Correlation between the embolism area and pulmonary arterial systolic pressure as an indicator of pulmonary arterial hypertension in patients with acute pulmonary thromboembolism

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Abstract. – OBJECTIVE: We tested whether correlation between embolism area and pulmonary arterial pressure may serve as an indicator of pulmonary arterial hypertension in patients with acute pulmonary thromboembolism.

PATIENTS AND METHODS: In total, 204 patients who underwent spiral computed tomography (CT) pulmonary angiography and ultrasonic cardiogram were enrolled. The patients were stratified according to their pulmonary arterial systolic pressure into those with normal values, or those with mild, moderate, or severe pulmonary arterial hypertension. The embolism area was quantified using Qanadli score.

RESULTS: We found that embolism area correlated positively with pulmonary arterial systolic pressure (r = 0.514). Specifically, embolism areas of four study groups were, respectively, 17.72 ± 13.61%, 18.25 ± 13.78%, 33.39 ± 10.99%, 40.46 ± 15.75%, obviously increasing along with progression of the disease. Pulmonary arterial systolic pressure was above 41 mm Hg when the embolism area was >33%, and above 70 mm Hg with the embolism area of > 40%.

CONCLUSIONS: Assessment of the embolism area is useful in the clinical evaluation of pulmonary arterial systolic pressure, but appears to be more applicable to moderate and severe pulmonary arterial hypertension.

Keywords:
Acute pulmonary embolism, Pulmonary hypertension, Embolism area, Spiral CT pulmonary angiography, Ultrasonic cardiogram.

Introduction

Pulmonary arterial systolic pressure tends to increase following acute pulmonary thromboembolism (APTE), and patients are likely to experience changes of the cross-sectional diameter of pulmonary arteries. Pathology reports demonstrate a correlation between pulmonary arterial systolic pressure and increase in embolism areas. However, the strength of this correlation is not clear. In the present study, we evaluated pulmonary arterial systolic pressure, area and diameter of embolism in patients with APTE using echocardiography and spiral computed tomography (CT) pulmonary angiography. We further studied a feasibility of accurately estimating pulmonary arterial systolic pressure using the embolism area. Also, we assessed the relationship between pulmonary arterial systolic pressure, and the extent of pulmonary vascular dilation and embolism. The results of our study provide necessary information for early assessment of disease conditions to enable early interventions in pulmonary arterial hypertension.

Patients and Methods

Patients

Patients with APTE whose diagnosis was confirmed by spiral CT pulmonary angiography and who were admitted to the No. 2 Hospital, Hebei Medical University, from January 2012 to March 2013 were enrolled in our study. Further enrollment criteria included previous cardiac ultrasound examination and disease course of less than 3 months. Exclusion criteria were the following: prior history of cardiovascular disease, rheumatic diseases, and pulmonary hypertension of other etiologies. Patients were stratified according to the Classification of Pulmonary Arterial Hypertension[1] into those with normal pul-

monary arterial systolic pressure (< 36 mm Hg), and mild (36-40 mm Hg), moderate (41-70 mm Hg), and severe (> 70 mm Hg) pulmonary arterial hypertension[2-6].

The patients' demographic data were also collected, including gender, age, height, body weight, and body-mass index (BMI).

Instruments

Echocardiography was done as follows. Pulmonary arterial systolic pressure was estimated based on tricuspid regurgitation velocity. Cross-sections of four apical chambers were employed to determine the short axis of the left and right ventricles during at least five cardiac cycles. Average values of five cycles were used.

Spiral CT pulmonary angiography was done using Philips high-speed 256-row spiral CT, with the thickness of scanning section set to 1 mm. Captured images were transferred to workstation for further analysis. Diameters of main pulmonary artery, aortic diameter, right pulmonary artery, and vertebral diameter were measured based on the section that had maximal area. Further, the extent of vascular obstruction was assessed based on the segmental and sub-segmental pulmonary embolic profiles. Embolism areas were also estimated. In order to diminish assessment bias, two experienced radiologists worked together to evaluate the results.

Estimation of the embolism area

The Qanadli score was used to estimate the extent of embolism of 10 segmental pulmonary vessels for both left and right sides, and 20 sub-segmental vessels under spiral CT pulmonary angiography. For each segmental pulmonary artery, 0 points were assigned in the absence of embolism, 1 point was given when incomplete embolism was present, and 2 points meant complete embolism. If sub-segmental vessels were occluded, the involved segmental pulmonary vessel was considered as having incomplete embolism, and 1 point was to be assigned with a total score of no less than 2 points for each segmental pulmonary vessel. When emboli were present in the upper vessels of segmental pulmonary artery, a complete occlusion was to be assigned to segmental vessels, with 2 points assigned in total. The measurement values were summarized. The sum for each field could not exceed 20 points, with a total score of 40 points. The estimate formula was $[(n \times d)/40] \times 100]$, where "n" were 10 segmental pulmonary vessels for both left and right sides and "d" – 20

sub-segmental vessels. Quantitative results were expressed as the percentage of the embolism area.

Statistical analysis

Numerical data were analyzed by chi-square test and are presented as mean ± SD. Comparisons among multiple groups were carried out by the ANOVA test. The Spearman's rank correlation test was used to analyze non-normally distributed data. The linear correlation analysis was utilized to analyze the inter-variable correlation. A p value of < 0.05 was considered as statistically significant.

Results

A total of 204 patients with APTE patients were included. There were 92 (44.9%) male and 112 (54.6%) female patients. The patients' mean age was 59.75 ± 13.49 years, ranging from 24 to 88 years. One hundred and fifty-one (74.02%) patients were older than 65 years. The inter-group comparisons revealed no statistical differences in gender, age, height, body weight, or BMI.

Pulmonary arterial systolic pressure and the ratio of main pulmonary artery/aortic diameter were estimated based on echocardiography and spiral CT pulmonary angiography. Using the cut-off mark of 36 mm Hg,[2] there were 84 patients with pulmonary arterial hypertension, including 14 patients with mild, 48 with moderate, and 22 with severe hypertension. Using the main pulmonary artery/aortic diameter of > 1 as the diagnosis criterion for pulmonary arterial hypertension[4], there were 59 patients who met the criteria for pulmonary arterial hypertension, including 4 patients with mild, 37 with moderate and 18 with severe pulmonary arterial hypertension. Moderate PAH was assigned if the embolism area was >33%, while severe PAH was assigned if the embolism area was > 40%.

Sensitivities of the main pulmonary artery/aortic diameter ratio to detect pulmonary arterial hypertension based on echocardiography analysis were, respectively, 70.2%, 28.6%, 77.1%, and 81.2% for mild, moderate, and, severe forms (Figure 1). Among the included patients, 120 patients had normal (i.e., ≤ 36 mm Hg) pulmonary arterial systolic pressure, including 33 patients with the main pulmonary artery/aortic diameter ratio of ≤ 1. The specificity of diagnosis of pulmonary arterial hypertension by spiral CT pulmonary angiography was estimated to be 72.5%.
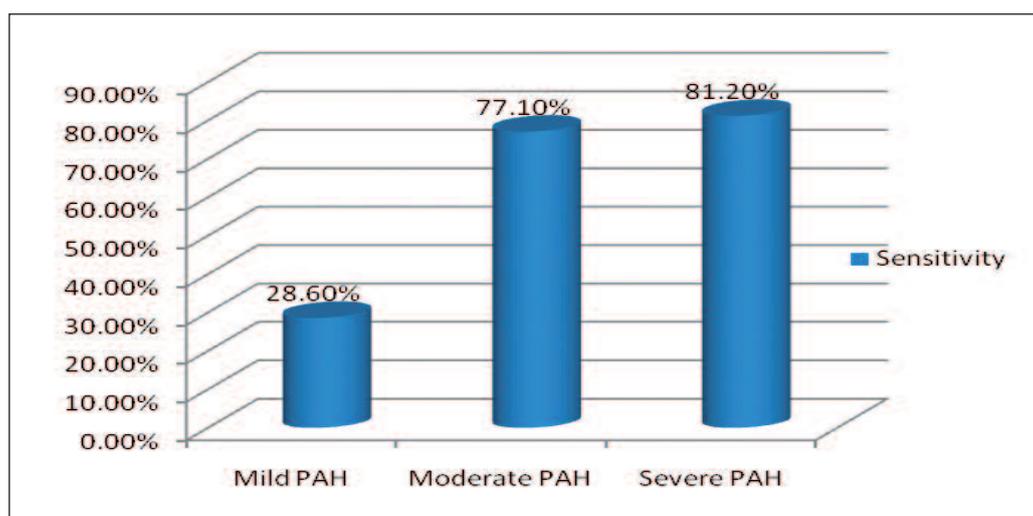
Figure 1. Sensitivity of CTPA in the diagnosis of PAH.

The right/left ventricle ratio, main pulmonary artery, main pulmonary artery/aortic diameter, right pulmonary artery, main pulmonary artery/vertebral artery, and embolism area were found to positively correlate with pulmonary arterial systolic pressure (respectively, r = 0.396, 0.35, 0.46, 0.13, 0.25, and 0.514). In moderate pulmonary arterial hypertension, the right/left ventricle ratio and main pulmonary artery/aortic diameter ratio increased significantly and remained stable, and were not affected by increased pressure. Pulmonary artery and pulmonary artery/vertebral artery also tended to increase with increasing pulmonary arterial systolic pressure; however, this increase did not reach statistical significance until the development of severe pulmonary arterial hypertension. A significant enlargement of the right pulmonary artery was observed only in patients with severe pulmonary arterial hypertension (Table I).

Discussion

Thromboembolic pulmonary arterial hypertension causes high morbidity worldwide, and its diagnosis and treatment remain challenging. Residual pulmonary arterial hypertension persists in both acute and chronic embolism[4-6]. Previous studies showed that pulmonary arterial systolic pressure increases sharply within 30 minutes of embolism and reaches a peak within 1-2 hours after an APTE episode. The emboli may be eliminated in the early stages, and most thrombolysis process is complete by, approximately, day 28 after APTE. Pulmonary arterial systolic pressure may recover back to stable conditions around day 38 to 42[6,7]. Approximately 80% of patients with APTE suffer from pulmonary arterial hypertension, and 0.5-4% of them will ultimately develop chronic thromboembolic pulmonary hypertension[6].

Table I. Difference between the diameter of pulmonary vascular and pulmonary artery obstruction areas with the level of PASP.

	PA (mm)	PA/AA	PA/vertebral diameter	RPA (mm)	Embolism area (%)	RV/LV
Normal PA pressure	28.8 ± 5.03	0.91 ± 0.17	1.34 ± 0.37	20.14 ± 4.48	17.7 ± 13.6	0.553 ± 0.32
Mild PAH	30.8 ± 4.01	0.97 ± 0.16	1.48 ± 0.42	17.9 ± 2.50	18.3 ± 13.8	0.46 ± 0.22
Moderate PAH	32.5 ± 6.67	1.06 ± 0.18	1.47 ± 0.38	20.05 ± 3.46	33.4 ± 10.9	0.67 ± 0.23
Severe PAH	35.5 ± 5.76	0.17 ± 0.11	1.63 ± 0.34	23.25 ± 4.47	40.6 ± 15.7	1.48 ± 3.55
p_1	< 0.0001	< 0.0001	0.004	0.007	< 0.0001	< 0.0001
R	0.383	0.469	0.25	0.186	0.514	0.33
p_2	< 0.0001	< 0.0001	< 0.0001	0.008	< 0.0001	< 0.0001

Footnote: p_1 = p values for comparisons among groups; p_2 = p values for correlation analysis. PA = pulmonary artery; AA = aortic artery; RPA = right pulmonary artery.

There are many calculation methods to evaluate spiral CT pulmonary angiography, such as Mastora, Miller, Walsh, and Qanadli scores. The Qanadli score is closely related to angiography of right heart catheterization and pulmonary artery, and has advantages of being a simple and repeatable procedure. Therefore, this method was used by us in this study. Based on our findings, pulmonary arterial systolic pressure is > 41 mm Hg if the embolism area is > 33%, and > 70 mm Hg if the embolism area is > 40%.

Poor prognosis and high mortality are seen in patients with APTE and pulmonary arterial hypertension. The prognosis is defined by initial pulmonary artery pressure, timely treatment, adequate changes of pulmonary arterial systolic pressure in the course of treatment, cardiopulmonary reservation, embolism area, time to thrombosis, and self-fibrinolytic activities. In patients with low initial pulmonary arterial systolic pressure, good prognosis can be expected, and the pressure tends to decrease after therapy in patients without cardiovascular diseases. However, poor prognosis is expected in patients with initial pulmonary arterial systolic pressure of > 50 mm Hg and age of > 65 years, even if disease is stable. Due to its non-specific clinical characteristics, pulmonary arterial hypertension tends to be overlooked, while its early diagnosis is very valuable in the treatment and prognosis of patients with APTE.

The right heart catheterization is the gold standard for diagnosis, however, its wide application is limited by its invasive character. Therefore, clinically, most pressure evaluations are based on tricuspid regurgitation velocity by echocardiography. However, echocardiography can only be used to crudely estimate the sizes of emboli. The assessments may be affected by cardiac cycle and breathing. Therefore, more accurate approaches are desired. Spiral CT pulmonary angiography could directly evaluate the extent of expansion by determining the diameter of pulmonary arteries and the embolism area of segmental pulmonary artery. The results are consistent with those achieved from right heart catheterization and pulmonary angiography.

Right ventricular function is the key factor contributing to the survival of patients with pulmonary arterial hypertension[8], and right ventricular function may be involved as a result of initial elevation of pulmonary arterial systolic pressure, with right ventricular hypertrophy being the main presentation[9]. In previous studies with patients with post-APTE pulmonary arterial hypertension, the ratio of right to left ventricular functions was > 0.6, and dramatic elevation of pulmonary arterial systolic pressure was seen in patients with this ratio of > 1.5[7 10 11]. In our study, we also found that this ratio increases along with increases in pulmonary arterial systolic pressure, and that moderate and severe pulmonary arterial hypertension can be identified with the ratio of > 0.6. Since this is not the case in patients with mild disease, we speculate that structural changes in the right ventricle of these patients may not be as prominent yet. Indeed, structural changes in the right ventricle are pronounced only at pulmonary arterial systolic pressure of > 41 mm Hg.

In this study, the sensitivity and specificity of diagnosis of pulmonary arterial hypertension (respectively, 70.2% and 72.5%) were very similar to prior studies[12 13]. However, the diagnostic sensitivity of spiral CT pulmonary angiography in mild pulmonary arterial hypertension was much lower than in the moderate and severe forms of this disease (respectively, 28.6%, 77.1%, and 81.2%). Therefore, this approach is highly sensitive in the diagnosis of moderate-to-severe pulmonary arterial hypertension, with the highest sensitivity in severe form.

In our study, we documented positive correlation between diameter of the main pulmonary artery and pulmonary arterial systolic pressure. Shortly after development of pulmonary arterial hypertension, most diameters of the main pulmonary arteries are expected to exceed 29 mm. In severe form, most diameters exceed 35 mm. The magnitude of expansion of the diameter of the main pulmonary artery is affected by mechanical effects of high blood volume and pulmonary fibrosis of adjacent vessels, which both lead to passive expansion of pulmonary vessels[14]. Further factors determining the diameter include age and body surface area. Clinically, the factors related to the expansion of the diameter of the main pulmonary artery should be discriminated.

Prior studies proposed to use the ratio of main pulmonary artery to the diameter of aorta of > 1 as a sign for pulmonary arterial hypertension[11,15]. However, pulmonary arterial hypertension cannot be completely excluded in patients with the ratio of ≤ 1[13]. In our study, we documented positive correlation between the ratio and pulmonary arterial systolic pressure. Further, the ratio of main pulmonary artery and aorta of > 1 was only observed in patients with moderate-to-severe disease, which is consistent with the literature[9]. Thus, we also believe that pulmonary arterial hypertension cannot

be completely excluded in patients with the ratio of ≤ 1, especially in those with mild disease.

The changes in pulmonary arterial systolic pressure are closely related to the area of embolism after APTE episodes[16,17]. As autopsy results demonstrate, mean pulmonary arterial pressure begins to increase when the pulmonary vascular bed obstruction reaches > 25%-30%, and increases to 40 mm Hg if the pulmonary vascular bed obstruction is 40%-50%. The mortality increases if PVB obstruction reaches > 60%[18], and sudden death may occur if the obstruction reaches > 80%.

Conclusions

The above studied factors and embolism area may serve as indicators for pulmonary arterial hypertension. The diameter and embolism area determined by spiral CT pulmonary angiography can be used to assess the condition in patients with this disease.

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Conflict of interest

The Authors declare that they have no conflict of interests.

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