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Changes in main pulmonary artery diameter during follow-up have prognostic implications in pulmonary arterial hypertension

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Abstract

Background and objective—A dilated pulmonary artery (PA) is a common finding in patients with pulmonary arterial hypertension (PAH). Little is known on the variations in PA size over time and whether these changes track with disease severity and/or predict long-term survival.

Methods—We included patients with PAH who had at least two computed tomography (CT) scans of the chest done on different visits. Both scans matched the use of i.v. contrast.

Results—Pairs of CT scans were compared in 113 PAH patients. During a median (interquartile range (IQR)) time difference between scans of 8 (IQR: 3.5–20.0) months, we noted an increase in main PA diameter of 0.5 ± 1.8 mm (mean $\pm$ SD) ($P = 0.008$). When CT scans were performed >12 months apart ($n = 47$), the main PA diameter increased or decreased by >1 mm in 40% and 13% of the patients, respectively. An increase in main PA diameter was associated with lower PA compliance, higher right ventricular (RV) systolic pressure, worse RV function and a decline in 6-min walk distance. During a median (IQR) follow-up of 33 (IQR: 4.5–47) months, 53 (46.9%) patients died. The change in PA diameter was a significant predictor of mortality (hazard ratio (HR) per mm increase: 1.33 (95% CI: 1.11–1.61), $P = 0.002$) when adjusted for difference in time and slice thickness between CT scans, age, gender, PAH aetiology and pulmonary vascular resistance.

Conclusion—In PAH patients, an increase in CT-derived main PA diameter over time is associated with progression in pulmonary pressures, RV dysfunction, a decline in functional capacity and higher mortality.

Keywords

outcomes; pulmonary arterial hypertension; pulmonary artery diameter; survival

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a group of conditions characterized by an increased pulmonary vascular resistance (PVR) that may lead to right heart failure and death.¹ This increased PVR with resulting higher pulmonary artery (PA) pressures and wall tension causes central PA dilation.² A dilated PA may be seen on plain radiography or echocardiography; however, a computed tomography (CT) scan or MRI of the chest allows for a more accurate measurement.^{2,3}

The finding of an enlarged main PA can facilitate the recognition of pulmonary hypertension²; furthermore, a dilated PA can compress the left main coronary artery, left recurrent laryngeal nerve and tracheobronchial tree,⁴ or predispose to PA dissection and rupture.⁵ Abundant information exists on the prevalence and degree of PA dilation in patients with PAH^{2,3}; however, little is known on the degree and direction of main PA diameter changes over time and particularly its prognostic implications in patients with PAH. We hypothesized that patients with PAH⁶ have PA dilation that worsens with time and is associated with worse prognosis. To test our hypotheses, we studied patients with PAH who had at least two CT scans of the chest for a variety of reasons. We investigated changes in main PA diameter over time, factors associated with PA dilation and effect on survival.

METHODS

This retrospective study was approved by the Cleveland Clinic Institutional Review Board (study number 10-1127). Written informed consent was waived. Patients needed to have at least two CT scans of the chest done at our institution on different visits and both under the same condition regarding i.v. contrast administration, that is both scans had to be acquired either with or without the use of IV contrast. Hence, only non-contrast to non-contrast and contrast to contrast CT scans were compared. CT scans were performed from February 2007 to December 2013 and were ordered for worsening dyspnoea, persistent cough, concern for pulmonary embolism, interstitial lung disease, emphysema and further evaluation of parenchymal opacities, nodules or enlarged mediastinal lymph nodes on chest radiography.

Patient selection

We included patients with PAH, defined by a mean PA pressure ≥ 25 mm Hg, PA wedge pressure ≥ 15 mm Hg and PVR > 3 Wood units during right heart catheterization.⁷ We excluded patients with conditions other than PAH (group 1 of the classification updated by the Fifth World Symposium on Pulmonary Hypertension⁶), acute or chronic thromboembolic pulmonary disease and subjects who received lung and/or heart transplantation either before the first or second CT scan of the chest. Of the 795 patients with PAH in the Cleveland Clinic Pulmonary Hypertension Registry, 129 had at least two CT scans of the chest available for review and 113 (88%) had matched scans regarding i.v. contrast administration, that is both studies done either with or without i.v. contrast; patients with one CT performed with and another without contrast were excluded. We recorded data on demographics and results of 6-min walk test (6MWT), echocardiogram and right heart catheterization done closer to the CT scan of the chest. We selected the study performed the closest to the diagnostic right heart catheterization as the initial CT scan.

Studies around the time of CT scanning

In all patients, we reviewed the echocardiograms and 6MWTs performed at the time of the first and second CT scans of the chest. Echocardiographic measurements were available for 108 and 107 patients, meanwhile 6-min walk determinations were available for 92 and 91 patients, at the time of the first and second CT scans, respectively. Transthoracic echocardiography was performed by well-trained sonographers and interpreted by experienced cardiologists following current guidelines.⁸ Right ventricular (RV) systolic pressure (RVSP) was estimated by the simplified Bernoulli equation and RV function was assessed by combining visual estimation and tricuspid annular plane systolic excursion (TAPSE).^{8,9} The 6MWT was performed based on American Thoracic Society (ATS) standards.¹⁰ Right heart catheterization was obtained following customary protocols and measuring pulmonary vascular pressures at end expiration. Pulmonary compliance was calculated as the ratio between stroke volume and PA pulse pressure (difference between systolic and diastolic pressures).

Technical aspects

Two experienced radiologists (S.J. and R.Y.), blinded to clinical information, reviewed all the CT scans and performed measurements of the PA size. Scans were obtained with patients in supine position with breath-holding at full inspiration. For each study, we documented the type of scanner and protocol employed (i.e. slice thickness), the use of i.v. contrast and quality of the study. We were very careful in assuring that measurements were comparable in the pair of CT scans. Methodology for measuring the PA was previously described.² Briefly, we measured the main PA diameter along a line that originated at the centre of the adjacent aorta (Ao) and run perpendicular to the long axis of the PA, as this method has shown to be reproducible (intra- and interobserver variability bias of 0.17 and 0.28 mm, respectively) and has a good correlation with mean PA pressure ($R = 0.51$).¹¹ We measured the vascular lumen in contrasted scans and the vascular lumen plus the vessel wall in non-contrasted studies. For non-contrasted studies, our intra- and interobserver variability bias in measuring main PA diameter were 0.3 (95% CI: -0.98 to 0.38) mm and 0.4 (95% CI: -0.51 to 1.3) mm, respectively. Meanwhile, for contrasted studies, the intra- and interobserver variability bias were -1.2 (95% CI: -2.01 to 0.39) mm and 0.3 (95% CI: -1.56 to 0.96) mm, respectively.

Right and left main PA diameters were measured at the widest point in the axial plane proximal to the first branching, in a location where the vessel walls appeared as parallel as possible.¹¹ At radiology workstations, we determined the cross-sectional area of the main PA after multiplanar reformatting and manipulation, to obtain a view orthogonal to the long axis of the vessel, ideally at the same level where main PA diameter was measured. We circumscribed the outer wall of the vessel and the software calculated the cross-sectional area.

Statistical analysis

We summarized continuous variables using mean $\pm$ SD or median and interquartile range (IQR) when appropriate. Categorical variables are presented as n (%). We compared numerical variables using t-test and categorical variables with chi-square test. Groups of numerical variables in which normal distribution could not assumed were tested with Mann–

Whitney Wilcoxon test. Matched pairs of continuous values were tested with paired sample t-test. We used the McNemar–Bowker test for the comparison of RV function at the time of first and second CT scans. Association between continuous variables was tested with the Pearson correlation test. Linear regression was used to test variables that could predict the change in PA diameter or area. Survival analysis was performed using Cox proportional hazards modelling adjusted for prespecified variables. The starting point for the analysis was the date of the second CT scan. Patients were followed until death or end of the study in July 2016. Patients were censored at the time of lung transplantation. Results of Cox analyses are expressed as hazard ratios (HRs) with the corresponding 95% CIs. We performed complete case analysis for those with missing echocardiographic or 6-min walk measurements. A *P*-value of <0.05 was considered as indicative of statistical significance. Statistical analyses were performed using the statistical package SPSS version 17 (SPSS Inc., Chicago, USA.) and MedCalc version 14.12.0 (*MedCalc Software bvba*, Ostend, Belgium).

RESULTS

Patient's characteristics

We included a total of 113 patients with PAH with a mean $\pm$ SD age at the time of the first CT scan of 54 ± 13 years and 81 (72%) of female gender. Race was white in 87 (77%), African/American in 25 (22%) and Asian in 1 (1%). The aetiology of PAH was idiopathic, heritable, associated with anorexigens/toxins, connective tissue disease, congenital heart disease or portal hypertension in 34 (30%), 5 (4%), 2 (2%), 50 (44%), 12 (11%) and 10 (9%), respectively.

The diagnostic right heart catheterization was performed a median (IQR) of 0 (IQR: -7.5 to $+3$) months from the initial CT scan. This right heart catheterization showed right atrial, mean PA and PA wedge pressures of 9.8 ± 6.5 , 46.9 ± 13.5 and 12.9 ± 6.6 mm Hg, respectively. Pulse pressure was 41.6 ± 14.2 mm Hg. Cardiac index by thermodilution was 2.8 ± 0.6 L/min/m², PVR of 7.2 ± 4.3 Wood units and PA compliance of 1.96 ± 1.36 mL/mm Hg. During the time between the two CT scans of the chest, patients received PAH-specific treatment with parenteral prostacyclin analogues ($n = 36$, 32%), inhaled prostacyclin analogues ($n = 13$, 12%), endothelin receptor antagonists ($n = 42$, 37%) and/or phosphodiesterase-5 inhibitors ($n = 79$, 70%).

CT scans of the chest

The i.v. contrast was used for the pair of CT scans in 81 patients while in the rest ($n = 32$, 28%) both scans were performed without contrast. Study quality was rated as limited in only two (2%) patients on both CT scans. Vascular measurements in the first and second CT scans are shown in Table 1. The median (IQR) time between the CT scans of the chest was 8 (IQR: 3.5–20.0) months, during which time the main PA diameter increased by 0.46 ± 1.82 mm ($P = 0.008$).

When the second CT scan was done >12 months apart ($n = 47$, median (IQR) difference of 24 (16–33) months), the main PA diameter increased or decreased by >1 mm in 40% and 13% of the patients, respectively (Table 2, *n*Fig. 1). Individuals with a main PA diameter

reduction of 1 mm (= 6) also had a significant reduction in PA area (median (IQR): -186 (-259 to -176) mm² vs +96 (+24 to +195) mm², $P < 0.001$) and PA/Ao ratio (median (IQR): -0.11 (-0.27 to -0.11) vs 0.03 (-0.02 to +0.11), $P = 0.003$).

Time of the first and second chest CT scans

Echocardiograms were obtained close to the time of first and second CT scans of the chest at a median (IQR) of 0 (-13 to +3) and 0 (-14 to +4) days. In these echocardiograms, the RVSP was 74 ± 26 and 70 ± 28 mm Hg ($P = 0.12$), RV basal diameter was 4.7 ± 0.9 and 4.9 ± 1.1 cm ($P = 0.11$), TAPSE was 1.6 ± 0.7 and 1.6 ± 0.6 cm ($P = 0.64$) and RV function ($n = 107$) was normal in 36 (32%) and 31 (27%) ($P = 0.67$) patients, respectively. The median (IQR) time between 6MWTs and the first and second CT scans of the chest was 0 (IQR: -19 to 6) and 0 (IQR: -32 to +6) days, respectively. The distance walked in 6 min was 315 ± 101 and 304 ± 105 m ($P = 0.62$), respectively.

Factors influencing the degree of PA dilation

Time between CT scans was directly associated with the increase in PA diameter (β : 0.04, SE: 0.014, $P = 0.004$) or area (β : 2.42, SE: 0.89, $P = 0.008$). Difference in slice thickness between scans (mean difference: 0.17 ± 1.3 mm) was not associated with change in PA diameter. When adjusted by time between scans and difference in slice thickness, the variables associated with a more pronounced main PA diameter included a higher PA pulse pressure and lower compliance during right heart catheterization, higher RVSP and worse RV function on the echocardiograms performed close to the first and second CT scans. A decline in 6MWT distance was also associated with PA dilation during follow-up. In addition, patients with portopulmonary hypertension had a significant reduction in PA diameter compared with idiopathic PAH individuals (Table 3). In fact, of the 10 patients with portopulmonary hypertension, 5 had a reduction in PA diameter 1 mm, while 2 experienced no change and 3 had an increase of 1 mm.

Number of PAH-specific therapies or use of parenteral prostacyclin analogues, oral endothelin receptor antagonist or phosphodiesterase-5 inhibitors did not significantly impact the degree of change in main PA diameter over time.

Survival analysis using PA measurements

The median (IQR) follow-up was 33 (IQR: 4.5–47) months during which 53 (46.9%) patients died and 6 were censored at the time of lung transplant. Survival at 1 and 2 years was 64.9% and 61.1%, respectively. Both main PA diameter at baseline (HR per 1 mm increase: 1.07 (95% CI: 1.02–1.12), $P = 0.005$) and during follow-up (HR per 1 mm increase: 1.08 (95% CI: 1.03–1.13), $P < 0.001$) were significant predictors of mortality, when adjusted by difference in time and slice thickness between CT scans, age, gender and PVR. Importantly, the change in main PA diameter was also a significant predictor of mortality (HR per 1 mm increase: 1.28 (95% CI: 1.06–1.55), $P = 0.009$) when adjusting for the same factors (Fig. 2) or when adding the diameter of the main PA at baseline (HR per 1 mm increase: 1.27 (95% CI: 1.05–1.53), $P = 0.01$), aetiology of PAH (HR per 1 mm increase: 1.33 (95% CI: 1.11–1.61), $P = 0.002$) or time from the diagnostic right heart

catheterization and initial CT scan of the chest (HR per 1 mm increase: 1.28 (95% CI: 1.06–1.54), $P=0.01$).

Change in PA area (HR per 1 mm² increase: 1.003 (95% CI: 1.00–1.01), $P=0.035$) significantly impacted survival; however, the change in other determinations such as main PA/Ao diameter ratio (HR per 0.1 mm increase: 4.01 (95% CI: 0.15–107.9), $P=0.41$), right PA diameter (HR per 1 mm increase: 1.1 (95% CI: 0.94–1.27), $P=0.28$) and left PA diameter (HR per 1 mm increase: 1.12 (95% CI: 0.98–1.28), $P=0.10$) were not significant predictors of survival when adjusted by difference in time and slice thickness between CT scans, age, gender, PVR and PAH aetiology.

DISCUSSION

This is the first study to assess changes in PA diameter over time in PAH patients. We found that the main PA diameter increased by at least 1 mm in 40% of the PAH patients after 12-month follow-up. Meanwhile, in a smaller proportion of individuals (13%), the diameter decreased. We found that a higher PA pressures, lower PA compliance, worse RV function and functional capacity were predictors of main PA dilation. Importantly, an increase in main PA diameter predicted a worse survival.

The pulmonary vascular remodelling and dilation of the PA in patients with PAH likely depends on a combination of genetic predisposition, intrinsic characteristics of the vessel and an adaptive response to elevated PA pressures.^{2,12} Boerrigter *et al.* using cardiac MRI in patients with PAH noted a progressive increase in PA diameter over time.¹³ In our cohort, during both CT scans of the chest, all but six (5%) patients had an enlarged main PA diameter based on the 90th percentile upper limit of normal described in the Framingham Heart study (males: 28.9 mm and females: 26.9 mm).¹⁴

We observed that a small number of patients had a decrease in main PA diameter during follow-up (Fig. 3). In fact, six individuals had a reduction of 1 mm and five (11%) of 3 mm when the CT scans were performed at least 12 months apart. This finding appears reliable as it tracked the PA/Ao diameter ratio and the main PA area by multiplanar reformatting. Aetiologies of PAH in the six subjects with a reduction in PA diameter of 1 mm were connective tissue disease ($n=3$), idiopathic ($n=1$) and portal hypertension ($n=2$). Boerrigter *et al.*¹³ described a decrease in PA diameter >2 mm in 3 out of 51 (6%) patients with PAH, during a mean follow-up of 942 days. In these three patients, investigators noted an almost normalization of the mean PA pressure. The reasons for the interval decrease in the PA diameter over time are unclear; however, it appears that reverse remodelling due to improvement in pulmonary haemodynamics and decrease in intravascular volume play an important role.¹⁵ Changes in intravascular volume may be particularly relevant in patients with portopulmonary hypertension who more commonly had a reduction in main PA diameter during follow-up than subjects with idiopathic PAH.

During the first year, the change in main PA diameter remained within 1 mm in most subjects, but after 12 months the PA diameter increased >1 mm in 40% of the subjects; tracking with a lower PA compliance, higher RVSP, worse RV function and functional class;

all parameters that reflect a more severe disease. Boerrigter *et al.*¹³ found a direct association between PA dilation and time between imaging studies but no correlation with baseline haemodynamics. In addition, this group of investigators did not observe an association between changes in main PA diameter and variations in mean PA pressure or cardiac output.¹³ Similarly, in our study, although we noted a direct association between changes in main PA diameter and the estimated RVSP at the time of first and second CT scans, we did not observe a significant association with the degree of change in RVSP between echocardiograms. Interestingly, an improvement in TAPSE significantly tracked with a reduction in main PA diameter.

Importantly, we noted that for every 1-mm expansion in main PA diameter, there is a 28% increase in mortality. As far as we know, an increase in main PA diameter in serial assessments has not been previously linked to mortality in PAH patients. Zylkowska *et al.* noted that PA diameter at initial evaluation was an independent risk factor of death unexplained by RV failure or comorbidities (HR per 1 mm increase: 1.06, 95% CI: 1.03–1.08) in a cohort of patients with PAH and inoperable chronic thromboembolic pulmonary hypertension.¹⁶

Our study has several limitations: (i) reasons for the CT scans varied and the results may not be applicable to asymptomatic patients, (ii) CT scans were not done at the same intervals; however, we adjusted our analyses for time between them, (iii) in about one-fourth of the patients, both scans were performed without i.v. contrast, (iv) plasma brain natriuretic peptide was only available in a limited number of patients close to the time of the CT scans and (v) direct haemodynamic determinations were not available at the time of the second CT scan of the chest. In spite of these limitations, our study is the first to assess changes in PA size during follow-up in PAH patients, identify factors associated with PA dilation and conclude that an increase in the main PA diameter entails worse survival. Results of this study encourage further investigations of modalities that permit serial determinations of main PA diameter which may become a tool to measure the long-term vascular effects of PAH and provide valuable prognostic information.

In conclusion, the main PA diameter and area tend to increase over time in PAH patients; however, in a small percentage of individuals the opposite occurs. Higher PA pulse pressure, lower PA compliance, worse RV function and functional capacity track with main PA dilation. An increase in PA diameter over time is associated with worse survival.

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Abbreviations

6MWT	6-min walk test
Ao	aorta
ATS	American Thoracic Society

BMI	body mass index
CT	computed tomography
HR	hazard ratio
i.v	intravenous
IPAH	idiopathic PAH
IQR	interquartile range
MRI	magnetic resonance imaging
PA	pulmonary artery
PAH	pulmonary arterial hypertension
PH	pulmonary hypertension
PoPH	portopulmonary hypertension
PVR	pulmonary vascular resistance
RHC	right heart catheterization
RV	right ventricular
RVSP	right ventricular systolic pressure
TAPSE	tricuspid annular plane systolic excursion

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SUMMARY AT A GLANCE

It remains unclear whether the increase in main pulmonary artery (PA) diameter over time has prognostic implications in patients with pulmonary arterial hypertension. In the present study, we found that an increase in main PA diameter was associated with higher PA pressures, lower PA compliance, worse right ventricular function and reduced survival.

Figure 1. Histogram of the change in pulmonary artery (PA) diameter. Intervals between computed tomography (CT) scans of the chest: <6 months (A), 6–11.9 months (B) and 12 months (C). Number of patients is shown on the y axis, while the difference in main PA diameter between scans is depicted in the x axis.

Figure 2.

Cox survival analysis plotting the adjusted change in main pulmonary artery (PA) diameter. The y axis shows the cumulative survival and the x axis the follow-up time in months from the second computed tomography (CT) scan of the chest to death, lung transplantation or end of the study. Patients were censored at the time of lung transplantation or end of the study. The three curves represent a change in main PA diameter between scans of: <1 mm and increase or decrease >1 mm (—, reduction; ···, no change; ---, increase). Patients who experienced an increase in main PA diameter of >1 mm had a significant increase in mortality (hazard ratio (HR): 2.11 (95% confidence interval (CI): 1.09–4.07), $P = 0.026$), when adjusted by age, gender, pulmonary arterial hypertension (PAH) aetiology, time between the CT scans, differences in slice cuts and pulmonary vascular resistance (PVR).

Figure 3.

Main pulmonary artery (PA) diameter measurement during first and second computed tomography (CT) scans of the chest. Panels (A) and (B) correspond to a pulmonary arterial hypertension (PAH) patient in whom the main PA diameter decreased by 3.5 mm, while panels (C) and (D) showed the axial CT cuts of another PAH patients in whom the main PA diameter increased by 4 mm during follow-up.

Table 1

Vascular measurements in the first and second CT scans of the chest

Variables	First CT scan Mean $\pm$ SD	Second CT scan Mean $\pm$ SD	Difference between CT scans Mean $\pm$ SD	P (paired Student's t-test)
Main PA diameter (mm)	35.2 $\pm$ 6.1	35.8 $\pm$ 6.4	0.46 $\pm$ 1.82	0.008
Main PA area (mm ²)	1151 $\pm$ 413	1178 $\pm$ 408	27 $\pm$ 137	0.04
Right PA diameter (mm)	25.8 $\pm$ 4.9	26.4 $\pm$ 5.0	0.53 $\pm$ 2.00	0.006
Left PA diameter (mm)	24.9 $\pm$ 4.5	25.2 $\pm$ 4.6	0.32 $\pm$ 2.11	0.11
Right + left PA diameters (mm)	50.7 $\pm$ 8.6	51.5 $\pm$ 9.0	0.85 $\pm$ 3.13	0.005
Ao diameter	30.5 $\pm$ 5.0	30.7 $\pm$ 5.1	0.19 $\pm$ 2.03	0.31
Main PA/Ao diameter ratio	1.18 $\pm$ 0.25	1.19 $\pm$ 0.25	0.01 $\pm$ 0.10	0.31

Ao, aorta; CT, computed tomography; PA, pulmonary artery; SD, standard deviation.

Table 2

Variation in main PA diameter at different time intervals between CT scans of the chest

Variables	<6 months <i>n</i> (%)	6–11.9 months <i>n</i> (%)	12 months <i>n</i> (%)	<i>P</i> (chi-square)
<i>n</i>	39	27	47	
Main PA diameter change				
<1 mm	27 (69.2)	22 (81.5)	22 (46.8)	0.036
Increase > 1 mm	8 (20.5)	4 (14.8)	19 (40.4)	
Decreased > 1 mm	4 (10.3)	1 (3.7)	6 (12.8)	

CT, computed tomography; PA, pulmonary artery.

Table 3

Factors associated with change in main PA diameter between CT scans of the chest

Variables (unit of change)	Beta	Standard error	P (linear regression) [‡]
PoPH compared with IPAH (PoPH)	-1.581	0.610	0.01
Haemodynamic determinations at the diagnostic RHC			
PA pulse pressure (1 mm Hg)	0.027	0.012	0.03
PA compliance (1 mL/mm Hg)	-0.45	0.136	0.001
Functional determinations			
Change in 6MWT distance (1 m)	-0.007	0.002	0.007
Echocardiographic determinations			
RVSP close to first CT scan (1 mm Hg)	0.019	0.007	0.006
RVSP close to second CT scan (1 mm Hg)	0.013	0.006	0.04
RV function close to first CT scan [‡]	0.437	0.167	0.01
RV function close to second CT scan [‡]	0.461	0.163	0.006
TAPSE close to second CT scan (1 cm)	-1.141	0.312	<0.001
Change in TAPSE (1 cm)	-0.789	0.292	0.009
RV diameter close to second CT scan (1 cm)	0.413	0.171	0.018

[‡]Linear regression was adjusted for time between scans and difference in slice thickness. Age, gender, race, BMI, smoking status, treatment with parenteral prostacyclin analogues, number of PH-specific therapies, change in RVSP or RV basal diameter on echocardiograms, PVR and main PA diameter during diagnostic RHC did not reach statistical significance as predictors of change in main PA diameter.

[‡]Worsening of RV function by one degree, i.e. normal to mild, mild to moderate or moderate to severe.

6MWT, 6-min walk test; CT, computed tomography; IPAH, idiopathic pulmonary arterial hypertension; PA, pulmonary artery; PH, pulmonary hypertension; PoPH, portopulmonary hypertension; PVR, pulmonary vascular resistance; RHC, right heart catheterization; RV, right ventricular; RVSP, right ventricular systolic pressure; TAPSE, tricuspid annular plane systolic excursion.