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Clinical and imaging manifestations of Takayasu's arteritis with pulmonary hypertension: A retrospective cohort study in China

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ABSTRACT

Background: Takayasu's arteritis with pulmonary artery involvement (PTA) is uncommon and part of which may be accompanied by pulmonary hypertension (PH). This study herein investigated the clinical presentation, imaging features, and outcomes in PTA patients with and without PH.
Methods: A total of 57 PTA patients were selected at the Beijing Chao-Yang Hospital from January 2011 to July 2017. Patients were placed into two groups, PTA-with-PH or PTA-without-PH. The clinical characteristics, imaging features, and outcomes of patients in these two groups were investigated.
Results: Among the 57 PTA patients, 24 were in the PTA-without-PH group and 33 were in the PTA-with-PH group. The disease duration in PTA-with-PH patients was longer than that of PTA-without-PH patients. The mean follow-up duration of 43 patients was 33.5 ± 20.3 months, while three patients in the PTA-with-PH were deceased. The PTA-with-PH group had significantly higher prevalence of chest tightness and dyspnea, shorter 6-minute walk distance (6MWD) and higher Borg scores after walk than that the PTA-without-PH group. Imaging analyses revealed that patients had five different arterial lesions (stenosis, occlusion, vascular wall thickening, in situ thrombosis, and aneurysm), but aneurysms were only detected in patients in PTA-with-PH patients at 42%. Compared with PTA-without-PH patients, PTA-with-PH patients tended to have occlusion lesions, but less likely to have vascular wall thickening.
Conclusions: Compared with PTA-without-PH patients, PTA-with-PH patients had longer disease duration, more severe symptoms and tended to be deceased during the follow-up time. In addition, PTA-with-PH patients tended to have aneurysm and occlusion vessel lesions.

1. Introduction

Takayasu's arteritis (TA), also known as aortic arch syndrome or pulseless disease, is a chronic large vessel granulomatous vasculitis, which predominantly affects young females. The disease commonly involves the aorta and its major branches, including the ascending aorta, abdominal aorta, and descending thoracic aorta. TA may also involve the pulmonary artery (PTA) [1]. Our and others previous studies had reported that the prevalence of PTA in all TA patients were widely varied from 6.9% to 36.7% [2–4]. There were also clinical features' differences between PTA and total TA patients [5], as well as higher mortality of 23% than total TA patients [6].

The early stages of TA and PTA present with nonspecific symptoms, such as fever, fatigue, and chest pain [7], however, the progression of PTA into later disease stages results in serious complications, including pulmonary artery stenosis, occlusion, and pulmonary hypertension (PH) [8]. Given that pulmonary artery involvement in TA increases the chances for developing PH, which is known to negatively affect cardiovascular function [9], we hypothesized that PTA-with-PH might present distinct clinical and imaging features and outcomes when compared with PTA-without-PH. However, limited studies have compared the clinical features of PTA patients with and without PH, except for one study found the differences of biomarkers between two groups [10].

In the present study, we investigated the clinical and imaging features, along with the outcomes of PTA patients with and without PH. The objective of this study was to define the imaging characteristics

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and explore the relationship of outcomes with the clinical characteristics of PTA patients with and without PH.

2. Patients and methods

2.1. Patients

The study protocol was approved by the Beijing Chao-Yang Hospital Ethics Committee (2017-K-127) and all participants were aware of and agreed to participate in this study. All suspected PTA patients ($n = 86$) who had one of the respiratory symptoms, chest pain, chest tightness, hemoptysis, dyspnea, cough and fever, between January 2011 and July 2017 were first screened, and underwent computed tomographic pulmonary angiography (CTPA) and echocardiography (ECHO) for all these patients. Finally, 57 patients diagnosed as PTA were included, and 29 patients were excluded. Depending on ECHO, we classified 57 patients into a high probability of PH ($n = 36$) and low probability ($n = 21$) of PH. Following confirmation of PH with right heart catheterization (RHC), patients were then classified into PTA-with-PH group ($n = 33$) and PTA-without-PH group ($n = 24$) based on the RHC results. The flowchart detailing the procedures of subject enrollment and classification were showed in Supplementary Fig. 1. All patients underwent ECHO performed by a senior echo cardiologist to initially evaluate the probability of PH. The ECHO criteria for the high probability of PH included tricuspid regurgitation velocity great than 3.4 m/s with or without a pulmonary artery systolic pressure greater than or equal to 50 mm Hg [11]. The patients with the high probability of PH underwent RHC for confirmation of the PH diagnosis.

Demographic characteristics, laboratory data, clinical imaging, and right heart catheterization (RHC) results, were analyzed in these 57 PTA patients retrospectively. All patients satisfied the modified Ishikawa's diagnostic criteria for TA by Sharma et al. [12], fulfilling one or more major criteria and two or more minor criteria. Examples of the major criteria included a left or right mid-subclavian artery lesion, characteristic signs and symptoms lasting one month or longer. Examples of the minor criteria included a high erythrocyte sedimentation rate (ESR), carotid artery tenderness, hypertension, and aortic regurgitation or annuloaortic ectasia, along with lesions of the pulmonary artery, mid-common carotid artery, distal brachiocephalic trunk, descending thoracic aorta, abdominal aorta, and coronary artery.

2.2. Clinical features and laboratory examination

Demographic and basic clinical data, including age, gender, World Health Organization heart function classification (WHO FC), disease duration, history of certain diseases, symptoms, 6-minute walk distance (6MWD), Borg scores after walk and physical examination, of each participant were collected immediately after hospitalization. The laboratory testing results, which included ESR, C-reactive protein (CRP), immunoglobulin A/G/M, N-terminal prohormone brain natriuretic peptide (NT-proBNP) and arterial oxygen partial pressures (PaO_2) were recorded at first admission.

2.3. Computed tomography pulmonary angiography (CTPA)

CTPA examinations were carried out using a 64 detector CT scanner (LightSpeed VCT, GE, Waukesha, Wisconsin, USA). Eighty mL of contrast medium was intravenously administered at 4.5 mL/s. Scans started with an injection-to-scan delay of approximately 14 s. Scan parameters were 120 kV and 400 mA, using a thin collimation of 64×0.625 mm. Patients underwent CTPA in the supine position while holding their breath, and scanning was performed from 2 cm above the aortic arch to the diaphragm. An effective axial slice thickness of 1.25 mm was required for interpretation. These images were assessed on a GE workstation (AW4.2P and AW4.3P) by two senior radiologists, who assessed the main, lobar, segmental, and sub-segmental arteries. The complete visualization of the main, lobar, and segmental arteries required these arterial branches to be followed to their respective bifurcations.

2.4. Right heart catheterization

RHC was performed in the Department of Interventional Radiology (Beijing Chao-Yang Hospital) using a Philips monitoring system (Shenzhen Goldway Industrial Inc., China). Briefly, a Swan-Ganz catheter was inserted via the jugular vein to assess the pressure in the right chambers and the pulmonary artery, recording mean values for PAP [mPAP], systolic PAP [sPAP], and diastolic PAP [dPAP], and to obtain oximetry samples. The pulmonary artery wedge pressure (PAWP) was determined to exclude post-capillary PH. Cardiac output (CO) was estimated by thermodilution and measured in triplicate to obtain a mean value. Pulmonary vascular resistance (PVR) was calculated as PVR = (mPAP − PAWP) / CO. PTA-with-PH patients were identified as mPAP ≥25 mm Hg and PAWP ≤15 mm Hg [11].

2.5. Statistical analysis

Statistical analyses were performed using the SPSS 13.0 software (SPSS Inc., Chicago, IL, USA). The normally distributed continuous data were presented as the mean ± standard deviation (SD), while the skewed data were expressed as the median or interquartile range (IQR: 25th and 75th percentiles). Categorical data (counts or frequencies) were presented as percentages. Mean levels of variables with a normal distribution were compared using the Student's *t*-test, and those data with a non-normal distribution were compared using the Mann-Whitney *U* test. Categorical variables were analyzed using the Fisher exact test, and survival curves were derived using the Kaplan–Meier method. A *p*-value of <0.05 was considered statistically significant.

3. Results

3.1. Comparison of demographic and basal clinical characteristics of PTA patients with and without PH

A total of 57 PTA patients were included in the study. Among these patients, 24 were in the PTA-without-PH group, and 33 patients were in the PTA-with-PH group. The clinical characteristics of PTA patients with and without pulmonary hypertension were showed in Table 1. From the PTA-with-PH group, 15 patients were WHO FC of I-II and 18 patients were WHO FC of III-IV. The average ages of patients in the PTA-without-PH and PTA-with-PH groups were 41.5 (26.5, 53) and 49 (34.5, 56) years old ($p > 0.05$), respectively. Females accounted for 67% of the patients in the PTA-without-PH group and 79% in the PTA-with-PH group ($p > 0.05$). The PTA-with-PH group had significantly longer disease duration than the PTA-without-PH group [24 (6, 72) vs. 6 (3, 24) months, $p < 0.05$]. Of all the participants, four had a prior history of TA, one had a history of rheumatoid arthritis, nine had a history of hypertension, three had a history of coronary artery diseases, diabetes mellitus and tuberculosis respectively. Compared with the PTA-without-PH group, the PTA-with-PH group had a significantly higher prevalence of chest tightness (79%) and dyspnea (88%), while the prevalence of hemoptysis, cough, and chest pain was similar between the two groups. Fever and fatigue were rare in our patients with a prevalence of only 8.8% and 5.3% in the PTA patients without significant difference between two groups. Compared with the PTA-without-PH group, the occurrence of edema of lower limbs in the PTA-with-PH group was higher (21% vs. 0, $p < 0.05$). In addition, The PTA-with-PH group had significantly shorter 6MWD (314 ± 92 m vs. 436 ± 57 m, $p < 0.05$), higher Borg scores after walk, [2 (1,4) vs. 1 (0,1), $p < 0.05$], higher level of NT-proBNP, [921.3 (209.2, 2400) pg/mL vs. 50.1 (26.1, 147.6) pg/mL, $p < 0.05$], and lower PaO_2 (64.8 ± 14.8 mm Hg vs. 76.9 ± 13.6 mm Hg, $p < 0.05$) in comparison with that of the PTA-without-PH group.

However, there were no differences in ESR and CRP values between these two groups.

The hemodynamic data of 33 patients from PTA-with-PH group and 3 patients from PTA-without-PH group were also listed in Supplementary Table 1.

3.2. Comparison of outcomes of PTA patients with and without PH

Among 57 patients, 43 were followed up after discharge, while 14 patients were lost (9 from the PTA-with-PH group, and 5 from the PTA-without-PH group), with a mean follow-up duration 33.5 ± 20.3 months. Among these 43 patients, 36 had ameliorated symptoms, with 18 patients in the PTA-without-PH group and 18 patients in the PTA-with-PH group. Three patients in the PTA-with-PH group died, with two deaths attributed to chronic right heart failure (average disease duration of eight years), and one patient death resulted from a failed pulmonary thrombectomy in the patient's third year of the disease. RHC showed that the mPAP of these three deceased patients were 47, 78, and 60 mm Hg, respectively, and the WHO FC scores were III. The cumulative survival rate of PTA-with-PH group seemed to be lower than that of PTA-without-PH group, but without a significant difference ($p = 0.109$) (Fig. 1). Among the 4 symptom-exacerbated patients, 3 patients' symptoms in PTA-with-PH group were agitated due to right heart failure, and 1 patient's symptom in PTA-without-PH group was agitated due to the activity of disease. During the follow-up period, the symptom-aggravated and deceased patients displayed higher systolic pulmonary artery pressures, as measured by ECHO, and a higher

Table 1
Clinical characteristics of PTA patients with and without pulmonary hypertension.

	Total ($n = 57$)	PTA with PH ($n = 33$)	PTA without PH ($n = 24$)	p-Value
Clinical characteristics				
Age, years	46 (31.5,55)	49 (34.5,56)	41.5 (26.5,53)	0.093
Female, n (%)	42 (74%)	26 (79%)	16 (67%)	0.368
BMI, kg/m^2	22.1 (19.8, 23.8)	23.0 (19.6,23.8)	22.1 (20.3,24.6)	0.783
WHO FC I-II	–	15	–	
WHO FC III-IV	–	18	–	
Duration from symptom onset to diagnosis, month	22.1 (19.8, 23.8)	24 (6, 72)	6 (3,24)	0.020
Arteritis apart from pulmonary artery	38 (67%)	22 (67%)	16 (67%)	1.000
Comorbidities				
Coronary artery disease, n (%)	3 (5.3%)	3 (9%)	0 (0%)	0.256
Diabetes mellitus, n (%)	3 (5.3%)	3 (9%)	0 (0%)	0.256
Hypertension, n (%)	9 (16%)	7 (21%)	2 (8.3%)	0.277
Tuberculosis, n (%)	3 (5.3%)	1 (3%)	2 (8.3%)	0.173
Rheumatoid arthritis, n (%)	1 (1.8%)	0 (0%)	1 (4.2%)	0.421
Takaysu's arteritis	4 (7%)	0 (0%)	4 (17%)	0.029
Symptoms				
Chest tightness	37 (65%)	26 (79%)	11 (48%)	0.013
Dyspnea	39 (68%)	29 (88%)	10 (44%)	0.000
Hemoptysis	25 (44%)	14 (42%)	11 (48%)	1.000
Chest pain	19 (33%)	8 (24%)	11 (48%)	0.099
Cough	24 (42%)	12 (36%)	12 (52%)	0.224
Syncope	2 (3.5%)	1 (3%)	1 (4%)	1.000
Fever	5 (8.8%)	3 (9%)	2 (8%)	0.640
Fatigue	3 (5.3%)	1 (3%)	2 (8%)	1.000
Body examination				
Asymmetric artery pressure	15 (26%)	11 (33%)	4 (17%)	0.226
Bruits of other arteries	25 (44%)	18 (55%)	7 (29%)	0.059
Bruits of pulmonary	30 (53%)	18 (55%)	12 (50%)	0.788
Edema of lower limbs	7 (12%)	7 (21%)	0 (0%)	0.016
6MWD, m	365 ± 99	314 ± 92	436 ± 57	0.000
Borg score	1 (0.5,3)	2 (1,4)	1 (0,1)	0.000
ECHO				
RAD, mm	40.7 ± 11.8	46.4 ± 11.3	32.9 ± 7.0	0.000
RVD, mm	37.6 ± 9.8	42.6 ± 8.3	30.7 ± 7.3	0.000
LAD, mm	32.4 ± 5.7	32.0 ± 6.7	32.8 ± 3.9	0.627
LVEDD, mm	42.2 ± 6.8	39.3 ± 7.0	46.1 ± 4.0	0.000
sPAP, mm Hg	–	90 ± 27	–	
Blood test				
Increased ESR (>value)	23 (40%)	11 (33%)	12 (50%)	0.276
Increased CRP (>value)	27 (47%)	14 (42%)	13 (54%)	0.429
NT-proBNP	307 (72.5, 1812)	921.3 (209.2, 2400)	50.1 (26.1, 147.6)	0.000
PaO_2, mm Hg	69.8 ± 15.4	64.8 ± 14.8	76.9 ± 13.6	0.006

PTA: Takayasu's arteritis with pulmonary artery involvement, PH: pulmonary hypertension, BMI: Body Mass Index, WHO FC: World Health Organization heart function classification, PaO_2: Arterial oxygen partial pressure, 6MWD: 6-minute walk distance, RAD: Right Atrial Diameter, RVD: Right Ventricular Diameter, LAD: Left Atrial Diameter, LVEDD: left Ventricular End Diastolic Diameter, sPAP: Pulmonary Arterial Systolic Pressure, ESR: erythrocyte sedimentation rate, CRP: C reactive protein, NT-proBNP: N-terminal prohormone brain natriuretic peptide, WHO FC: World Health Organization heart function classification, PA: pulmonary artery.

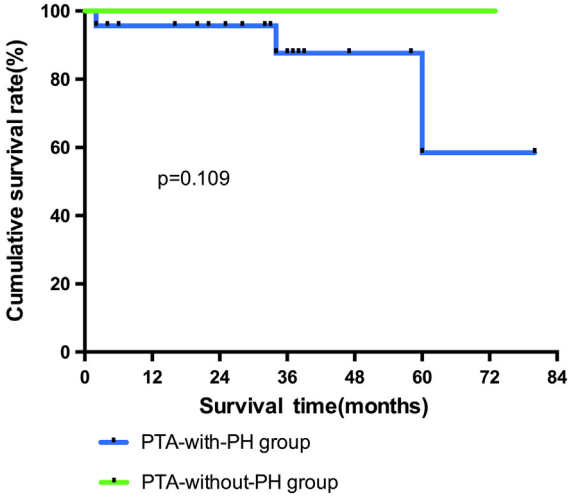

Fig. 1. Kaplan–Meier estimation of survival in PTA patients with or without PH. Kaplan–Meier cumulative survival curves showing cumulative rates of survival for 43 PTA patients, stratified by with or without PH. The survival rate in PTA-with-PH group tended to be lower than that in PTA-without-PH group. $p = 0.109$.

level of NT-proBNP than the baseline (Supplementary Table 3). In addition, 17 patients in the PTA-without-PH group and 9 patients in the PTA-with-PH group were treated with glucocorticoids and immunosuppressant. Also, 23 and 25 patients accepted aspirin and warfarin, respectively. In the PTA-with-PH group, 29 patients were treated with diuretics, and 15 patients had accepted treatment for PH.

3.3. Comparison of findings from CTPA between PTA patients with and without PH

All 57 patients underwent CTPA, which revealed a total of five different arterial lesions in our patients: stenosis, occlusion, thickening of the vascular wall, in situ thrombosis and aneurysm (Table 2, Fig. 2). Surprisingly, all aneurysms were found in patients of the PTA-with-PH group (42% of patients), and compared with PTA-without-PH patients, the PTA-with-PH group had higher incidence of occlusions in both sides of the pulmonary artery (36% vs. 4%, $p < 0.05$) and tended to have a lower incidence of vascular walls thickening in the right lobar pulmonary artery (12% vs. 42%, $p = 0.073$) (Supplementary Table 2). Among the three deceased and four symptom-aggravated patients, four had aneurysms, and one had in situ thrombosis (Supplementary Table 3). The incidence of predominant lesion involvement in the right main

Table 2
Comparison of five vessel lesions between PTA patients with and without pulmonary hypertension.

PA lesions types	PTA with PH ($n = 33$)	PTA without PH ($n = 24$)	p-Value
In situ thrombosis, n (%)	9 (27%)	6 (25%)	1.000
Occlusion, n (%)	31 (94%)	18 (75%)	0.059
Stenosis, n (%)	22 (67%)	14 (58%)	0.585
Aneurysm, n (%)	14 (42%)	0 (0%)	0.000
Vascular walls thickening, n (%)	10 (30%)	12 (50%)	0.172

PTA: Takayasu's arteritis with pulmonary artery involvement, PH: pulmonary hypertension, PA: pulmonary artery.

pulmonary artery and right lobar pulmonary arteries was common in all PTA patients, and rat-tail stenosis and occlusions of the right main pulmonary arteries were detected in 19 patients (33%). Also, 67% of patients in both groups showed involvement of other arteries, apart from pulmonary arteries, among which the subclavian, carotid, and aorta arteries were the most commonly involved with a prevalence of 36% vs. 33%, 30% vs. 13%, and 24% vs. 33% in the PTA-with-PH and PTA-without-PH group, respectively.

4. Discussion

PTA is considered to be a rare disease, which is usually reported as clinical cases [13–15]. A proportion of PTA patients may develop PH; however, whether there were any differences in the clinical manifestations and outcomes of PTA patients with and without PH has not been well explored. To the best of our knowledge, this study is the first to compare the clinical and imaging features, as well as the outcomes, between PTA patients with and without PH in a relatively large sample size, given that PTA is not a prevalent type of TA. There were several major findings from this study. Firstly, PTA-with-PH patients had a longer disease duration from the disease onset to the diagnosis, shorter 6MWD, higher Borg scores after walk, lower PaO_2 and higher level of serum NT-proBNP than that of PTA-without-PH patients. Secondly, aneurysm formation was closely related to PH and was a valuable predictor of worse prognosis, including symptom deterioration and death in PH patients, and also PTA-with-PH patients had higher incidence of occlusions in both sides of the pulmonary artery. Finally, PTA-with-PH patients tended to be deceased during follow-up time, and to have symptom exacerbation due to the right heat failure, but without significant difference.

The 1990 ACR diagnostic criteria for TA were commonly used in previous studies [16]; however, these criteria emphasize aortic involvement more than other arteries, which limits its clinical applicability. In the present study, we used the modified Ishikawa's diagnostic criteria created by Sharma et al. for diagnosing TA [12], because the modified criteria included pulmonary artery lesions as one of the diagnostic criteria. Although the gold standard of PTA remains the pathological diagnosis, due to the difficulty in obtaining pulmonary artery tissues, only one of our patients achieved the pathological diagnosis. In the present study, the diagnoses of all PTA-with-PH patients were confirmed by RHC to have met the standard PH criteria, including the mPAP ≥25 mm Hg and PAWP ≤15 mm Hg, as recommended by the guidelines for PH diagnosis [11].

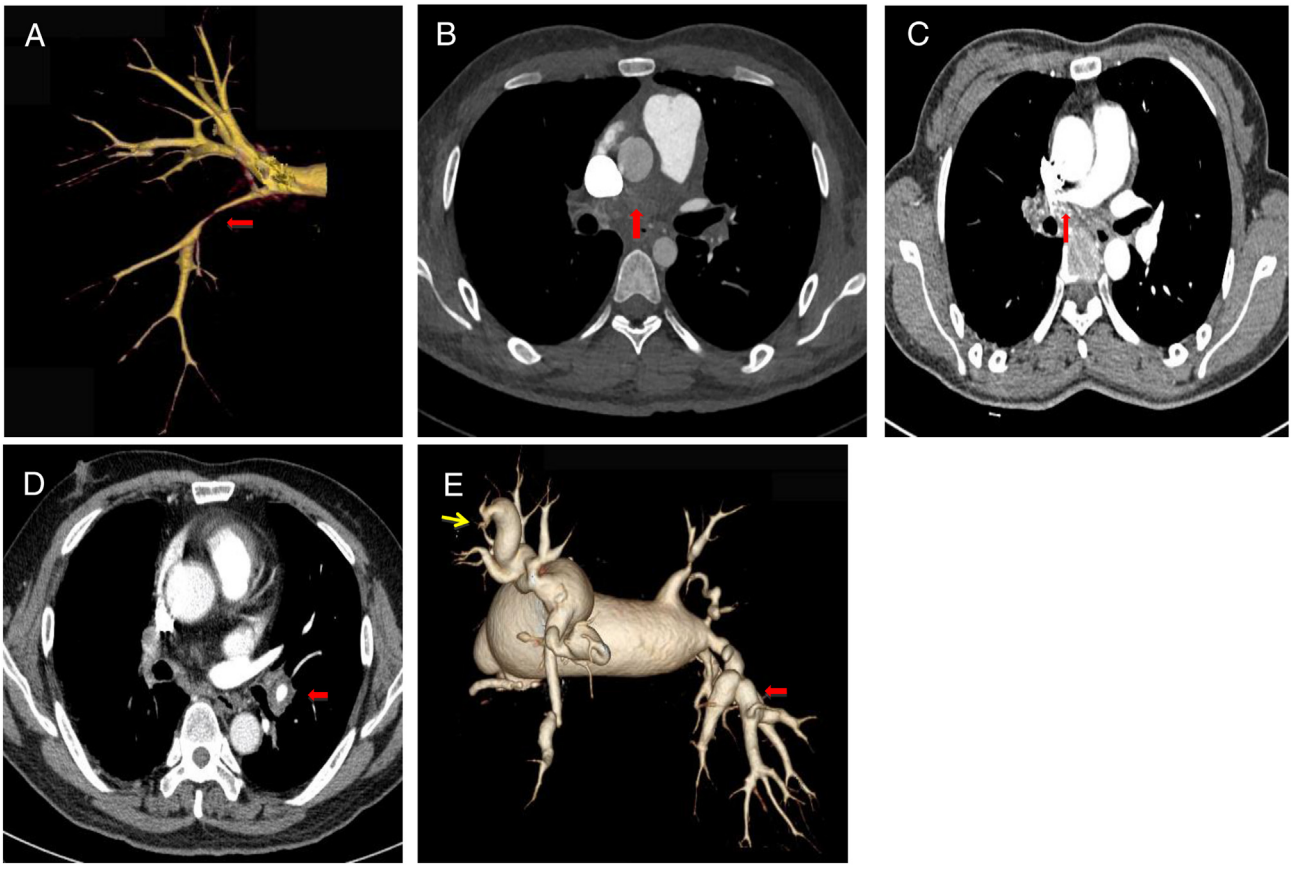

Fig. 2. Representative images showing PTA and related vessel lesions in patients. (A) Rat-tail stenosis of the right lower lobar pulmonary artery (red arrow) (volume rendering reconstruction) in a 48-year-old male PTA patient without PH. (B) In situ thrombus was formed in the dilated right main pulmonary artery and extended to the pulmonary artery trunk (red arrow) in a 22-year-old male PTA patient with PH. (C) Rat-tail occlusion of the right main pulmonary artery, which is a typical PTA imaging feature (red arrow) in a 40-year-old female PTA patient without PH. (D) Ring-shaped vascular wall thickening in left lower lobar pulmonary artery (red arrow) in a 48-year-old male PTA patient with PH. (E) Aneurysm was formed on the left upper lobar pulmonary artery (yellow arrow), and stenosis occurred on the right lower lobar pulmonary artery (red arrow), in a 62-year-old female PTA patient with PH (volume rendering reconstruction).

Currently, there are no data regarding mortality rates in PTA-with-PH patients, although several studies explored the mortality rates for total TA and PTA patients. For example, one study showed that the 15-year survival was 66.3% and 96.4% for TA patients with and without a major complication, respectively [17]. Also, they showed that systemic hypertension, while a major complication, was an independent predictor of a poor prognosis. Another study, in which the patients were followed up for a mean duration of 5.0 ± 0.2 years, revealed a 5.7% mortality rate for TA patients, with systemic hypertension being a significant prognostic marker, and PTA patients had a higher mortality of 23% than total TA patients during a 4.5 years follow-up period [6]. In the present study, we investigated the mortality rate of PTA patients within a mean follow-up period of 33.5 ± 20.3 months and found that the mortality rate was 9% for PTA-with-PH patients and 0% for PTA-without-PH patients, indicating that the presence of PH is a major predictor of mortality in PTA patients. We also found that PH progression and right heart failure were the main causes of the death in PTA patients. Thus, our study provides a strong rationale for aggressively monitoring and targeting PH in PTA patients. Additionally, there was a longer time delay from symptom onset to diagnosis for PTA-with-PH patients, suggesting that PTA-with-PH patients were likely to experience longer disease durations or higher rates of misdiagnoses, which may contribute to the unnoticed development and progression of PH in PTA patients.

Angiographic assessment, which can determine the structural changes in blood vessels, including occlusion or stenosis of the aorta and pulmonary artery [18], is essential to make an accurate diagnosis of TA. Previous studies found that stenosis, occlusion, thickening of vascular walls, and vascular dilation were the primary vascular lesions in large vessel vasculitis, including PTA [19,20]; however, the correlation between the outcomes and these imaging features of PTA patients was not explored. In the present study, we found that the above mentioned four vascular lesions and in situ thrombosis were observed in PTA patients. Surprisingly, aneurysms were only observed in PTA-with-PH patients, including two with symptom deterioration and two decreased, suggesting that aneurysms may represent the later stage of PTA and that the high pressure caused by PH may be a contributor to aneurysm formation. This is supported by previous reports showing that dilatation/aneurysms were evident after three years of TA disease onset [21]. Additionally, a close correlation has been found between aneurysm formation and systemic hypertension [22]. Also, in the present study, we found that PTA-with-PH patients had more occlusions on both sides of pulmonary arteries (36% vs. 4%, $p < 0.05$), and tended to have less thickening of vascular walls on right pulmonary arteries (12% vs. 42%, $p = 0.073$), suggesting that occlusions were related with disease severity and that vascular wall thickening may reflect an early stage of the disease. Given that a close correlation exists between circumferential wall thickening of arteries and disease activity [23–25], and that the imaging features reflected stages of disease progression, it is, therefore, imperative to appraise the disease using CTPA. The above clinical features will not only help to discriminate PTA from other pulmonary vascular diseases, such as CTEPH which also has vascular stenosis and occlusion [26–28], but it will also help to predict the occurrences and outcomes in PTA patients with PH.

PTA with in situ thrombosis can be easily misdiagnosed as pulmonary thromboembolism (PTE) [29], which also has non-specific symptoms and is associated with a high mortality rate [30]. Despite the low prevalence of in situ thrombosis formation in PTA patients, it is important to distinguish it from PTE as these two diseases require different treatments. For instance, some PTE patients may be suitable for pulmonary thrombectomy, while PTA patients may not be suitable candidates for surgical intervention. This was supported by the failed surgery of the 22-year-old male in our study, who was misdiagnosed as PTE. Cases of in situ thrombosis in PTA patients were rare, and some case studies only reported on TA-related abdominal aortic thrombosis [31,32]. Our study revealed one major difference in the in situ thrombosis between PTA and PTE, which was that most cases of in situ thrombosis in TA patients formed on the proximal pulmonary artery, especially on the right main artery, while thrombosis in PTE patients was normally in different segmental arteries [33].

In the present study, the occurrence rate of small-volume hemoptysis was 44% in both groups. The exact mechanisms of PTA-induced hemoptysis are not completely clear. One study suggested that PTA-linked hemoptysis was due to the rupture of collateral vessels or micro-aneurysms [34]. We believe that pulmonary infarction was also one of the causes underlying PTA-triggered hemoptysis. These proposed mechanisms were different from hemoptysis caused by PH, which was associated with bronchial artery hypertrophy [35]. Our findings suggest that hemoptysis is a relatively common symptom in PTA patients. Thus, it may be helpful to screen PTA in young females with idiopathic hemoptysis.

The primary limitation of this study is that it was done retrospectively, with only 43 patients being followed up after being discharged from the hospital, although, the patient loss rates were similar between the two groups. Another limitation was that this study was performed in a pulmonary vascular center, and we only included suspected PTA patients with one of the respiratory symptoms in the present study. Therefore, it was possible that part of PTA who was less of pulmonary symptoms might be undetected [36]. In addition, the present study had relatively short follow-up period, which did not allow us to evaluate the long-term survival rates of PTA patients with and without PH. Also, the disease was inactive in 54% of our patients, so we were unable to obtain the clinical characteristics and imaging features from the initial disease stages. In addition, this study was performed at a single center. Therefore, future prospective studies should be performed with multi-center support to further corroborate these findings.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2018.08.047.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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