



# Pulmonary hypertension due to left heart disease: diagnostic value of pulmonary artery distensibility

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## Abstract

**Objectives** To evaluate how pulmonary artery (PA) distensibility performs in detecting pulmonary hypertension due to left heart disease (PH-LHD) in comparison with parameters from ungated computed tomography (CT) and echocardiography.

**Methods** One hundred patients (79 men, mean age =  $63 \pm 17$  years) with either severe heart failure with reduced ejection fraction (HFrEF), aortic stenosis, or primary mitral regurgitation prospectively underwent right heart catheterization, ungated CT, ECG-gated CT, and echocardiography. During the ECG-gated CT, the right PA distensibility was calculated. In ungated CT, dPA, dPA/AA, the ratio of dPA to the diameter of the vertebra, segmental PA diameter, segmental PA-to-bronchus ratio, and the main PA volume were measured; the egg-and-banana sign was recorded. During echocardiography, the tricuspid regurgitation (TR) gradient was measured. The areas under the ROC curves (AUC) of these signs were computed and compared with DeLong test. Correlation between PA distensibility and PA pressure (PAP) was investigated through Pearson's coefficient.

**Results** PA distensibility was lower in patients with PH than in those without PH (11.4 vs. 21.2%,  $p < 0.001$ ) and correlated negatively with mean PAP ( $r = -0.72$ ,  $p < 0.001$ ). Age, PA size, and mean PAP were independent predictors of PA distensibility. PA distensibility  $< 18\%$  detected PH-LHD with 96% sensitivity and 73% specificity; its AUC was 0.92, larger than that of any other sign at ungated CT and TR gradient (AUC ranging from 0.54 to 0.83, DeLong:  $p$  ranging from 0.020 to  $< 0.001$ ).

**Conclusion** PA distensibility on an ECG-gated CT can detect PH-LHD better than the parameters reflecting PA dilatation in ungated CT or TR gradient in the echocardiography of patients with severe HFrEF, aortic stenosis, or mitral regurgitation.

## Key Points

- In left heart disease, pulmonary artery distensibility is lower in patients with PH than in those without pulmonary hypertension (11.4 vs. 21.2%,  $p < 0.001$ ).
- In left heart disease, pulmonary artery distensibility detects pulmonary hypertension with an area under the receiver operating curve of 0.92.
- In left heart disease, the area under the receiver operating curve of pulmonary artery distensibility for detecting pulmonary hypertension is larger than that of all other signs at ungated CT ( $p$  from 0.019 to  $< 0.001$ ) and tricuspid regurgitation gradient at echocardiography ( $p = 0.020$ ).

**Keywords** Pulmonary hypertension · Computed tomography · Echocardiography · Heart failure

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## Abbreviations

ABR	Pulmonary artery to bronchus ratio
AUC	Area under the receiver operating characteristic curve
dPA	Diameter of the main pulmonary artery
dPA/AA	Diameter of the main pulmonary artery to the diameter of the ascending aorta ratio
dPA/V	Diameter of the main pulmonary artery to the diameter of the vertebral body ratio
HFrEF	Heart failure with reduced ejection fraction
PA	Pulmonary artery
PAP	Pulmonary artery pressure
PAWP	Pulmonary artery wedge pressure
PH	Pulmonary hypertension
PH-LHD	Pulmonary hypertension due to left heart disease
TR	Tricuspid regurgitation

## Introduction

Pulmonary hypertension (PH) due to left heart disease (PH-LHD) is defined as a mean pulmonary artery (PA) pressure greater than or equal to 25 mmHg; it is associated with a PA wedge pressure greater than 15 mmHg as measured by right heart catheterization [1]. PH-LHD carries a worse prognosis by increasing the right ventricular afterload [2–4]. Patients with left heart disease are routinely evaluated using echocardiography that provides a noninvasive estimation of pulmonary pressure. The tricuspid regurgitation (TR) gradient computed from the TR velocity by the continuous wave spectral Doppler is the more routinely used method for detecting PH at echocardiography [1]. However, possible diagnostic inaccuracies of such TR gradient have been widely reported, due to weak or absent TR jet at spectral Doppler, lack of parallel alignment of the ultrasound beam to the TR jet, and intraday variation due to patient-related factors including blood volume status [5]. Thus, despite its invasiveness, right heart catheterization remains the standard of reference in the diagnosis and severity assessment of PH [1].

Various parameters have been reported for noninvasive detection of PH in ungated chest computed tomography (CT), mainly based on PA measurements, including the diameter of the main PA (dPA) [6–16], the ratio between dPA and the diameter of the ascending aorta (dPA/AA) [8–18], the ratio between dPA and the diameter of the thoracic vertebra (dPA/V) [17], the volume of the main PA [19, 20], the segmental PA diameter [17], the segmental PA-to-bronchus ratio (ABR) [7, 12, 17], and the so-called egg-and-banana sign [12, 15]. These parameters have been separately assessed and are all of limited value unless combined with echocardiography [17].

In ECG-gated CT, the PA distensibility—defined as the relative difference between the systolic and diastolic PA cross-sectional areas—performs well in detecting PH [21].

Nevertheless, the diagnostic value of PA distensibility in PH-LHD, as well as its diagnostic value when compared with ungated CT and echocardiography, remains unknown. In addition, most of the CT vascular parameters have been evaluated in patients with precapillary or mixed types of PH, although PH-LHD is the most common [2]. The purpose of this study was, therefore, to assess the respective values of CT vascular parameters in a group of patients with PH-LHD, considering right heart catheterization as the independent method of reference.

## Materials and methods

### Study group

Our local ethics committee approved the protocol of this prospective investigation. All patients gave written informed consent. Between October 2015 and April 2019, patients who were scheduled to undergo clinically indicated right heart catheterization for either heart failure with reduced ejection fraction (HFrEF) considered for heart transplantation, aortic stenosis considered for transcatheter aortic valve implantation, or primary mitral regurgitation considered for surgery were invited to participate to this investigation. Patients with contraindications to the injection of an iodinated contrast medium (i.e., intolerance to contrast medium or renal insufficiency with an estimated glomerular filtration rate of  $< 30$  mL/min/1.73 m<sup>2</sup>), except those under dialysis, were not invited to participate. Patients younger than 30 year old, with congenital heart disease or acute heart failure defined as rapid onset, or with worsening of symptoms and/or signs of heart failure were also not invited to participate [22]. One hundred and three patients were invited and consented to participate.

Of the 103 enrolled patients, three patients were excluded because of major CT artifacts in their ECG-gated CT due to extrasystolic beats in two patients and severe arrhythmia during RHC in one patient, resulting in incomplete data. Thus, our final study group consisted of 100 patients: 79 men (79%), mean age of  $63 \pm 17$  years, with either HFrEF (54 patients), aortic stenosis (31 patients), or primary mitral regurgitation (15 patients). The median time intervals between CT and right heart catheterization and between echocardiography and right heart catheterization were 1 day (interquartile ranges, 0–1 day and 1–2 days, respectively).

### Right heart catheterization and echocardiography

Right heart catheterization was performed using the standard technique, with measurements of mean PA pressure (PAP), PA wedge pressure (PAWP), cardiac output, and computation of pulmonary vascular resistance [1]. PH-LHD was defined as mean PAP  $\geq 25$  mmHg and PAWP  $> 15$  mmHg. Combined

pre- and post-capillary PH was defined as mean PAP  $\geq 25$  mmHg, PAWP  $> 15$  mmHg, associated with pulmonary vascular resistance  $> 3$  Wood Units, and/or diastolic pulmonary gradient (diastolic PAP – mean PAWP)  $\geq 7$  mmHg [1]. Echocardiography was performed on IE33 or Epic sonographs (Philips Medical Systems, Cleveland, OH) by experienced cardiologists (all  $> 10$  years of experience). In accordance with the most recent guidelines, the TR gradient was used to detect PH [1].

### ECG-gated and ungated CT

CT examinations were performed using a 256-detector row scanner (ICT, Philips Healthcare). First-pass perfusion images were acquired on a single transversal slice through both ventricles with the following parameters: slice thickness, 10 mm; rotation time, 270 ms; tube potential, 100 kV; and tube current, 20 mA. The contrast injection protocol consisted of 40 mL of 400 mg iodine/mL iodinated contrast medium (Iomeron®, Iomeprol, Bracco Diagnostics) injected at a flow rate of 5 mL/s through a right antecubital vein via an 18-gauge catheter and followed by 20 mL of saline bolus chaser at 5 mL/s. The acquisition was discontinued as soon as the contrast density visually decreased in the descending aorta.

Immediately thereafter, a second acquisition consisted of a retrospective ECG-gated cardiac CT after an additional injection of 60 mL of contrast medium at 2 mL/s, with bolus tracking in the ascending aorta. The acquisition was debuted when the attenuation had increased to 180 HU. The parameters were collimation,  $128 \times 0.625$  mm; rotation time, 270 ms; tube potential from 100 to 120 kV, depending on the patient's weight; and tube current from 300 to 800 mAs, depending on the automatic tube current modulation. All contrast medium injections were performed with a power injector (Medrad Stellant, Bayer Healthcare), and CM was heated using syringe heating.

Finally, a third acquisition consisted of a thoracoabdominal scan, 60 s after the end of the second acquisition with the following parameters: tube potential, 120 kV; tube current from 40 to 150 mAs, depending on automatic tube current modulation. The effective delivered radiation dose was calculated as follows: dose-length product provided by the scanner unit multiplied by 0.017 [23]. The average radiation exposure delivered by ungated CT and ECG-gated CT acquisitions was  $3.4 \pm 0.9$  mSv and  $11.5 \pm 1.8$  mSv, respectively.

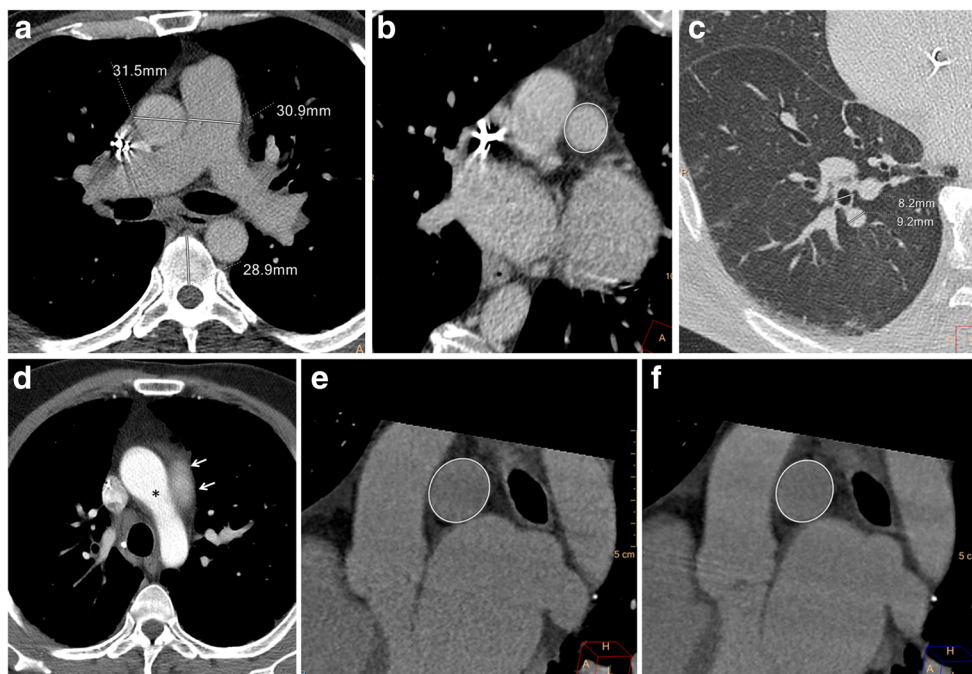
The CT images were analyzed with commercially available software (CT viewer and CT cardiac viewer, Philips Healthcare) by observer Nr1 (G.V.), who had 3 years of experience in cardiac imaging, and blinded to right heart catheterization results. In ungated CT, dPA, dPA/AA, and dPA/V were measured as previously reported [8–18]. The small segmental PA diameter was measured in four lobes on axial sections: the apical segment of the right upper lobe, the posterior

segment of the left upper lobe, the posterior basal segment of the right lower lobe, and the posterior basal segment of the left lower lobe [17]. The average segmental PA diameter was calculated from these four measurements. The segmental ABR was calculated as the segmental PA diameter divided by the small outer diameter of the adjacent bronchus and was considered as enlarged if  $> 1.25$  [17]. Segmental ABR was scored from 0 to 4, on the basis of the number of enlarged ABR in the four lobes. The main PA volume was calculated as follows: a center line was traced from the center of the pulmonary valve to the main PA bifurcation. The length of this center line was considered to be the main PA length. The PA cross-sectional area was measured at each 10-mm segment of the center line, and a mean area was computed. The PA volume was calculated as mean PA area multiplied by the PA length, expressed in milliliter. The egg-and-banana sign was present when the main PA was visible at the bottom level of the aortic arch [15].

For ECG-gated CT, the right PA distensibility was measured as proposed by Revel et al [21]. From a parasagittal view, the cross-sectional area of the right PA was obtained after a double oblique adjustment on axial and coronal views, 1 cm distal to the main PA division, and manually delineated every 10% of the cardiac cycle. PA distensibility, expressed as a percentage, was defined as the following ratio: (maximal cross-sectional area minus minimal cross-sectional area)/maximal cross-sectional area [21]. In addition, the dPA and dPA/AA were measured on axial slices for every 10% of the R-R interval in the same way as described for ungated CT. The maximal and minimal values for dPA and dPA/AA were noted. Examples of CT measurements are illustrated in Fig. 1. In order to assess interobserver agreement, PA distensibility was independently calculated by observer Nr2 (G.C.), who had 8 years of experience in cardiac imaging. In order to assess intraobserver agreement, observer Nr1 (G.V.) redid the PA distensibility calculation more than 1 month later.

### Statistical analysis

Continuous variables were expressed as means  $\pm$  standard deviations or as medians with interquartiles. Categorical variables were expressed as counts and proportions. Groups were compared using Student's unpaired *t* test or  $\chi^2$  test when appropriate. A non-parametric test (Kruskal–Wallis) was used to compare the median values of ABR. Interobserver agreement for PA distensibility was assessed by using Lin's concordance correlation coefficient. The relationships between mean PA pressure, CT parameters, and TR gradient were tested using linear regression analysis and Pearson's correlation coefficient. The Pearson correlation coefficient was used to assess the relationship of PA distensibility with patient characteristics, PA size, and hemodynamics. Multivariable analysis



**Fig. 1** Computed tomography measurements in a 57-year-old man with ischemic dilated cardiomyopathy and severe left ventricular systolic dysfunction. **a** At ungated CT, the pulmonary artery diameter was 30.9 mm, the aortic diameter was 31.5 mm, and the diameter of the vertebral body was 28.9 mm. **b** Measurement of the pulmonary artery area after double oblique reformation. **c** Measurement of the right posterior basal segmental artery-to-bronchus ratio. The segmental artery diameter was 9.2 mm

and the adjacent bronchus diameter was 8.2 mm, allowing an artery-to-bronchus ratio of 1.12. **d** Egg-and-banana sign consisting in the visibility of the pulmonary artery (arrows) at the level of the aortic arch (\*). At gated CT, the right pulmonary artery distensibility was calculated at 11%; the right pulmonary cross-sectional area was measured at 570 mm<sup>2</sup> in systole (30% of the RR interval, **e**) and 508 mm<sup>2</sup> in diastole (0% of the RR interval, **f**)

using backward elimination was performed with all variables associated in univariable analysis ( $p < 0.10$ ).

The value of CT parameters and TR gradient for diagnosing PH-LHD was assessed through the area under the receiver operating characteristic curves (AUCs). The AUCs were compared against 0.5 and one another using the DeLong test. A  $p$  value  $< 0.05$  was considered to be statistically significant. All statistical analyses were performed using NCSS 12 Statistical Software (LLC).

## Results

At right heart catheterization, 56 patients had PH, while 44 patients had no PH. All 56 patients with PH had PH-LHD. Among them, 27 patients had associated combined pre- and postcapillary PH with pulmonary vascular resistance  $> 3$  Wood Units and among these, twelve patients had also elevated diastolic pulmonary gradient  $\geq 7$  mmHg. Eight patients (8%) had chronic lung disease (five patients with chronic obstructive pulmonary disease, one patient with hypersensitivity pneumonitis, one patient with pulmonary fibrosis, and one patient with nonspecific interstitial pneumonia).

The patient characteristics and echocardiography, hemodynamics, ungated CT, and ECG-gated CT parameters of patients with and without PH are compared in Table 1.

There was no significant difference between patients with and those without PH regarding age, gender, body mass index, ischemic heart disease, and chronic lung disease. Patients with PH had higher heart rate ( $p \leq 0.001$ ) and had more frequently atrial fibrillation ( $p = 0.014$ ) than those without PH. Among CT parameters, dPA, dPA/AA ratio, and dPA/V ratio, as well as main PA mean cross-sectional area and volume, were significantly larger in patients with PH as compared with those in patients without PH (all  $p < 0.001$ ). By opposition, main PA length, segmental PA diameter, median segmental ABR score, and egg-and-banana sign were not significantly different between both groups (all  $p > 0.05$ ). The AUCs of each parameter assessed in ungated CT, ECG-gated CT, and echocardiography for detecting PH are listed and compared with 0.5 in Table 2. The correlations between these parameters and mean PA pressure are also listed in Table 2.

PA distensibility  $< 18\%$  detected PH-LHD with 96% sensitivity and 73% specificity. Its AUC (0.92) was significantly larger than that of the TR gradient, dPA/AA (Fig. 2), dPA, main PA cross-sectional area, and all other ungated CT



**Table 1** Patient characteristics, hemodynamics, echocardiography, and CT parameters

	Whole study group ( <i>n</i> = 100)	Patients without PH ( <i>n</i> = 44)	Patients with PH ( <i>n</i> = 56)	<i>p</i> value
<b>Patient characteristics</b>				
Age, years	63 ± 17	61 ± 15	64 ± 17	0.337
Men	79 (79)	34 (77)	45 (80)	0.706
BMI, kg/m <sup>2</sup>	26 ± 5	26 ± 5	26 ± 4	0.653
BSA, m <sup>2</sup>	1.89 ± 0.22	1.89 ± 0.20	1.89 ± 0.24	0.965
Ischemic heart disease	39 (39)	20 (45)	19 (34)	0.241
Heart rate, bpm	71 ± 15	65 ± 11	76 ± 13	< 0.001
Atrial fibrillation	23 (23)	5 (11)	18 (32)	0.014
NHYA class III or IV	33 (33)	9 (20)	23 (41)	0.028
Chronic lung disease	8 (8)	2 (5)	6 (11)	0.259
HFrEF	54 (54)	22 (41)	32 (59)	< 0.001
Aortic stenosis	31 (31)	11 (35)	20 (65)	< 0.001
Mitral regurgitation	15 (15)	11 (73)	4 (27)	< 0.001
<b>Hemodynamics</b>				
Systolic PAP, mmHg	43 ± 17	27 ± 6	55 ± 13	< 0.001
Diastolic PAP, mmHg	21 ± 9	12 ± 4	27 ± 7	< 0.001
Mean PAP, mmHg	29 ± 12	18 ± 4	38 ± 8	< 0.001
PAWP, mmHg	19 ± 8	11 ± 4	25 ± 5	< 0.001
Cardiac output, L/min	4.4 ± 1.3	5.0 ± 1.4	4.0 ± 1.1	< 0.001
Cardiac index, L/min/m <sup>2</sup>	2.3 ± 0.7	2.7 ± 0.7	2.1 ± 0.7	< 0.001
PVR, Wood Unit	2.6 ± 1.8	1.5 ± 0.7	3.4 ± 1.9	< 0.001
DPG, mmHg	1 ± 0	1 ± 2	2 ± 5	0.336
<b>Echocardiography parameter</b>				
TR gradient, mmHg	32 ± 17	21 ± 13	40 ± 11	< 0.001
<b>Ungated CT parameters</b>				
dPA, mm	29 ± 5	27 ± 4	32 ± 4	< 0.001
dPA/AA, ratio	0.89 ± 0.15	0.80 ± 0.10	0.96 ± 0.13	< 0.001
dPA/V, ratio	1.07 ± 0.20	0.98 ± 0.16	1.14 ± 0.20	< 0.001
Main PA volume, ml	23 ± 10	19 ± 8	25 ± 10	< 0.001
Main PA mean CSA, mm <sup>2</sup>	806 ± 211	690 ± 175	898 ± 193	< 0.001
Main PA length, mm	27 ± 6	27 ± 6	28 ± 6	0.550
Segmental PA diameter, mm	7 ± 1	7 ± 1	8 ± 1	0.061
Segmental ABR, median score*	1 (0–2)	1 (0–1)	1 (0–2)	0.095
Egg-and-banana sign	19 (19)	5 (11)	14 (25)	0.084
<b>ECG-gated CT parameters</b>				
dPA max, mm	31 ± 5	28 ± 4	33 ± 4	< 0.001
dPA/AA max	0.92 ± 0.15	0.84 ± 0.11	0.99 ± 0.14	< 0.001
dPA min, mm	28 ± 5	25 ± 4	30 ± 5	< 0.001
dPA/AA min	0.87 ± 0.15	0.77 ± 0.11	0.95 ± 0.14	< 0.001
Right PA maximal CSA, mm <sup>2</sup>	583 ± 178	507 ± 143	643 ± 180	< 0.001
Right PA minimal CSA, mm <sup>2</sup>	497 ± 174	401 ± 125	571 ± 171	< 0.001
Right PA distensibility, %	15.7 ± 6.9	21.2 ± 5.4	11.4 ± 4.4	< 0.001

Values are mean ± standard deviation, *n* (%), or median\* (25th–75th percentile)

*ABR* pulmonary artery to bronchus ratio; *BMI* body mass index; *BPM* beat per minute; *BSA* body surface area; *CSA* cross-sectional area; *CT* computed tomography; *dPA* diameter of main pulmonary artery; *dPA max* maximal diameter of main pulmonary artery; *dPA min* minimal diameter of main pulmonary artery; *dPA/AA* ratio between pulmonary artery and aorta diameters; *dPA/AA max* maximal ratio between pulmonary artery and aorta diameters; *dPA/AA min* minimal ratio between pulmonary artery and aorta diameters; *dPA/V* ratio between pulmonary artery and vertebra diameters; *DPG* diastolic pulmonary gradient; *HFrEF* heart failure with reduced ejection fraction; *NHYA class* New York Heart Association functional class; *PA* pulmonary artery; *PAP* pulmonary artery pressure; *PAWP* pulmonary artery wedge pressure; *PH* pulmonary hypertension; *PVR* pulmonary vascular resistance; *SD* standard deviation; *TR* tricuspid regurgitation

parameters (AUC ranging from 0.54 to 0.83, DeLong test: *p* ranging from 0.020 to < 0.001). PA distensibility was reproducible between ( $r = 0.89$ ,  $p < 0.001$ ) and within ( $r = 0.96$ ,  $p < 0.001$ ) observers. The correlations between PA distensibility and patient characteristics, PA size, and pulmonary hemodynamics are listed in Table 3. The correlation between PA distensibility and PAP ( $r = -0.72$ ,  $p < 0.001$ ) is illustrated in Fig. 3. In multivariable analysis, PA distensibility was independently associated with mean PAP ( $\beta = -0.41$ ,

$p < 0.001$ ), minimal right PA area ( $\beta = -0.008$ ,  $p = 0.019$ ), and age ( $\beta = -0.07$ ,  $p = 0.019$ ).

## Discussion

This study shows two main results. First, in patients with HFrEF, aortic stenosis, or primary mitral regurgitation, right PA distensibility was decreased in those with PH as opposed

**Table 2** Alone and combined echocardiography, ungated CT, and ECG-gated CT parameters: AUC for the diagnosis of PH and correlation with mean PAP

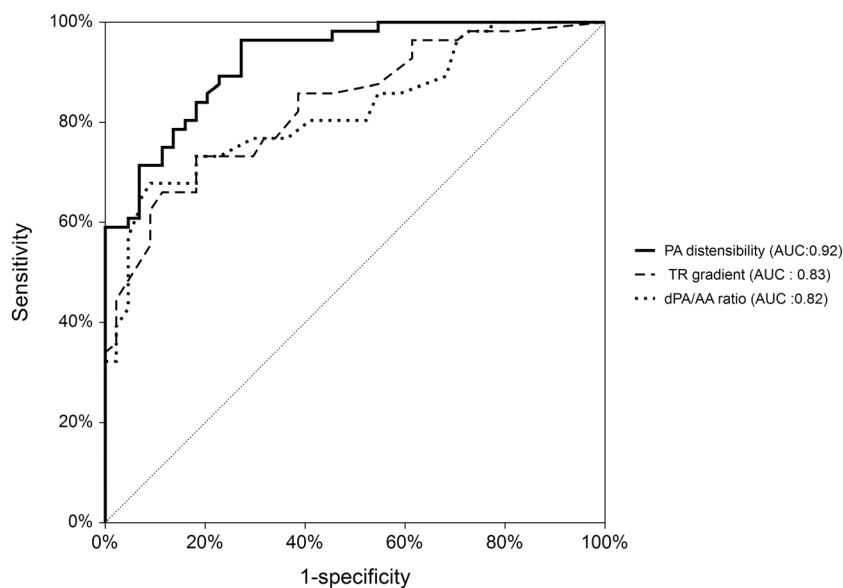
	PH diagnosis		Correlation with mean PAP	
	AUC (95% CI)	<i>p</i> value	<i>r</i>	<i>p</i> value
Echocardiography				
TR gradient, mmHg	0.83 (0.79–0.90)	< 0.001	0.58	< 0.001
Ungated chest CT				
dPA, mm	0.81 (0.69–0.88)	< 0.001	0.55	< 0.001
dPA/AA, ratio	0.82 (0.72–0.89)	< 0.001	0.54	< 0.001
dPA/V, ratio	0.75 (0.63–0.83)	< 0.001	0.43	< 0.001
Main PA volume, mL	0.73 (0.61–0.82)	< 0.001	0.30	0.002
Main PA mean CSA, mm <sup>2</sup>	0.80 (0.67–0.89)	< 0.001	0.48	< 0.001
Main PA length, mm	0.54 (0.42–0.65)	0.237	0.01	0.902
Segmental PA diameter, mm	0.59 (0.46–0.69)	0.066	0.32	0.002
Segmental ABR score (0–4)	0.59 (0.48–0.69)	0.044	0.22	0.028
Egg-and-banana sign	0.57 (0.49–0.63)	0.036	0.16	0.117
ECG-gated chest CT				
dPA max, mm	0.77 (0.66–0.85)	< 0.001	0.45	< 0.001
dPA/AA max, ratio	0.80 (0.69–0.87)	< 0.001	0.47	< 0.001
dPA min, mm	0.81 (0.70–0.88)	< 0.001	0.54	< 0.001
dPA/AA min, ratio	0.84 (0.74–0.90)	< 0.001	0.55	< 0.001
Right PA max CSA, mm <sup>2</sup>	0.72 (0.60–0.80)	< 0.001	0.38	< 0.001
Right PA min CSA, mm <sup>2</sup>	0.80 (0.69–0.87)	< 0.001	0.49	< 0.001
Right PA distensibility, %	0.92 (0.86–0.96)	< 0.001	–0.72	< 0.001

Abbreviations as in Table 1

to those without PH and correlated negatively with mean PA pressure. Second, among all tested parameters, PA distensibility performed the best for detecting PH, better than all vascular signs available from ungated CT and TR gradient in echocardiography. These findings deserve further discussion with regard to the diagnostic value of these CT signs and the

physiological relationships between PA pressure and PA distensibility.

With regard to the diagnostic value, our study shows that, for detecting PH, PA distensibility performs well with the AUC reaching 0.92, a value very close to that reported by Revel et al (i.e., 0.95) in mixed types of PH [21]. Most

**Fig. 2** ROC curves for PH detection in patients with left heart disease. The AUC of PA distensibility (0.92) at ECG-gated CT was significantly larger than that of dPA/dAA ratio at ungated CT (0.82,  $p = 0.019$ ) and TR gradient at echocardiography (0.83,  $p = 0.020$ )

**Table 3** Relationship of PA distensibility with patient characteristics, PA size, and hemodynamics

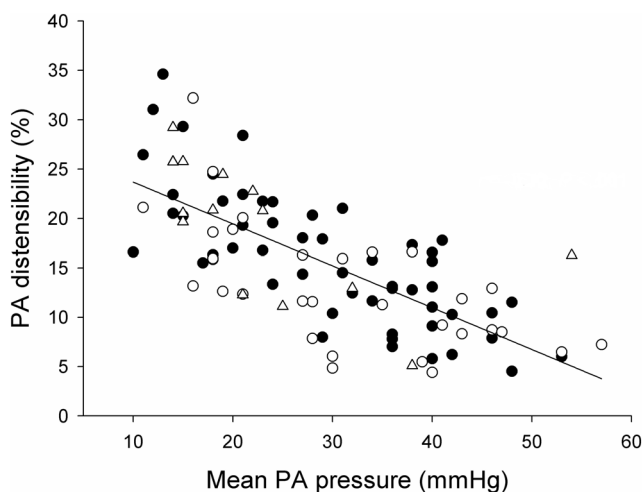
	Correlation coefficient ( <i>r</i> )	<i>p</i> value
Age, years	-0.35	<0.001
BMI, kg/m <sup>2</sup>	0.16	0.111
BSA, m <sup>2</sup>	0.17	0.089
Ischemic heart disease	0.06	0.529
Heart rate, bpm	-0.40	<0.001
Atrial fibrillation	-0.27	0.006
Chronic lung disease	-0.11	0.289
Mean PAP, mmHg	-0.72	<0.001
PAWP, mmHg	-0.65	<0.001
PVR, WU	-0.59	<0.001
Cardiac index	0.38	<0.001
Right PA minimal CSA, mm <sup>2</sup>	-0.59	<0.001
Right PA maximal CSA, mm <sup>2</sup>	-0.42	<0.001

Abbreviations as in Table 1

importantly, PA distensibility performed better than TR gradient in echocardiography and any measurement or sign of proximal and peripheral PA dilatation in ungated CT.

In ungated CT, dPA and dPA/AA had the highest value, but their corresponding AUCs were still lower than that of PA distensibility in ECG-gated CT. Thus, evaluation of PA size changes during cardiac cycle through PA distensibility at gated CT performs better than single PA size measurement at ungated CT.

With regard to physiological relationships, correlations between mean PA pressure and PA distensibility, also called relative area change [24], PA pulsatility [25], or PA strain [26], using either maximal cross-sectional area [21, 27–29]



**Fig. 3** Correlation between ECG-gated CT-derived right PA distensibility and mean PA pressure ( $r = -0.72$ ,  $p < 0.001$ ) in patients with HFrEF (black dots), aortic stenosis (white dots), and mitral regurgitation (white triangle)

or minimal cross-sectional area [24–26] as denominator, have been recently reported in studies based on ECG-gated CT [21, 27, 28] and magnetic resonance imaging [24–26, 29] in patients with exclusive [24–27, 29] or almost exclusive [21, 28] precapillary PH. Our study shows that, in patients with left heart disease, PA distensibility is lower in those with PH than in those without PH (11.4% vs. 21.2%). These results are within the same order of magnitude as values reported by Revel et al (12.2% vs. 22.6%), using ECG-gated CT in 45 patients with mixed types of PH [21], and by Porter et al (10.8% vs. 17.0%), using intravascular ultrasound in 30 patients with HFrEF [30]. In fact, CT-derived PA distensibility also correlates with mean PA pressures in PH-LHD. Our study confirms the decrease of PA distensibility in patients with PH-LHD as well, despite the different mechanisms leading to PH.

Although our results show that PA distensibility is a reliable parameter for PH detection, we acknowledge that PA distensibility computation has several technical issues that might limit its clinical use, including higher radiation exposure associated with retrospective ECG-gated CT, the need for contrast IV injection (although further studies should investigate unenhanced ECG-gated CT in this setting), and the time needed for measurements of cross-sectional area throughout the cardiac cycle. Thus, the added diagnostic value of ECG-gated CT should be balanced with these technical issues before considering its potential clinical interest. However, the use of ECG-gated CT before cardiac interventions is growing, and the diagnosis of PH is very important because of the higher overall mortality rate in patients with PH than in those without PH after cardiac procedures, including transcatheter aortic valve implantation [12]. PA distensibility could thus detect PH in patients who have ECG-gated CT as part of their work-up.

Our study has several limitations. First, CT and right heart catheterization were not obtained simultaneously, and we cannot exclude some variations in PA pressure between both procedures. However, patients were stable, and the time interval between CT and right heart catheterization was quite short. Second, CT acquisition was performed during breath-holding after deep inspiration, while PA pressure was recorded at the end of the expiratory phase during free breathing. Third, the causes of left heart disease were multiple, including HFrEF, mitral regurgitation, and aortic stenosis, each of them carrying different physiological pathways. Our results, therefore, cannot be generalized to any patient with left heart disease. Fourth, we did not evaluate whether the PA distensibility was sensitive to serial changes in mean PA pressure due to ethical reasons regarding repeated CT and subsequent radiation exposure. Fifth, in accordance with PH guidelines, only the TR gradient was used for PH detection in echocardiography [1]. However, left ventricular filling pressures may be estimated through other echocardiography parameters that were not evaluated in this study [31]. Sixth, the low temporal

resolution of CT (140 ms) could have underestimated the actual PA distensibility, especially in patients with high heart rates. Finally, this study was monocentric with a rather small study group.

In conclusion, in patients with severe HF<sub>r</sub>EF, aortic stenosis, or mitral regurgitation, PA distensibility in ECG-gated CT can detect PH-LHD better than the parameters reflecting PA dilatation in ungated CT or TR gradient in echocardiography.

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## Compliance with ethical standards

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**Conflict of interest** The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

**Statistics and biometry** No complex statistical methods were necessary for this paper.

**Informed consent** Written informed consent was obtained from all subjects (patients) in this study.

**Ethical approval** Institutional Review Board approval was obtained.

## Methodology

- prospective
- diagnostic or prognostic study
- performed at one institution

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