ORIGINAL ARTICLE

Electrocardiogram Patterns during Hemodynamic Instability in Patients with Acute Pulmonary Embolism

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Background: We have previously described new electrocardiogram (ECG) findings for massive pulmonary embolism, namely ST-segment elevation in lead aVR with ST-segment depression in leads I and V₄–V₆. However, the ECG patterns of patients with acute pulmonary embolism during hemodynamic instability are not fully described.

Methods: We compared the differences between the ECG at baseline and after deterioration during hemodynamic instability in twenty patients with acute pulmonary embolism.

Results: Compared with the ECG at baseline, three ischemic ECG patterns were found during clinical deterioration with hemodynamic instability: ST-segment elevation in lead aVR with concomitant ST-segment depression in leads I and V₄–V₆, ST-segment elevation in leads V₁–V₃/V₄, and ST-segment elevation in leads III and/or V₁/V₂ with concomitant ST-segment depression in leads V₄/V₅–V₆. Ischemic ECG patterns with concomitant S1Q3 and/or abnormal QRS morphology in lead V₁ were more common (90%) during hemodynamic instability than at baseline (5%) ($P = 0.001$).

Conclusions: Hemodynamic instability in acute pulmonary embolism is reflected by signs of myocardial ischemia combined with the right ventricular strain pattern in the 12-lead ECG

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acute pulmonary embolism; electrocardiogram; myocardial ischemia; right ventricular strain; hemodynamic instability

Acute pulmonary embolism (APE), a relatively common cardiovascular emergency, may lead to acute life-threatening, but potentially reversible right ventricular (RV) failure.¹ APE is often misdiagnosed as acute coronary syndrome because many symptoms and electrocardiogram (ECG) characteristics of APE are similar to acute coronary syndrome.^{2,3} Our group published a case report of three patients with APE, where ST-segment elevation (STE) in lead aVR and ST-segment depression (STD) in leads I and V₄–V₆ were observed during hemodynamic instability.⁴ This ECG pattern is

often found in patients with acute coronary syndrome and is associated with left main coronary artery or multivessel coronary artery disease.⁵ STE in leads V₁–V₃/V₄ similar to acute anteroapical myocardial infarction is not a rare phenomenon in high-risk patients with APE and signifies RV transmural ischemia.⁶ Echocardiogram can help to differentiate these two clinical entities. ECG may be the most convenient and easily available diagnostic tool for differential diagnosis in patients with suspected APE. Especially in patients with hypotension or shock, immediate recognition of

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ECG patterns suggestive of APE combined with echocardiography, when available, may lead to earlier diagnosis and appropriate therapy, and thus to decreased mortality. As the ECG patterns during hemodynamic instability in APE, including hypotension or cardiogenic shock, have not been fully defined, the aim of this study was to compare the ECGs at baseline and after deterioration during hemodynamic instability.

METHODS

Patient population

From January 2008 to September 2012, 206 patients were diagnosed APE in the Shiyan Taihe Hospital. We retrospectively found 26 patients fulfilled the following inclusion criteria: (1) clinical signs and symptoms suggesting APE, such as acute onset of dyspnea, tachypnea, palpitations, hemoptysis, presyncope, syncope, hypotension, cardiogenic shock, or cardiac arrest; (2) APE confirmed by high-resolution computed tomographic pulmonary angiography during hospitalization; (3) hemodynamic stability at admission deteriorating into hemodynamic instability during hospitalization, including hypotension and cardiogenic shock, according to the guidelines of the European Society of Cardiology risk stratification of APE¹; (4) available ECG of good technical quality both on admission, when the patients were hemodynamically stable, and during hemodynamic instability; and (5) no obvious history of cardiopulmonary disease or symptoms of chest pain or dyspnea before onset of clinical signs and symptoms suggesting APE. Both patients, who were diagnosed as APE at hospital admission and those, in whom the diagnosis was made later during the hospital stay, were included. Six patients were excluded due to ECG signs of an old myocardial infarction, complete left branch bundle block, left ventricular hypertrophy and ventricular pacing, or presentation with electrolyte abnormalities, medication with antiarrhythmic agents or digoxin. Hence, 20 patients were included in this study.

ELECTROCARDIOGRAM

At admission or after deterioration during hemodynamic instability, an ECG using a paper speed of 25 mm/s and a standardization of 1 mV/10

mm was recorded. The TP segment was used as the isoelectric line; the PR segment was used when the T wave and the P wave merged. The J point was determined for each lead independently. Both STE and STD were measured at the J point in all leads. Two investigators, without knowledge of the patients' clinical data and recording date, evaluated the ECGs separately in a random order. Any disagreement between the investigators was resolved by consensus. The ECG analyses were in accordance in 18 patients, while there were differences in the interpretation of the ST-segment changes in lead III in one patient and in lead V₁ in one patient due to the beat-to-beat alternation and unstable isoelectric line in these two leads. After consensus, both changes were classified as STE. The following ECG parameters previously shown to be associated with pulmonary embolism were analyzed and compared:

- (1) heart rate;
- (2) S1Q3 or S1Q3T3 pattern defined according to the criteria of McGinn and White⁷;
- (3) depth of negative T wave in V₂-V₄ ≥ 1.0 mm;
- (4) depth of negative T wave in III and aVF ≥ 1.0 mm;
- (5) QRS morphology in V₁, including normal (QS or rS morphology), notched S wave, and complete or incomplete right bundle branch block (RBBB) according to conventional criteria, and Qr sign;
- (6) ST deviation in each lead, including STE or STD;
- (7) amplitude of S wave in V₄ and V₅.

ECHOCARDIOGRAM

RV dysfunction (RVD) on the echocardiogram was defined as the presence of at least one of the following criteria: (1) RV dilatation, defined as end-diastolic diameter >30 mm in the parasternal long axis view; (2) RV free-wall hypokinesia; (3) flattening or paradoxical movement of the interventricular septum.

Clinical Adverse Events during Hospitalization

The following clinical events were recorded: death from all causes, cardiac arrest, need for inotropic support, and mechanical ventilation for respiratory support.

Table 1. Demographic and Clinical Data of Enrolled Patients

(n = 20)	Value
Age (years)	58 ± 10
Female	12 (60%)
Predisposing factors for acute pulmonary embolism	
Oral contraception	1 (5%)
Immobilization due to surgery	8 (40%)
Immobilization due to bone fracture	1 (5%)
Infection	8 (40%)
Cancer	5 (25%)
Obesity	6 (30%)
Symptoms before hemodynamic instability	
Free of symptoms pertaining pulmonary embolism	9 (45%)
Dyspnea	8 (40%)
Chest discomfort	6 (30%)
Cough	2 (10%)
Syncope	6 (30%)
Symptoms or signs during hemodynamic instability	
Hypotension	3 (15%)
Cardiogenic shock	17 (85%)
Clinical events during hospitalization	
Death	7 (35%)
Cardiac arrest	9 (45%)
Need for inotropic support	15 (75%)
Mechanical ventilation for respiratory support	14 (70%)

Statistical analysis

All data were analyzed by SPSS 12.0 for Windows. Data were expressed as mean ± standard deviation for continuous variables and as rates (%) for categorical variables. For comparison of continuous variables, the *T* test was used. For comparison of categorical variables, the chi-square test or the Fisher's exact test was used. A two-tailed probability value <0.05 was considered statistically significant.

RESULTS

Demography and Clinical Data (Table 1)

Of the 20 patients, 8 acquired APE with hemodynamic instability during hospitalization—6 after and 2 during surgery. Of the remaining 12 patients, 7 were diagnosed as APE before and 5 after clinical deterioration. Of these, 11 patients had acute onset of symptoms suggesting APE, while 1 patient had no symptoms indicating the disease.

After deterioration, 3 patients had hypotension, 17 patients were in cardiogenic shock and all the 20 patients showed RVD, severe tricuspid regurgitation and elevated right ventricular systolic pressure (49 ± 12 mmHg) on the echocardiogram. After deterioration, there were 7 (35%) deaths, 9 (45%) patients presenting cardiac arrest, 15 (75%) patients needing inotropic support, and 14 (70%) patients needing mechanical ventilation for respiratory support. After deterioration, systolic and diastolic blood pressure was significantly lower and the heart rate higher ($P < 0.001$) than at admission.

Electrocardiographic Findings (Tables 2 and 3 and Figs. 1–4)

Compared with the admission ECG, the following parameters were significantly more common after deterioration: S1Q3, abnormal QRS morphology in lead V₁, STE in leads V₁, V₂, aVR, and III, and STD in leads I and V₄–V₆. Regarding ST-segment changes patterns, we found three ischemic ECG patterns during hemodynamic instability: 2 patients presenting STE in lead aVR with concomitant STD in leads I and V₄–V₆, 2 patients presenting STE in leads V₁–V₃/V₄, and 16 patients presenting STE in leads III and/or V₁/V₂ with concomitant STD in leads V₄/V₅–V₆. In comparison, only one patient presented STE in lead aVR with concomitant STD in leads I and V₄/V₅–V₆ at baseline. There were significant differences ($P < 0.001$) regarding ischemic ECG patterns between the baseline and during hemodynamic instability. Ischemic ECG patterns with concomitant S1Q3 and/or abnormal QRS morphology in lead V₁ was more common (90%) during hemodynamic instability than at baseline (5%) ($P = 0.001$). Regarding the QRS morphology changes in lead V₁, there were seven (35%) patients showing new onset of the Qr sign, five (25%) patients showing new onset of RBBB, three (15%) patients with new notched S wave, one (5%) patient with a change from notched S wave to RBBB, one (5%) patient shifting from notched S wave to the Qr sign, and one (5%) patient from RBBB to the Qr sign.

DISCUSSION

Our study indicates that ECG signs of RV strain combined with three ischemic ECG patterns are

Table 2. Blood Pressure, Heart Rate, and ECG Parameters at Baseline and during Hemodynamic instability

Parameter	At baseline (n = 20)	During hemodynamic instability (n = 20)	P value
Systolic BP (mmHg)	113 ± 18	67 ± 21	<0.001
Diastolic BP (mmHg)	69 ± 13	36 ± 13	<0.001
Heart rate (beats/min)	83 ± 19	109 ± 26	0.002
S1Q3	6 (30%)	15 (75%)	0.004
S1Q3T3	5 (25%)	9 (45%)	0.185
Negative T wave in V ₂ -V ₄	7 (35%)	7 (35%)	1.000
Negative T wave in III and aVF	8 (40%)	9 (45%)	0.749
Abnormal QRS morphology in V ₁	4 (20%)	19 (95%)	0.001
STE in V ₁	1 (5%)	17 (85%)	0.001
STE in V ₂	1 (5%)	9 (45%)	0.003
STE in V ₃	1 (5%)	2 (10%)	1.000
STE in III	0 (0%)	13 (65%)	0.001
STE in III and aVF	0 (0%)	4 (20%)	0.106
STE in aVR	1 (5%)	19 (95%)	0.001
STD in V ₄ -V ₆	2 (10%)	18 (90%)	0.001
STD in V ₅ -V ₆	0 (0%)	2 (10%)	0.487
STD in I	1 (5%)	20 (100%)	0.001
Amplitude of S wave in V ₄ (mm)	4.6 ± 4.8	5.1 ± 3.2	0.564
Amplitude of S wave in V ₅ (mm)	3.1 ± 3.3	4.2 ± 3.1	0.08
Sum of the amplitude of S wave in V ₄ -V ₅ (mm)	7.5 ± 7.8	9.3 ± 6.0	0.273
ST-segment changes patterns			<0.001
STE in lead aVR with concomitant STD in leads I and V ₄ -V ₆	1 (5%)	2 (10%)	
STE in leads V ₁ -V ₃ /V ₄	0 (0%)	2 (10%)	
STE in leads III and/or V ₁ /V ₂ with concomitant	0 (0%)	16 (80%)	
STD in leads V ₄ /V ₅ and V ₆			
Without ST-segment deviation	19 (95%)	0 (0%)	
STE and STD with concomitant S1Q3 and/or abnormal QRS morphology in lead V ₁	1 (5%)	18 (90%)	0.001

BP = blood pressure; STE = ST elevation; STD = ST depression.

Table 3. Changes of Patterns of the QRS Morphology in Lead V₁ Between Baseline and Hemodynamic Instability

Change pattern	Value
New onset of notched S wave	3 (15%)
New onset of RBBB	5 (25%)
New onset of Qr sign	7 (35%)
From notched S wave to RBBB	1 (5%)
From notched S wave to Qr sign	1 (5%)
From RBBB to Qr sign	1 (5%)

RBBB = right bundle branch block.

common findings in patients with APE during hemodynamic instability. Although all patients included in this report had APE confirmed by computed tomographic pulmonary angiography, the presence or absence of important coronary

artery disease is not ascertained in this population. However, based on our systematic review of the literature of ECG patterns during hemodynamic instability in APE, ECG presentations in patients without coronary artery disease or paradoxical coronary embolism are similar to the three ischemic ECG patterns that are described in this study population. Accordingly, the three ischemic ECG patterns with concomitant RV strain parameters, such as S1Q3, S1Q3T3, notched S wave in lead V₁, RBBB or Qr sign in lead V₁, are important markers for suspected pulmonary embolism. In patients with hemodynamic instability, echocardiography is an appropriate diagnostic tool to diagnose RVD, tricuspid regurgitation and elevated right ventricular systolic pressure caused by pulmonary embolism, leading to earlier thrombolytic therapy or mechanical intervention.

Figure 1. The ECGs of a patient, who acquired acute pulmonary embolism during hospitalization. The admission ECG (left), when the patient was free of symptoms pertaining acute pulmonary embolism, was normal, with the exception of frontal plane left QRS axis deviation. The deterioration ECG (right) shows new appearance of S1Q3, Qr sign in lead V₁, ST-segment elevation in lead aVR, and ST-segment depression in leads I, aVL, V₃-V₆.

Figure 2. The ECGs of a patient with acute onset of dyspnea and palpitation. The admission ECG (left) shows incomplete RBBB and minor ST-segment elevation in leads V₃ and V₄. The ECG after deterioration (right) shows S1Q3, Qr sign in lead V₁, significant ST-segment elevation in leads II, III, aVF, V₁-V₄, and ST-segment depression in leads I, aVL, and V₆.

Significance of Notched S Wave, RBBB or Qr Sign in Lead V₁

RBBB is an ECG sign of acute RV strain (RVS) and dilation, accompanied by ischemia of the right bundle branch.⁸ The appearance of RBBB has been found to be more frequent in cases of massive pulmonary trunk obstruction than in peripheral pulmonary embolism.⁹ In APE, typical RBBB morphology in lead V₁ is a frequent phenomenon and contains prognostic significance.^{9,10} Meanwhile, Qr sign in V₁ is closely related to the presence of

RVD, and is an independent predictor of adverse clinical outcome.^{11,12} Notched S wave in lead V₁ is also a common phenomenon in patients with APE¹² and may be associated with acute RV strain.^{13,14} Our group has analyzed the QRS morphology in leads V_{3R}-V_{5R} in 15 adults/senior individuals with notched S wave in lead V₁.¹⁵ The majority (13 in 15) showed triphasic QRS morphology with final R' wave in their QRS complexes in leads V_{3R}-V_{5R}. This QRS morphology in association with a notched S wave in lead V₁ is suggestive of the possibility of concealed incomplete or complete RBBB.¹⁵ In 18 of

Figure 3. The ECGs of a patient with chest discomfort on exertion. The admission ECG (left) was normal. The ECG after deterioration (right) shows sinus tachycardia, S1Q3T3, Qr in lead V₁, ST elevation in leads aVR, III, and V₁ to V₂, and ST depression in leads I, II, aVL, V₄–V₆.

our 20 patients, new changes of QRS morphology in lead V₁ were noted after hemodynamic instability: new onset of the Qr sign in 7, new onset of RBBB in 5, new notched S wave in 3, change from notched S wave to RBBB in 1, shifting from notched S wave to the Qr sign in 1, and from RBBB to the Qr sign in 1. Our results not only suggest that notched S wave in lead V₁ may be the early presentation of RBBB but also suggest that the Qr sign may be a more severe ECG sign than RBBB. In patients with suspected APE, these abnormalities of the QRS morphology in lead V₁ may be useful to aid in the diagnosis of APE. Also, these abnormalities are useful in risk stratification in confirmed APE.

Significance of ST-Segment Elevation in Leads V₁, V₂, aVR, and III, and ST-Segment Depression in Leads I and V₄–V₆

Hypotension, hypoxemia and RV strain during hemodynamic instability in APE can cause left ventricular (LV) subendocardial ischemia and RV transmural ischemia.⁴ Accordingly, leads reflecting mainly LV electrical activity, while situated remotely from the RV, such as I and V₄–V₆, will record STD. Meanwhile, leads reflecting local and remote (reciprocal) regional activity or the border zone between the ventricles, such as aVR, V₁, and III, will record a net effect of electrical activity from both the LV and the RV. STE in lead aVR reflects ischemia of the RV outflow tract and/or the right paraseptal region, but may also represent a reciprocal phenomenon of LV subendocardial ischemia.¹⁶ In line with these observations, lead aVR showed STE in 19 out of 20 patients in this study. Lead III faces the inferior region of the RV and lead V₁ faces the anterior region of the RV.¹⁷ If the RV is enlarged, lead V₂ and sometimes also V₃ will face the anterior region of the RV. In case of severe transmural ischemia of the RV, these leads will show STE. In this study, we found three ischemic ECG patterns during hemodynamic instability: dominant LV subendocardial ischemic pattern presenting STE in lead aVR with concomitant STD in leads I and V₄–V₆ (as shown in Fig. 1 after deterioration), dominant RV transmural ischemic pattern presenting STE in leads V₁–V₃/V₄ (as shown in Fig. 2 after deterioration), and LV subendocardial with concomitant RV transmural ischemic pattern presenting STE in leads III and/or V₁/V₂ with concomitant STD in leads V₄/V₅–V₆ (as shown in Figs. 3 and 4 after deterioration). Obviously, these three ischemic ECG patterns are not only consistent with the ECG characteristics described in previous literature^{6,12} but also indicative of LV subendocardial ischemia and/or RV transmural ischemia. We think that these three ischemic ECG patterns mainly result from hypotension, hypoxemia, RV strain and catecholamine surge.^{4,18,19} Another possible explanation for STE in APE is paradoxical coronary embolism through an atrial septal defect or patent foramen ovale. We found eight patients with presumed paradoxical coronary embolism with concomitant APE in the literature.^{20–27} Only one patient showed STE in leads V₁–V₄ and incomplete

Figure 4. The ECGs of a patient with dyspnea and syncope. The admission ECG (left) shows sinus tachycardia and negative T waves in the precordial leads. The deterioration ECG (right) shows S1Q3T3, notched S wave in lead V₁, ST-segment elevation in leads aVR, III, V₁ and V₂, and ST-segment depression in leads I, II, aVL, V₄-V₆.

RBBB with concomitant occluded conus artery,²⁰ which is similar to the dominant RV transmural ischemic pattern we have described in this study. Indeed, occlusion of the conus branch or artery can cause STE in leads V₁-V₃/V₄.²⁸ Variable STE patterns in the remaining seven patients are evidently different from the three ischemic ECG patterns we have described. Obviously, concomitant paradoxical coronary embolism only accounts for STE in a minority of patients with APE.

Significance of Negative T Waves in Inferior and Right Precordial Leads

Our group has described the correlation between STE and negative T waves by two patient cases with APE and their evolving serial ECGs.⁶ We found that negative T waves developed later than STE. We speculate that negative T waves in APE may represent an evolutionary "postischemic" stage following STE, which is a sign of transmural myocardial ischemia of the RV. In APE, transmural ischemia may develop in the RV and thus right precordial leads and inferior leads may present STE, especially in patients with hemodynamic instability. Therefore, negative T waves in the inferior and right precordial leads are common findings in APE.^{29,30} In this study, we did not find a correlation between negative T waves and high patient risk. Eight of our patients acquired APE during hospitalization, and none of them presented negative T waves in precordial leads after the acute onset of symptoms because of ongoing transmural ischemia and absence of previous transmural ischemia in these patients (as shown in Fig. 1). This finding is also consistent to the previous reports.^{6,31}

Significance of S1Q3

The S1Q3T3 and S1Q3 signs have been associated with RV strain.⁸ According to the description above, we think that also the negative T wave in lead III observed in the S1Q3 sign is a "postischemic" change. The S1Q3 sign is also a marker of RV strain and thereby useful in risk stratification.

CONCLUSIONS

In APE there is an association between hemodynamic instability and ECG signs of RV strain and myocardial ischemia. We found three distinct ECG patterns, indicating different manifestations of myocardial ischemia: STE in lead aVR with concomitant STD in leads I and V₄-V₆ (LV subendocardial ischemia), STE in leads V₁-V₃/V₄ (RV transmural ischemia) and STE in leads III and/or V₁/V₂ with concomitant STD in leads V₄/V₅-V₆ (LV subendocardial ischemia with concomitant RV transmural ischemia). Echocardiographic RVD aids in the diagnosis and in risk stratification of confirmed APE, and may be of benefit when

deciding about thrombolytic therapy or mechanical intervention.

Study Limitations

Our study is limited by its retrospective nature in a single center, the small number of patients and lack of a control group. Although coronary angiography was performed in 5 patients (3 during hemodynamic instability) and showed mild atherosclerosis in 3 patients and normal coronary artery in 2 patients, concomitant coronary artery disease, which could have affected the ischemic ECG changes, was not ruled out in the remaining 15 patients. One question that our study does not give answers to is whether hemodynamic deterioration in APE could be predicted by follow-up ECGs during hemodynamic stability. Further studies with larger sample size are needed to verify these results.

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