest 0.5 mm at the J point [4,13–21]. A negative T wave was defined as a depth of at least 0.1 mV [22–24]. The frequency of the negative T wave in each lead was examined.

ECG findings indicative of pulmonary thromboembolism were examined during the acute phase (onset) of APE and at follow-up. Complete disappearance of the pulmonary thromboembolism was confirmed by contrast-enhanced CT before discharge (follow-up).

Statistical analyses

Continuous data are expressed as mean \pm standard deviation (SD), and categorical data are expressed as numbers and percentages. A paired t-test was used to compare continuous variables between the onset and follow-up phases. The chi-square test was used to compare categorical variables. To detect the independent contribution of negative T wave in each lead for APE that could be a positive screening, we performed a multiple logistic

Table 1
Baseline characteristics of APE patients ($n = 56$).

	Value
Age, years	66.7 ± 13.3
Elderly, >75 years	14 (25.0)
Sex, male	18 (32.1)
BMI, kg/m^2	24.8 ± 4.0
Complaints	
Dyspnea	33 (58.9)
Chest pain	9 (16.1)
Shock/Syncope	7 (12.5)
Fever	4 (7.1)
Risk factors for APE	
Obesity (BMI $> 25.0 \text{ kg/m}^2$)	26 (46.4)
Malignancy	13 (23.2)
Immobilization (Bedrest > 3 days)	13 (23.2)
History of surgery	10 (17.9)
Coagulation abnormality	8 (14.3)
Inflammatory disease	4 (7.1)
Echocardiography ($n = 50$)	
LV ejection fraction (%)	63.5 ± 19.1
RV dysfunction	29 (58.0)
Severity of APE ($n = 50$)	
Massive PE	2 (4.0%)
Submassive PE	27 (54.0)
Non-massive PE	21 (42.0)

All values are shown as the means \pm standard deviation (SD) or n (%). APE, acute pulmonary embolism; BMI, body mass index; LV, left ventricular; RV, right ventricular.

Table 2
Electrocardiographic findings.

	Onset (n = 56)	Follow-up (n = 56)	p-Value
Heart rate, beats/min	89.7 ± 21.0	72.4 ± 13.3	<0.001
Tachycardia	18 (32.1)	1 (1.8)	<0.001
Atrial fibrillation	5 (8.9)	4 (7.1)	0.728
Paroxysmal	1 (1.8)	0	
Persistent	4 (7.1)	4 (7.1)	
Standard 12-lead ECG			
P pulmonale	0 (n = 51)	0 (n = 52)	NA
Right-axis deviation	8 (14.3)	0	0.003
Left-axis deviation	8 (14.3)	3 (5.4)	0.112
S ₁ S ₂ S ₃ pattern	8 (14.3)	1 (1.8)	0.015
S ₁ Q ₃ T ₃ pattern	18 (32.1)	5 (8.9)	0.002
Low voltage	8 (14.3)	3 (5.4)	0.112
RV hypertrophy	2(3.6)	0	0.154
Clockwise rotation	12 (21.4)	1 (1.8)	0.001
ST segment elevation	0	0	NA
ST segment depression	3 (5.4)	1 (1.8)	0.309
Synthesized right-sided chest ECG			
Q wave	27 (48.2)	16 (28.6)	0.033
ST segment elevation	1 (1.8)	1 (1.8)	1.000
ST segment depression	11 (19.6)	9 (16.1)	0.622

All values are shown as the mean ± SD or n (%).
ECG; electrocardiogram; RV, right ventricular; NA, not available.

regression analysis including lead III, V2, and syn-V3R. Odds ratios (OR) with a 95% confidence interval (CI) were calculated. Differences were considered statistically significant at *p* < 0.05. The data were analyzed using SPSS for Windows software (ver. 19.0; SPSS Inc., Chicago, IL, USA).

Results

Patient characteristics

Baseline characteristics of the patients are shown in Table 1. The major complaint of APE patients was dyspnea (58.9%). The most

prevalent risk factors for APE were obesity (46.4%), malignancy, and immobilization (both 23.2%). The major severity of PE was submassive PE (54.0%) and non-massive PE (42.0%). In all patients, the pulmonary thromboembolism had completely disappeared and the physical condition was stable before discharge. The duration from the diagnosis of APE to the disappearance of pulmonary thromboemboli confirmed by CT was 47.1 ± 20.1 days.

ECG findings of APE

ECG findings indicating APE were compared between the onset and follow-up phases (Table 2). Standard ECGs at onset were more closely associated with tachycardia, right-axis deviation, the S₁S₂S₃ and S₁Q₃T₃ patterns, and clockwise rotation than the follow-up ECGs. However, the frequencies of these findings were not high (32.1%, 14.3%, 14.3%, 32.1%, and 21.4%, respectively). Atrial arrhythmias were of paroxysmal (n = 1) and persistent (n = 4) atrial fibrillation, and the frequency was not different between APE phases. ST segment elevation and depression were rarely observed in the onset phase.

In synthesized right-sided chest ECGs, Q wave at onset was seen in more cases than that in the follow-up phase. The frequencies of ST segment elevation and depression were not high (1.8% and 19.6%, respectively). Fig. 1 shows a representative ECG of a patient with APE at onset, including synthesized right-sided chest ECGs.

Negative T waves

During APE onset, the presence of a negative T wave in a standard 12-lead ECG was most frequently observed in lead V1 (60.7%). However, there were no differences in the frequency of such T waves between the onset and follow-up ECGs (Fig. 2). By contrast, a negative T wave was observed more frequently in lead syn-V3R (66.1%) than in lead V1 at onset and this finding significantly (*p* < 0.01) decreased at the follow-up. Similar to syn-V3R, negative T waves in syn-V4R (62.5%) and -V5R (51.8%) at

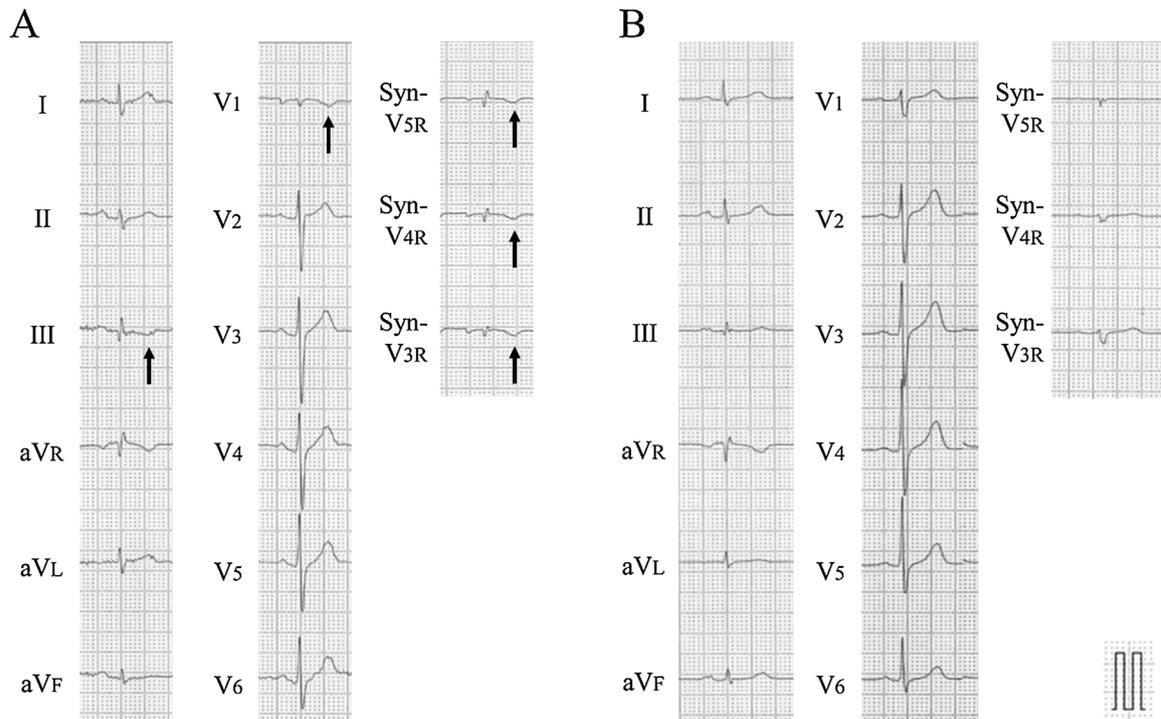


Fig. 1. Representative electrocardiogram (ECG) of a patient with acute pulmonary embolism (APE): synthesized right-sided chest ECGs at APE onset (A) and follow-up (B) phases. Arrows at the onset show negative T waves that disappeared at the follow-up. Syn, synthesized.

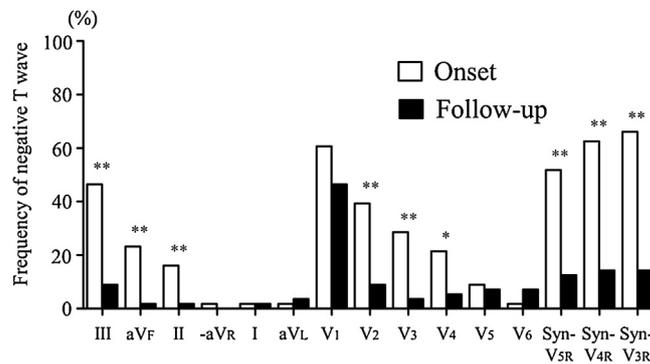


Fig. 2. Frequency of negative T waves in patients with acute pulmonary embolism (APE). White and black boxes show the frequency of negative T waves on standard 12-lead and synthesized right-sided chest electrocardiograms during the acute (onset) and follow-up phases of APE. * $p < 0.05$, ** $p < 0.01$ vs. follow-up.

Table 3

Univariate and multiple logistic regression analyses: Utility of a negative T wave for differentiating between acute and follow-up phases.

ECG lead	Univariate regression analysis			Multiple regression analysis		
	OR	95% CI	p-Value	OR	95% CI	p-Value
III	6.60	2.28–19.12	<0.001	2.28	0.65–8.05	0.200
V1	1.78	0.84–3.78	0.131			
V2	6.60	2.28–19.12	<0.001	2.28	0.65–8.05	0.200
Syn-V3R	11.68	4.61–29.64	<0.001	6.95	2.50–19.32	< 0.001

Odds ratios (ORs) are shown with 95% confidence intervals (CIs). ECG, electrocardiogram; Syn, synthesized.

onset were equivalently observed and significantly ($p < 0.01$) decreased at the follow-up.

Univariate logistic regression analyses revealed that ORs of negative T waves for differentiating between acute and follow-up phases were highest in lead syn-V3R (OR: 11.68, 95% CI: 4.61–29.63 $p < 0.001$) (Table 3). The OR in syn-V3R was higher than those of standard ECG leads (lead III, OR: 6.60, 95% CI: 2.28–19.12; lead V1, OR: 1.78, 95% CI: 0.84–3.78; and lead V2, OR: 6.60, 95% CI: 2.28–19.12). Multiple logistic regression analysis revealed that the negative T wave only in lead syn-V3R was significantly related with APE (OR: 6.95 95% CI: 2.50–19.32, $p < 0.001$).

Discussion

This study demonstrated that the presence of a negative T wave in synthesized right-sided chest ECG is frequent during the acute phase of APE.

ECG findings of APE

ECG abnormalities caused by APE, such as P pulmonale, right- and left-axis deviation, $S_1S_2S_3$ and $S_1Q_3T_3$ patterns, low voltage, and clockwise rotation, are highly variable and frequently transient [4,13–21]. In this study, several of these features were observed during the acute phase of APE, although not frequently. However, ECG changes in APE patients, such as right-axis deviation, the $S_1Q_3T_3$ pattern, and clockwise rotation, largely disappeared during hospitalization with treatment. Akula et al. reported that these ECG changes disappeared within 24 h of admission in 87.5% of APE patients [25]. In addition, ST segment elevation and depression that have been reported [4,14,15,17,20,21,24] were rare in this study. This difference is probably due to the period of examination from the actual onset of APE. ST segment depression tended to resolve faster than a negative T wave [4].

Negative T wave in right-sided chest ECGs in APE

A negative T wave is a common ECG finding in APE patients [4,24]. However, the mechanism underlying negative T waves remains unknown. Previous studies have suggested that a negative T wave in APE patients may reflect severe ischemia of the right ventricle due to rapid right ventricular pressure overload, impaired coronary blood flow, and hypoxia, caused by pulmonary artery embolism [4,13,14,26–31].

There are few reports on the findings of right-sided chest ECGs in APE patients. In some APE patients, the left-sided ECG is normal, but the right-sided ECG shows ST segment elevation [25]. Chia et al. reported ST segment changes in the right-sided chest ECGs of APE patients, and suggested that these abnormalities may result from ischemia of the right ventricular myocardium and/or dilation of the right ventricle, as mentioned above [32]. In this study, the presence of a negative T wave in synthesized right-sided chest ECGs during the acute phase of APE was frequently observed. If severe ischemia of the right ventricle in APE causes a negative T wave in right-sided chest ECGs, as previously described, it is reasonable to expect that the presence of a negative T wave would be observed most frequently in lead syn-V3R, which is the lead closest to the right ventricle [33]. However, it is difficult to determine the extent of RV infarction in APE patients.

Potential of synthesized right-sided chest ECGs for diagnosing APE

Negative T waves in the lead syn-V3R had larger ORs for differentiating the onset and follow-up phases of APE versus standard ECGs using leads III and V1 (for example), which have previously been reported to be useful [18–20]. Kozaci et al. reported the actual right-sided chest ECGs were useful to diagnose APE in patients with clinical PE suspicion [34]. The waveforms of the mathematically derived right-sided chest ECGs in this study were identical to the ECGs of patients with various diseases in other studies. Ventricular outflow tract arrhythmias of different origins have features that are dissociable on synthesized right-sided chest ECGs [9,10]. In addition, the usefulness of synthesized right-sided chest ECGs for diagnosing Brugada syndrome [7] and acute myocardial infarctions involving the RV wall [11,12] has been reported. Synthesized right-sided chest ECGs, which can be derived quickly and non-invasively from standard 12-lead ECG data, can be beneficial to both physicians and patients for early diagnosis and treatment of APE. Even if the APE patient is in poor condition at disease onset, a synthesized ECG can provide additional information to that of a standard 12-lead ECG regarding RV abnormality or dysfunction. Furthermore, V3R lead-derived ECGs may be useful for the diagnosis of APE, even without ECG synthesis.

Study limitations

Some limitations of this study must be considered. First, this was a retrospective investigation that included a relatively small number of APE patients who were not randomly selected from among the general population; therefore, the present results require validation in studies with larger patient populations. Second, the synthesized ECG software program that we used was designed on the basis of the findings of 12-lead ECGs in a limited number of Japanese subjects. Therefore, further studies are needed to clarify whether there are generational, racial, or sex differences in synthesized right-sided chest ECG findings. Third, we compared the two different phases of APE in the same patients to detect APE. Healthy individuals are desirable as controls to obtain more precise methods of diagnosis. However, a negative T wave that changed dramatically between the onset and follow-up phases in the same patients can indicate important information to notice APE that is often difficult to detect.

Conclusions

This study indicates that the presence of a negative T wave in a synthesized right-sided chest ECG, particularly in the V3R lead, is a new and distinctive finding denoting PE. To confirm the utility of this characteristic using synthesized right-sided chest ECGs for the diagnosis of APE, further studies with larger populations, including patients without APE, will be required.

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Disclosure of interest

The authors declare no conflicts of interest.

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