

Predictive value of insufficient contrast medium filling in pulmonary veins in patients with acute pulmonary embolism

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Abstract

This study is to investigate the predictive value of insufficient contrast medium filling (ICMF) in patients with acute pulmonary embolism (PE).

A total of 108 PE patients were enrolled and divided into group A and group B according to the presence of ICMF. PE index and ventricular axial lengths were measured. Heart cavity volumes were examined and right ventricle (RV) to left ventricle (LV) diameter ratio (RV/LV_(d)) and volume ratio (RV/LV_(V)) and right atrium (RA) to left atrium (LA) volume ratio (RA/LA_(V)) were calculated and compared. Group A was further divided into A1 and A2 based upon the pulmonary vein filling degree and each index was compared.

There were no significant differences between group A and B in general condition. PE index of group A was higher than that of group B. LA and LV in group A were smaller than that of group B, whereas RA in group A was larger than that of group B. RV/LV_(d), RV/LV_(V), and RA/LA_(V) in group A were significantly larger than that of group B. Embolism index of group A2 was higher than that of group A1, but without statistical significant difference. LA in group A2 was smaller than that of group A1, whereas RA, RV/LV_(d), and RV/LV_(V) were larger than that of group A1, all with significant differences.

PE increased with serious ICMF in pulmonary veins could be used as an indicator for risk stratification in patients with acute PE.

Abbreviations: COPD = chronic obstructive pulmonary disease, CTPA = computed tomography pulmonary angiography, ICMF = insufficient contrast medium filling, ICU = intensive care unit, LA = left atrium, LV = left ventricle, PE = pulmonary embolism, RA = right atrium, RV = right ventricle.

Keywords: acute pulmonary embolism, insufficient contrast medium filling, predictive value, x-ray computed

1. Introduction

Pulmonary embolism (PE) refers to clinical and pathophysiological pulmonary circulation disorder syndrome caused by endogenous or exogenous emboli-induced embolism in pulmonary artery and (or) its branches. PE is a common clinical emergency in cardiovascular diseases, and its mortality is only next to coronary heart disease and hypertension. Currently, computed tomography pulmonary angiography (CTPA) is the preferred method for the diagnosis of acute PE,^[1,2] and application of CTPA images for risk stratification of patients with acute PE has been emphasized more by clinician. Based on the rapid diagnosis of PE, CTPA could grade the danger of the patients so as to guide the clinician to take appropriate treatment and assessment of prognosis.

Generally, Qanadli method is applied for evaluation of the severity of PE via PE index. In addition, the diameter ratio of right to left ventricular (RV/LV_(d)) is used for the assessment of right ventricular dysfunction caused by PE,^[3,4] demonstrating that clinical risk and prognosis are highly consistent. Recently, some researchers put forward a new reference index of acute PE risk stratification by studying the correlation between the ratio of left and right atrial volume (LA/LV_(V)) and RV/LV_(d) with PE.^[5,6] With normal CTPA scanning, pulmonary vein imaging is clear, and its density uniform is consistent with that of left atrial. We found that in a considerable number of patients with acute PE, single or multiple pulmonary vein contrast medium filling occurred, with lower density and lower left atrial enhanced density. Whether this phenomenon is associated with the risk of acute PE is not clear. To this end, in this study the relationship between ICMF and PE risk grade was studied using CTPA.

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2. Materials and methods

2.1. Patients' data

In this study, a total of 317 cases of patients admitted to our hospital were suspected as acute PE from January 2015 to December 2015. After taking CTPA, 167 cases were finally diagnosed as acute PE. The exclusion criteria are listed as follows: patient with a history of previous myocardial infarction or cardiac insufficiency, and echocardiography showed that the ejection fraction was <55%; patients with congenital heart disease and rheumatic heart disease (mitral valve, tricuspid valve, and aortic stenosis or insufficiency); patients with constrictive pericarditis or pericardial effusion; patients with chronic

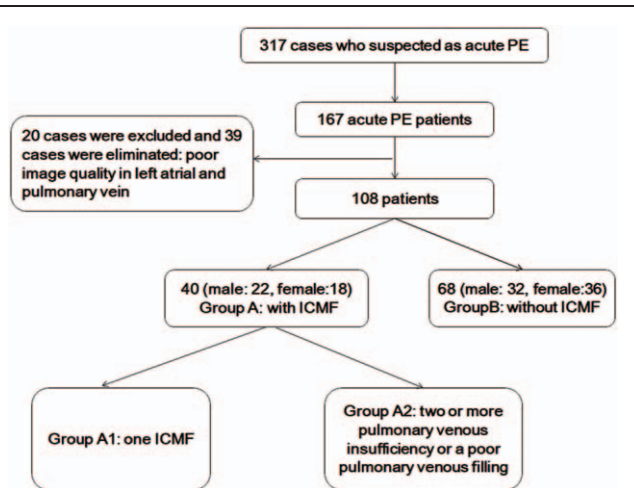


Figure 1. Flow chart of patient group assignment.

obstructive pulmonary disease (COPD) history or repeated episodes of chronic bronchitis and asthma history; and patients with emphysema, pulmonary edema, interstitial lung diseases (interstitial inflammation and fibrosis), or small airway disease revealed by plain CT scan. Flow chart of patient group assignment was represented in Figure 1.

Clinical data of the patients were retrieved by RIS database and manually registered, sex, age, and corresponding clinical symptoms including chest pain, chest tightness, hemoptysis, cough, and fever were recorded. Prior written and informed consent were obtained from the patients, and the study was approved by the ethics review board of Tianjin Chest Hospital.

2.2. CTPA examination

Somatom Definition DSCT (Siemens, Munich, Germany) or Brilliance iCT 256 (Philips International B.V., Amsterdam, The Netherlands) was for CTPA examination and respiratory training was performed so as to reduce respiratory artifacts. The patients were scanned from head to foot, and the scanning range was from thoracic inlet to lower edge of the rib. DSCT scanning parameters were as follows: the tube voltage was 120 kV, the tube current was 380 to 400 mA, the collimator width was 0.75 mm, the x-ray tube speed was 0.33 s/circuit, and the reconstruction of the convolution kernel was kernelB30f with the thickness of 1.5 mm, and the interval of 0.7 mm. As for 256 iCT scanning, the following parameters were applied. The tube voltage was 120 kV, the tube current was 800 to 1200 mAs, the collimator width was 128×0.625 mm, the x-ray tube speed was 0.27 s/circuit, and idose3 image reconstruction was applied with the thickness of 1.5 mm and the interval of 0.9 mm. Two-stage intravenous injection for contrast agent was applied. Briefly, 50 to 60 mL iopromide (Ultravist 370 mgI/mL; Bayer, Berlin, Germany) was injected followed by injection of 30 to 40 mL saline with a rate of 4.5 to 5.5 mL/s. The threshold trigger method was taken with the region of interest set in the main pulmonary artery. The CT trigger value was 60 HU and the scanning was delayed (5–7 s).

2.3. CTPA image assessment

CTPA image assessment was performed by 2 experienced radiologists and consensus view was made. All diagnosis was undertaken in workstation, and each cross-sectional image was observed one by one. Mediastinal window (window width of 350 HU and window

level of 50 HU) was used for pulmonary arteries observation, and pulmonary window (window width of 1500 HU and window level of 500 HU) was applied for lung situation diagnosis.

The diagnostic criteria for acute PE were low-density filling defects in the enhanced pulmonary artery cavity and central or eccentric arterial stenosis or complete occlusion. As for pulmonary vein filling poor judgments and classification, the cases were divided into group A and B according to whether there was ICMF. And group A was PE patients with ICMF, whereas group B was PE patients without ICMF. According to the number of ICMF and the corresponding pulmonary consolidation, patients in group A were further divided into 2 subgroups named group A1 and A2. Patients in group A1 had only 1 ICMF, whereas patients in group A2 had 2 or more pulmonary venous insufficiency or a poor pulmonary venous filling associated with lung consolidation in corresponding pulmonary segment.

2.4. Parameter definition

As for PE index determination, CTPA PE formula designed by Qanadli was applied: $(\sum(n \times d)/40) \times 100\%$.^[3] Here, the n represented the number of affected arteries, and as there are 20 pulmonary arteries in bilateral pulmonary, $1 \leq n \leq 20$. The d represented the weight coefficient of obstruction, where 0 indicated no embolism, 1 showed partial embolization, and 2 stood for complete embolization. When complete embolization of bilateral pulmonary occurred, the grading was 40 and the PE index was 100%.

Axial scanning images were transmitted to the Philips Intellispace Portal workstation for cardiac function determination. Cardiac Viewer software was applied for ventricular axis measurement and ventricular diameters were calculated. Atrium and ventricle were marked with different colors with CT Comprehensive Cardiac software and ventricular volumes were automatically measured (Fig. 2) as will detail below in the figure legends. The ratio of right ventricular (RV) to left ventricular diameter (LV) ($RV/LV_{(d)}$) and volume ($RV/LV_{(v)}$) together with the ratio of right atrium (RA) to left atrium (LA) volume ($RA/LA_{(v)}$) were thereby calculated.

2.5. Follow-up

Patients who were diagnosed PE by CTPA were hospitalized for treatment. We followed up the states of patient's treatment and recovery. Some patients with exacerbations were transferred from the general ward to the intensive care unit (ICU). The medical records of patients in group A and B, whether the condition was improved, and discharge or transferred to ICU were analyzed.

2.6. Statistical analysis

All statistical analyses were performed by using the SPSS 11.5 software (SPSS, Inc, Chicago, IL). Data were presented as mean \pm SD or percentage (%). Quantitative data analysis was performed using independent samples t test, and qualitative data analysis was undertaken with χ^2 test or Fisher exact probability method. A $P < .05$ was considered as statistically significant.

3. Result

3.1. General situation of the patients

At the beginning of the study, the candidate patients were screened with the exclusion criteria and 20 cases were excluded and 39 cases were eliminated because of poor image quality in left

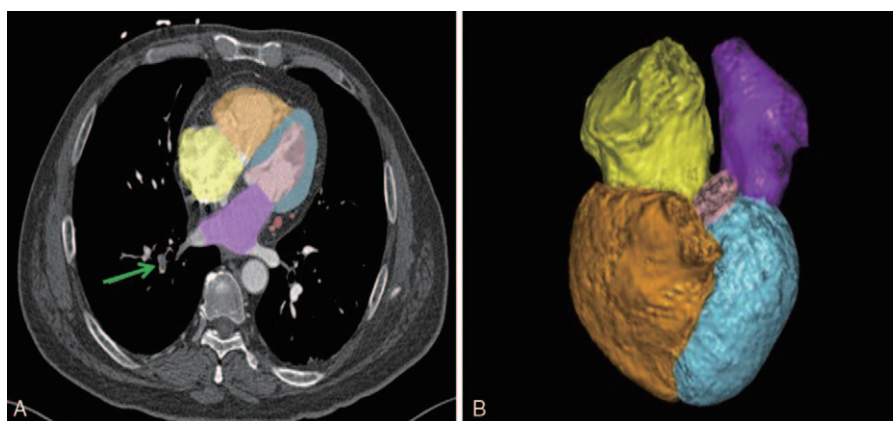


Figure 2. Atrial and ventricular volumes measured by the workstation. CTPA axial image (A) and colored map image (B) demonstrated the right lower lobar pulmonary artery embolism (green arrow) and atrial, ventricular volumes were measured by the workstation with different colors (purple: left atrium; yellow: right atrium; blue: left ventricle; brown: right ventricle).

Table 1
Comparison of clinical data between patients in the 2 groups.

	Group A (n=40)	Group B (n=68)	P
Age, y	60.55 ± 15.43	63.63 ± 10.04	.211
Sex			
Male	22	32	.425
Female	18	36	
Symptoms n (%)			
Chest pain	32 (80.00)	55 (80.88)	.911
Chest tightness	40 (100.00)	65 (95.59)	.294
Hemoptysis	4 (10.00)	5 (7.35)	.631
Cough	25 (62.50)	40 (58.82)	.706
Fever	10 (25.00)	15 (22.06)	.726

atrial and pulmonary vein. Finally, a total of 108 patients were included in this study, with both 54 cases of male and female. There were 40 cases of patients in group A (22 were male and 18 were female), with a mean age of 60.55 ± 15.43 years old and 68 cases in B group (32 were male and 36 were female), with a mean age of 63.63 ± 10.04 years old (Fig. 1). To identify whether there was no difference between the 2 groups in general situation, comparison was performed. As listed in Table 1, there was no significant difference between the 2 groups in age, sex, and clinical symptoms. The result indicated that the grouping was reasonable.

3.2. CTPA examination results

Generally, axial image of CTPA can show the filling of the pulmonary vein, whereas coronal image can better show pulmonary vein, pulmonary artery, and lung lesions. The higher the PE index, the higher degree the risk, and the badly need for timely clinical treatment for the patients. To make a correct diagnosis, CTPA examination was performed for the patients. Filling defects were found in all patients enrolled in this study; however, not all the patients were accompanied by pulmonary lesions (Fig. 3). As illustrated in Figures 4 and 5 RA and RV are increased in size, and LA is decreased in size, indicating the existence of ICMF.

3.3. Comparison of parameters of CT observation indexes between group A and B

To find out whether there is a more serious risk classification of ICMF for the patients, PE index and cardiac function parameters between the 2 groups were compared. As illustrated in Table 2, the PE index in group A was (63.73 ± 20.27%), which was significantly higher than that of group B (20.10 ± 10.66%) ($P < .5$). The volumes of LA and LV in group A were less than that in group B, whereas RA, RV/LV_(d), RV/LV_(v), and RA/LA_(v) in group A were higher than that of group B ($P < .5$). In total, the above heart function parameters indicated that the right heart function of patients in A group had become worse, indicating that

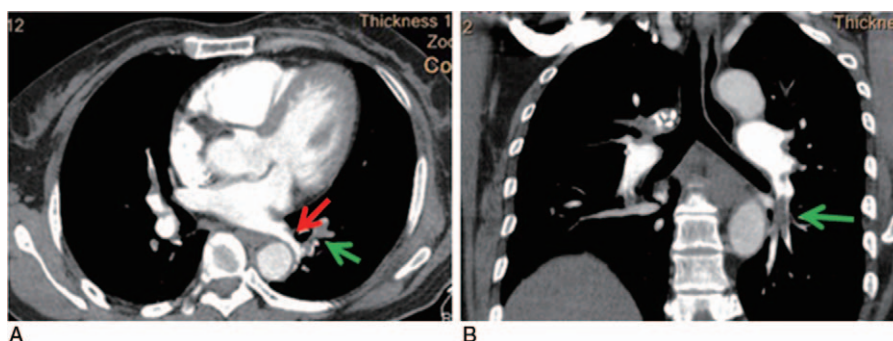


Figure 3. CTPA of one of the group B patients with acute pulmonary embolism (PE) but without insufficient contrast medium filling (ICMF). Axial (A) and Coronal (B) images demonstrated left lower pulmonary artery branch embolism (green arrow) without ICFM in the left inferior pulmonary vein (red arrow).

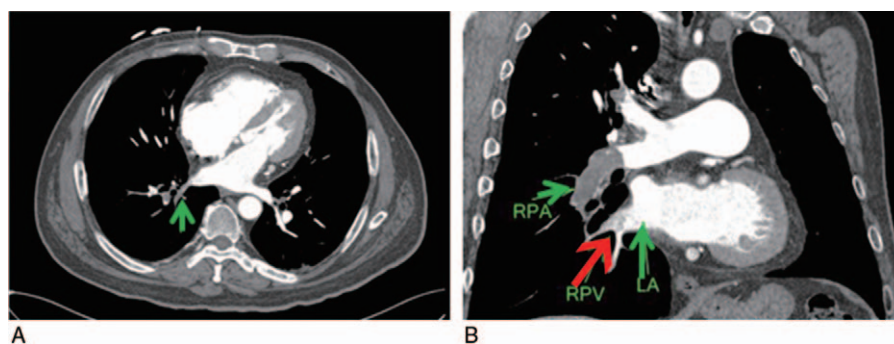


Figure 4. CTPA of one of the group A1 patients with acute pulmonary embolism (PE) and single insufficient contrast medium filling (ICMF). Axial (A) and Coronal (B) images demonstrated right lower lobar pulmonary artery embolism (green arrow) with ICFM in the right inferior pulmonary vein (red arrow).

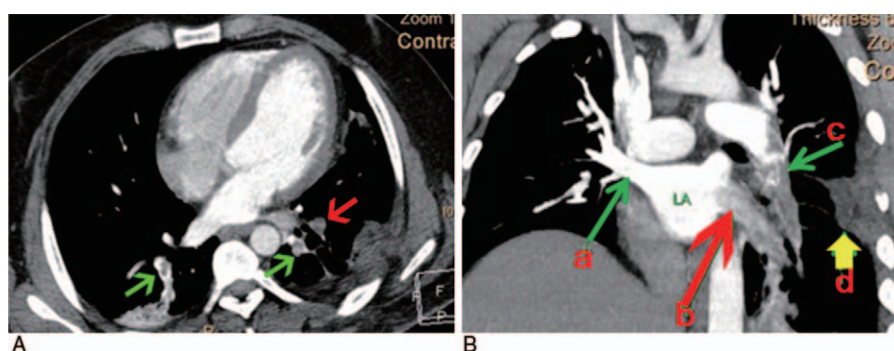


Figure 5. CTPA of one of the group A2 patients with acute pulmonary embolism (PE) and multiple insufficient contrast medium filling (ICMF). Axial (A) and Coronal (B) images demonstrated bilateral pulmonary emboli (green arrows) and multiple pulmonary venous ICFM (red arrows). Pleural based wedge shaped consolidation resembles pulmonary infarct (yellow arrow).

patients associated with ICMF were more serious than patients without ICMF.

3.4. Comparison of parameters of CT observation indexes between subgroup A1 and A2

To identify whether the degree of ICMF is associated with the severity of PE, patients with ICMF were further divided into subgroups A1 and A2 according to the number of poor pulmonary venous filling and relative parameters were compared. Although the PE index of group A2 was higher than that of group A1, the difference was not statistically significant (Table 3).

With the combination of the results that LA and LV in group A2 were lower than that in group A1 while RA, RV, RV/LV_(d), RV/LV_(v), and RA/LA_(v) all were higher than that of group A1, it is possible to assume that the right heart function of patients associated with more serious ICMF had the higher degree of risk than patients with lighter ICMF.

3.5. Follow-up results

The follow-up results were represented in Table 4. There were 20 cases (50%) transferred to ICU in group A patients, whereas there were 13 cases (19.1%) transferred to ICU in group B patients.

Table 2

Comparison of CTPA parameters between the patients in the 2 groups.

	Group A (n=40)	Group B (n=68)	P
PE index	63.73 ± 20.27%	20.10 ± 10.66%	.000
LA	66.02 ± 10.51	71.63 ± 14.33	.033
LV	69.47 ± 11.24	76.61 ± 16.80	.019
RA	95.80 ± 16.34	87.68 ± 21.12	.039
RV	122.84 ± 21.50	116.16 ± 32.56	.250
RV/LV _(d)	1.24 ± 0.45	1.07 ± 0.35	.031
RV/LV _(v)	1.77 ± 0.43	1.57 ± 0.50	.037
RA/LA _(v)	1.45 ± 0.38	1.25 ± 0.26	.002

LA = left atrium, LV = left ventricle, PE = pulmonary embolism, RA = right atrium, RV = right ventricle.

Table 3

Comparison of CTPA parameters between the patients of ICMF subgroups.

	A1 (n=23)	A2 (n=17)	P
PE index	60.28 ± 23.84	68.38 ± 13.4	.216
LA	68.89 ± 9.89	62.14 ± 10.95	.048
LV	72.12 ± 10.69	65.88 ± 12.04	.092
RA	93.75 ± 16.54	98.57 ± 16.12	.363
RV	119.65 ± 20.12	127.16 ± 22.05	.269
RV/LV _(d)	1.19 ± 0.39	1.31 ± 0.48	.389
RV/LV _(v)	1.59 ± 0.38	2.01 ± 0.46	.003
RA/LA _(v)	1.34 ± 0.44	1.59 ± 0.46	.044

LA = left atrium, LV = left ventricle, PE = pulmonary embolism, RA = right atrium, RV = right ventricle.

Table 4**Comparison of follow-up results between the patients.**

	A1 (n=23)	A2 (n=17)	P
Discharged	13 (56.5%)	7 (41.2%)	
Critical patients (ICU)	10 (43.5%)	10 (58.8%)	.055

	Group A (n=40)	Group B (n=68)	P
Discharged	20 (50%)	55 (80.9%)	
Critical patients (ICU)	20 (50%)	13 (19.1%)	.00

ICU=intensive care unit.

The number of patients with exacerbations in group A was significantly higher than that in group B ($P=.00$). There was no significant difference in the number of patients transferred to ICU between group A1 and A2 patients. However, the proportion of patients transferred to ICU in A2 group (58.8%) in which patients with more serious poor pulmonary venous filling than group A1 was significantly higher than that in group A1 (43.5%).

4. Discussion

Rapid and accurate classification of the severity of PE patients has important clinical significance^[7,8] for the guiding of the choice of treatment options and assessment of the prognosis. Currently, Qanadli method is commonly used for calculating PE index and $RV/LV_{(d)}$ of CTPA images so as to assess the severity of PE, whereas the study about pulmonary venous reflux status in patients with PE is very rare.^[3,4] This study showed that the proportion of ICMF in patients with acute PE was 23.9%, which was rather high. Patients diagnosed as PE with ICMF by CTPA were more serious than those who were without.

In CTPA images, the severity of PE is assessed from the degree of obstruction of the pulmonary vascular bed and the changes in the heart structure. For pulmonary vascular bed obstruction degree evaluation, scoring system designed by Qanadli is the most commonly used method. This system not only takes into account the embolism position, and is differentiated by the weighted method of complete and partial PE. This could objectively reflect the degree of obstruction of pulmonary arterial vascular bed in patients with PE. It is reported that for patients with PE index $>60\%$, the mortality increases, and Qanadli positive results on the CTPA system have very accurate prediction of death.^[9] Collomb et al found that the extent of PE determined by Qanadli scoring system could also reflect the hemodynamic state of severe PE. Patients with embolism index ($54 \pm 11\%$) have severe PE, and in need for thrombolysis or surgical treatment, whereas embolism index ($24 \pm 18\%$) is not serious.^[10] By comparing patients of acute PE death group with survival group, researchers have found that PE index increase is the risk factor of death in patients with acute PE and when PE index is $<40\%$, the death negative predictive value reached 100%.^[11] In this study, the pulmonary arterial embolization index of group A was $63.73 \pm 20.27\%$, whereas the index of group B was $20.10 \pm 10.66\%$, indicating that the degree of obstruction of the pulmonary vessels in group A was significantly greater than that of group B.

The lung has a double blood supply of bronchial artery and pulmonary artery and therefore usually pulmonary venous drainage is rarely affected. The results of this study showed that when PE caused severe obstruction of the pulmonary vascular bed, lung blood supply from pulmonary artery greatly decreased. And after the blood flowing through the pulmonary capillary, blood reflux in pulmonary vein branch decreased, thus leading to

decreased blood supply from pulmonary vein to the left atrium, this manifested as ICMF in pulmonary vein in CTPA image. We considered that ICMF essentially reflects the imbalance of ventilation perfusion ratio and indicates that the drainage of lung segment or lobe is in severe hypoxia.

CTPA can also be used to evaluate the heart changes caused by PE, such as the right ventricular dysfunction, the heart cavity diameter or volume changes, and so non. Right ventricular failure is the direct cause of death in patients with acute PE, and the measurement of right ventricular function is a more accurate indicator for assessing the severity of PE.^[12,13] Right heart dysfunction in patients with PE is the result of pulmonary vascular bed blocking, which indicates a gradual failure of cardiac function. If the thinning right ventricular wall could not be well compensate the sudden increase in wall pressure, right heart failure will be induced, including cardiac stroke volume reduction, tricuspid regurgitation, and venous blood flow decrease, which will finally lead to circulatory failure.^[14] Previous studies have showed that $RV/LV_{(d)}$ and PE index have a good consistency.^[13,15] In this study, $RV/LV_{(d)}$ values of the 2 groups were 1.66 ± 0.49 and 1.07 ± 0.35 , all were >1 , and the results of the study were consistent with previous studies.^[15-17] $RV/LV_{(d)}$ values of group A were significantly higher than that of group B, indicating that poor lung vein filling could reflect the severity of right heart failure in patients with acute PE. The result suggested that pulmonary vascular resistance increased significantly, hence resulted in significant pulmonary hypertension, which led to increase right ventricular after load and right ventricular dilatation. When the volume parameter $RV/LV_{(v)}$ was used for comparison, the group A was still higher than that of the group B. The difference of $RV/LV_{(d)}$ between the 2 groups was significantly higher than that of $RV/LV_{(v)}$, which might be the image motion artifacts caused by heartbeat changes as a result of non ECG gated CTPA acquisition. However, the 2 groups of data both indicated higher PE severity when pulmonary venous filling defects occurred.

To our knowledge, there are few studies about the changes of left and right atrial in PE patients and recent study has found that small increase of $RA/LA_{(v)}$ is linked to and elevated short-term mortality in acute PE patients.^[18] The results of this study showed that the volume of LA (60.52 ± 9.85 mL) in patients of group A was significantly lower than that in group B (71.63 ± 14.33 mL). In addition, $RA/LA_{(v)}$ had the same result, which was consistent with previous research.^[18] In previous study, the average volume of LA in patients with PE was 57.5 mL, which was significantly lower than that in the nondeath group (70.1 mL).^[18] ICMF displayed on CTPA reflected a decrease in pulmonary venous drainage. This could result in reduced left atrial volume, which leads to left ventricular blood volume deficiency, and finally resulting in systemic failure.

The results of follow-up showed that the danger degree (transferred to ICU) was significantly increased when the patients showed poor pulmonary vein filling, and we should pay more attention to risk degree of patients. When the poor pulmonary vein filling in patients occurred, the content of oxygen in the pulmonary vein decreased, and then the oxygen partial pressure in patients decreased and patients were exacerbations. In this study, there was no significantly difference in the follow-up results between group A1 and A2, but the proportion of critically ill patients in group A2 was significantly higher than group A1. These results may because that the blood oxygen level was further reduced and the risk was higher when multiple pulmonary venous infusions were associated with pulmonary lesions.

To sum up, this study set up a strict standard to exclude a variety of factors that can cause ICMF, as well as the development of scanning and time for remedy in gender development of left atrial and pulmonary vein. According to the existence of ICMF, the patients with acute PE were grouped. The results showed that pulmonary vascular obstruction and right heart failure degree in patients with ICMF were more serious than those who were without. This confirmed that acute PE patients with ICMF had higher clinical risk and needed for more positive clinical intervention. Further comparison of the number of ICMF showed that the severity was linked to risk degree.

There are some limitations for this study. First, ECG gating CTPA image acquisition was not applied to assess the heart parameters, which might affect the accuracy of the measurement data. Second, subjective evaluation method was used for ICMF evaluation. Third, the effect of ICMF on the treatment time and the treatment in patients with PE are still needed to be followed up.

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