Relationship Between ECG Findings and Pulmonary Artery Pressure in Patients With Acute Massive Pulmonary Thromboembolism

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Pulmonary thromboembolism (PTE) is associated with various electrocardiogram (ECG) abnormalities, but the utility of evaluating the severity of PTE based on ECG abnormalities alone has not been investigated in Japanese patients previously. The purpose of this study was to examine the relationship between ECG abnormalities and the mean pulmonary artery pressure (MPAP) in patients with acute massive PTE (AMPTE). ECG examination of 21 patients, who were diagnosed with AMPTE by pulmonary arteriography, found that S₁Q₃T₃ was the most frequently observed abnormality (in 67% of the patients), followed by negative T (62%), clockwise rotation (57%), and ST elevation (48%). When these patients were divided into 2 groups based on the level of MPAP, 8 of the 11 ECG findings, which were associated with PTE in a previous report, were more frequently observed in Group H (MPAP ≥40 mmHg) than in Group L (MPAP <40 mmHg). MPAP correlated significantly with the total number of ECG abnormalities ($r=0.82$, $p<0.001$). In particular, at least 5 ECG abnormalities were noted in patients with MPAP ≥45 mmHg. These results suggested that the total number of ECG abnormalities in patients with AMPTE can be used to evaluate the severity of APTE, including PAP level. (*Circ J* 2003; 67: 229–232)

Key Words: Acute massive pulmonary thromboembolism; Electrocardiography; Pulmonary hypertension

Acute pulmonary thromboembolism (APTE) is a very serious disorder in the United States because it occurs in 500,000–600,000 people every year and approximately 10% of them die within 1 h of its development. In addition, the mortality rate during hospitalization is approximately 10%.¹ The incidence of PTE in Japan has been increasing lately, although it is still lower (3,492 patients per year) than in the United States.² Pulmonary artery pressure (PAP) is an important prognostic factor of APTE and prognosis is often poor in patients with a mean PAP (MPAP) of 35 mmHg or less during the acute phase. Therefore, it is necessary to diagnose APTE immediately and accurately evaluate its severity.

At present, a definitive diagnosis of APTE is made by lung perfusion scintigraphy and pulmonary arteriography, but accurate diagnosis and severity evaluation using simpler diagnostic procedures, such as electrocardiogram (ECG), would be clinically advantageous in the provision of early treatment for APTE. Although specific ECG findings for various APTE have been reported,^{3–7} few could be used to establish a definitive diagnosis of APTE. Moreover, a consensus has not yet been established with regard to the relationship between the severity of APTE and ECG findings. In the present study, we evaluated the relationship between ECG findings and MPAP in patients with acute massive PTE (AMPTE) diagnosed by pulmonary arteriography.

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Methods

Subjects

Of the patients who were diagnosed with AMPTE based on the results of pulmonary arteriography or lung perfusion scintigraphy between March 1991 and December 2001, 21 (3 males, 18 females; mean age: 63.3 ± 9.8 years, $\pm$ SD) without an obvious past history of cardiopulmonary diseases were investigated retrospectively. Informed consent was given and the patients were divided into 2 groups based on a cutoff level of MPAP of 40 mmHg recorded during the acute phase: Group H of 9 patients (MPAP ≥40 mmHg) and Group L of 12 patients (MPAP <40 mmHg). Based on the criteria used in previous studies,^{8,9} AMPTE was defined as obstruction of either both main pulmonary arteries or 2 or more lobular arteries including those in the lingula.

Measurement of PAP and Pulmonary Arteriography

After admission to the Department of Internal Medicine, a Swan-Ganz catheter (Edwards Critical-Care Division, Irvine, CA, USA) was inserted via the internal jugular vein or the femoral vein for measurement of PAP. Subsequently, pulmonary digital subtraction angiography (DSA) was performed using a 7F balloon angiographic catheter (Harmac Medical Products Inc, Buffalo, NY, USA). The DSA images, which were acquired after injecting 30–40 ml of a nonionic contrast medium at a rate of 15–20 ml/s, were analyzed by 2 or more physicians.

PAP was measured again during the chronic phase, defined as improvement of subjective symptoms until New York Heart Association (NYHA) classification stage II was achieved, disappearance of tricuspid valve regurgitation (TR) findings on UCG, or when the TR pressure gradient (TRPG) measured by Doppler echocardiography dimin-

Table 1 Patients Characteristics

Case no.	Age (years)	Sex	MPAP (mmHg)	PO ₂ (mmHg)	PCO ₂ (mmHg)	DVT	Underlying disease	ECG findings	Time (day)
1	63	F	55	43.2	25.5	No	Uterine carcinoma p/o	5	1
2	68	F	28	53.0	20.0	Yes	Post angiography	1	1
3	78	F	35	64.0	17.3	No	None	3	10
4	67	M	46	56.4	25.5	Yes	Phlebitis	6	1
5	52	F	36	80.0	40.0	Yes	Uterine myoma p/o	3	1
6	66	F	35	66.0	31.1	Yes	None	3	6
7	75	F	62	47.0	26.7	No	Obesity	4	10
8	69	F	48	46.0	22.8	No	Varicose vein	6	10
9	47	F	26	63.0	20.6	Unknown	Prednisolone per os 1	2	
10	69	F	47	—	—	Unknown	None	5	3
11	54	M	26	—	—	Unknown	Chronic pancreatitis	2	Undefined
12	65	F	36	52.6	31.6	Yes	Renal cell carcinoma p/o	4	2
13	66	F	41	47.7	24.8	Unknown	Prednisolone per os 2	3	
14	60	F	58	53.0	42.6	No	Varicose vein	5	30
15	61	F	61	—	—	No	None	7	8
16	57	F	30	67.0	26.8	Unknown	None	3	1
17	50	F	28	—	—	No	Osteoarthritis of the knee p/o	3	1
18	70	F	23	—	—	Unknown	Nephrotic syndrome	2	1
19	71	F	42	58.0	24.2	No	None	3	10
20	78	F	25	—	—	Unknown	None	1	Undefined
21	43	M	26	—	—	Yes	Antiphospholipid antibody syndrome	1	4

MPAP, mean pulmonary artery pressure; DVT, deep vein thrombosis; Time, duration from onset to admission; p/o, post operation.

Table 2 Frequencies of ECG Findings on Admission

ECG finding	No. of Cases (%)	Group H	Group L
Arrhythmia	1 (5)	0	1
Pulmonary P	4 (19)	3	1
Right axis deviation	4 (19)	4	0
Left axis deviation	2 (10)	0	2
Right bundle branch block	4 (19)	3	1
S ₁ Q ₃ T ₃	14 (67)	8	6
Low voltage	4 (19)	3	1
Clockwise rotation (V _s)	12 (57)	8	4
ST elevation	10 (48)	6	4
ST depression	4 (19)	1	3
T inversion	13 (62)	7	6

ished to less than 20 mmHg.

Electrocardiography

The following parameters were analyzed on the ECG recorded on the day of measurement of PAP, based on the criteria defined by Stein et al.¹⁰

- (1) Arrhythmia.
- (2) P wave abnormalities including pulmonary P: P waves ≥ 0.25 mV in limb leads or those measuring ≥ 0.15 mV in lead V₁.
- (3) Abnormalities of the QRS complex, including (i) right axis deviation: QRS electrical axis $>90^\circ$; (ii) left axis deviation: QRS axis equal to or leftward of -30° ; (iii) clockwise rotation: transitional zone (R=S) located on V₅ or V₆ chest leads; (iv) right bundle branch block (RBBB): presence of S wave in lead I and R wave in lead V₁, incomplete RBBB (QRS intervals = 0.10–0.11 s) or complete RBBB (QRS intervals ≥ 0.12 s); (v) S₁Q₃T₃: the presence of S waves (≥ 0.15 mV) in lead I and Q waves (≥ 0.15 mV) and negative T in lead III; (vi) right ventricular hypertrophy: R waves ≥ 0.5 mV and R/S ≥ 1 in lead V₁; and (vii) low voltage: amplitude of QRS complex <0.5 mV in all limb leads.
- (4) ST-T abnormalities including (i) ST elevation: elevation of ST segments (≥ 0.1 mV) in one or more leads excluding aV_R without ST depression in any of these leads;

- (ii) ST depression: depression of ST segments (≥ 0.05 mV) in one or more leads excluding aV_R without bundle branch block (BBB) and ventricular hypertrophy; and (iii) negative T: presence of a negative T wave in one or more leads excluding aV_L, III, aV_R, and V₁ without BBB and ventricular hypertrophy.

Statistical Analysis

All data are expressed as mean $\pm$ SD. In both the H and L groups, PAP during the acute phase was compared with that during the chronic phase using the paired t-test. The correlation between MPAP and the frequency of ECG findings was analyzed by linear regression analysis using Spearman's rank correlation coefficients. P values less than 0.05 were considered significant.

Results

Table 1 shows the patients characteristics. Excluding 7 patients who received oxygen inhalation therapy on admission, arterial blood gas analysis was performed in 14 patients who did not receive supplemental oxygen but breathed room air only. Underlying diseases included phlebitis/varices of the lower extremities in 3 patients and anti-phospholipid antibody syndrome in 1 patient. Prior to the present study, 5 patients had undergone surgery of the uterus, kidney and lower extremities, 1 patient had undergone angiography, and 2 other patients had been on long-term steroid therapy. However, the medical histories were unclear in the remaining 7 patients. In addition, the presence of deep venous thrombosis was confirmed in 6 patients, not confirmed in 8 patients, and was unclear in 7 patients.

Table 2 shows the frequency of the respective ECG findings. S₁Q₃T₃ was the most frequently observed abnormality (in 67% of the patients), followed by negative T wave (62%), clockwise rotation (57%), and ST elevation (48%). When the frequencies of the respective ECG finding were compared between the H and L groups, 8 of the 11 ECG findings were more frequently observed in Group H than in

Fig 1. Correlation between the mean pulmonary artery pressure (MPAP) and total number of ECG findings.

Group L.

MPAP correlated significantly with the total number of ECG abnormalities, and 5 or more characteristic ECG abnormalities were observed in patients with MPAP ≥ 45 mmHg (Fig 1). However, the total number of ECG abnormalities did not correlate with either arterial oxygen tension (PaO₂) or arterial carbon dioxide tension (PaCO₂) on admission, or the period between disease onset and hospitalization. Although 2 patients died within 1 week after treatment, recovery of MPAP to normal levels was noted in 18 of the 19 surviving patients on discharge. Therefore, MPAP did not significantly differ between the H and L groups during the chronic phase of APTE (Fig 2).

Discussion

To date, various characteristic ECG abnormalities in PTE have been reported⁴⁻¹³ Stein et al investigated 50 patients with MPTE without a past history of cardiopulmonary diseases, and reported that negative T was the most common ECG abnormality (in 46% of the patients), followed by ST depression (28%), S₁Q₃T₃ (18%), ST elevation (18%), and clockwise rotation (10%).¹⁰ In Japan, Hasegawa et al investigated 225 APTE patients with and without a history of cardiopulmonary diseases, not taking the severity of APTE into account, and reported that negative T was the most frequent ECG abnormality (42%), followed by right axis deviation (25%), S₁Q₃T₃ (24%), clockwise rotation (24%), and RBBB (20%).¹⁴ Tayama et al reported that negative T in the anterior leads was the most frequent abnormality (82.9%), followed by Q wave in lead III (71.4%), and S wave in lead I (68.6%) in patients with acute massive/submassive pulmonary embolism.¹⁵ Moreover, they reported that more than 2 abnormal ECG findings were observed in 71.4% patients, and concluded that ECG is a useful tool for the diagnosis of APTE. However, the present study showed that S₁Q₃T₃ is the most frequent finding, which differs from the results of the previous studies. We also investigated whether the period between disease onset and hospitalization, complication of pulmonary infarction (including the concentration of lactate dehydrogenase on admission), and arterial blood gas levels, contributed to the ECG changes. However, there were no relationships between the frequency of S₁Q₃T₃ and these factors. The frequency of S₁Q₃T₃ tended to increase with increases in MPAP. S₁Q₃T₃ was noted in 8 (88.9%) patients with MPAP ≥ 40 mmHg but only in 6 (50%) patients with MPAP < 40 mmHg (Table 2). MacIntyre et al reported that the right ventricular (RV) pressure is limited in APTE

Fig 2. Changes in mean pulmonary artery pressure (MPAP) before and after treatment. Acute phase: values at admission before any treatment; chronic phase: values after the disappearance of respiratory symptoms after treatment; Group H: patients with MPAP ≥ 40 mmHg on admission; Group L: patients with MPAP < 40 mmHg on admission; NS, not significant.

patients without a history of cardiopulmonary diseases; MPAP does not exceed 40 mmHg in such patients.^{16,17} Nakamura et al also defined PTE patients with MPAP < 40 mmHg as APTE and those with persistently high RV afterload on ECG, including S₁Q₃T₃, as chronic PTE in their study of the Japanese Society of Pulmonary Embolism Research.¹⁸ Based on the findings of those studies, we divided our patients into 2 groups using a MPAP cutoff level of 40 mmHg. Thus, it could be considered that the present patients with MPAP ≥ 40 mmHg probably developed asymptomatic recurrent PTE; however, we assumed that the acute thrombosis in the pulmonary artery increased PAP in almost all patients because MPAP diminished to normal levels (< 20 mmHg) in all but 1 patient after treatment. Furthermore, S₁Q₃T₃ in these AMPTE patients disappeared during the chronic phase in all but 1 patient. Further studies are necessary to determine the reason for the different results reported here and by the other investigators.^{13,16,17} Apart from the type of ECG abnormality, the frequency of abnormal ECG findings on admission differed among most previous studies of APTE.^{5,8,10-14} The present results suggest that S₁Q₃T₃, negative T, and clockwise rotation are characteristic ECG findings of AMPTE during the acute phase, as they were observed in 67%, 62%, and 57% of the patients, respectively.

The ECG changes in APTE described in the present study were probably induced by rapid RV overload, but it is possible that myocardial ischemia, ischemia of the conduction system, hypoxemia, and various chemical mediators, such as catecholamine and histamine, are also involved in the appearance of these ECG changes.¹⁹⁻²³ In addition, it was reported that the hemodynamics of the right heart system are closely related to the obstructive pulmonary vascular volume, and MPAP increases only when 50% or more of pulmonary artery obstruction occurs.²⁴ Therefore, ECG findings of RV overload caused by pulmonary hypertension may depend on the obstructive pulmonary vascular volume. However, a uniform consensus has not yet been established with regard to the relationship between the frequency of ECG abnormalities and pulmonary hemodynamics, and the severity of APTE evaluated by pulmonary arteriography and lung perfusion scintigraphy. In the present study, the relationships between ECG abnormalities and PAP, PaO₂, PaCO₂ and the period between disease onset and hospitalization were only evalu-

ated in patients with AMPTE. MPAP alone correlated with abnormal ECG findings in APTE, as reported previously; the frequency of ECG abnormalities reported by Stein et al¹⁰ increased with increases in MPAP. In particular, 5 or more abnormal ECG findings were observed in patients with MPAP ≥ 45 mmHg. However, it was found that PaO₂, PaCO₂ and the period between disease onset and hospitalization were not independent factors that influenced ECG findings. Therefore, it is considered that PAP can be predicted by the severity of ECG changes during the acute phase of AMPTE. Our results are similar to those reported recently by Daniel et al who evaluated the relationship between ECG score and systolic PAP.²⁵ Although the majority of the earlier studies examined patients with PTE and MPAP ≤ 30 mmHg, the present study evaluated patients with AMPTE alone in whom MPAP was never less than 20 mmHg, and included those with MPAP ≥ 40 mmHg.

With regard to the consecutive ECG changes after therapy, we previously reported that the change in the amplitude of the negative T wave might reflect improvement in the cardiopulmonary hemodynamics.⁶ However, in the present study, treatment improved both the MPAP levels and the abnormal ECG findings in almost all patients, irrespective of the level of MPAP during the acute phase, which indicates that the ECG findings during APTE do not predict the posttreatment hemodynamic changes.

To our knowledge, the present study is the first to report that the level of PAP can be predicted by the number of ECG abnormalities in Japanese patients with markedly large obstructive pulmonary vascular volume.

Conclusions

We determined the ECG changes in AMPTE and found that the most common ECG changes on admission were S₁Q₃T₃, negative T, and clockwise rotation. Our results also showed that MPAP correlated with the total number of ECG findings, indicating that the level of PAP could be predicted by ECG changes recorded during the acute phase of AMPTE.

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