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Pulmonary vascular remodeling and right ventricular adaptation in precapillary pulmonary hypertension

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Background: In precapillary pulmonary hypertension (PH) as pulmonary arterial hypertension (PAH), chronic thromboembolic PH (CTPEH) and PH due to hypoxia and lung disease (HPH) the different pathomechanisms of vascular remodeling result in different right ventricular (RV) adaptation. Routine clinical factors which could predict vascular remodeling are lacking.
Purpose: Our aim was to investigate the differences in parameters of pulmonary vascular remodeling and RV adaptation in subgroups of precapillary PH and to correlate the severity of PH with these parameters.
Methods: Fifty-one patients (age 57±15 years) with precapillary PH (PAH N=18, CTEPH N=15, HPH N=18;) underwent right heart catheterization (RHC) and results of RHC, echocardiography and laboratory tests were analyzed retrospectively.
Results: The majority of parameters did not show difference among PH groups, but diastolic PAP was higher in PAH than in CTEPH and HPH ($p<0.05$) and RV outflow tract velocity time integral (RVOT VTI) and RV stroke work index were increased in PAH compared to HPH ($p<0.05$). Pulmonary vascular resistance (PVR) showed a significant relation to pulmonary arterial compliance (PAC) in the total cohort ($p<0.05$, $r=-0.661$) and in all subgroups (PAH $p<0.05$, $r=-0.70$; CTEPH $p<0.05$, $r=-0.525$; HPH $p<0.05$, $r=-0.793$). In PAH, all parameters including RVOT VTI and acceleration time (AT), tricuspid annular plane systolic excursion, RV diameter and right atrial area showed correlations with PVR. In the HPH group, only RVOT AT had a correlation with PVR, but no parameters in the CTEPH group showed a relationship to other factors.
Conclusion: In precapillary PH the different degree of RV adaptation in the subgroups is shown by RVSWI as an invasive parameter. The severity of PH is related to PAC in precapillary PH. Some parameters can better characterize the severity of vascular and cardiac changes in PAH than in CTEPH or HPH.

Keywords: precapillary pulmonary hypertension, right ventricular adaptation, arterial remodeling, pulmonary vascular compliance, right ventricular stroke work index

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Introduction

In healthy subjects, the pulmonary circulation is a low pressure circulatory system even in wide range of flow. The traditional upper limit of normal mean pulmonary arterial pressure (mPAP) is 25 mmHg. In this low resistant system, under normal condition the right ventricle works against low afterload with low stroke work (1). Precapillary pulmonary hypertension (PH) is a progressive disease. The new proposal for the definition of pulmonary arterial hypertension (PAH) during the 6th World Symposium in 2019 (3) which is expected to be included in the new guideline in the near future, places great emphasis on vascular resistance (PVR) and right ventricular stroke work index (RVSWI), as PVR and RVSWI best characterize the prognosis.

We believe that the parameters that best show the prognosis are most needed during follow-up. Therefore, we searched in our own patient database to see if PVR and RVSWI can separate PH groups of different etiologies and whether they can be replaced by more readily available echocardiographic parameters. Within precapillary PH, the most important groups in addition to PAH are chronic thromboembolic PH (CTEPH) and pulmonary hypertension due to lung diseases and/or hypoxia (HPH) (2).

Pathophysiological abnormalities and morphologic changes of the pulmonary arteries are not uniform in precapillary PH subgroups with different etiologies. In PAH, the primary mechanism is the remodeling of the pulmonary artery wall and development of plexiform lesions that result in lumen narrowing and stiffening of the arterial wall. These abnormalities, together with the development of in situ thrombus formation increase PVR (1, 4, 5). In HPH the rise of pulmonary pressure is multifactorial. These include structural damage of the lung parenchyma and the vascular bed, chronic hypoxia-induced vasoconstriction (6, 7) and remodeling, stiffening of both distal and proximal, large arteries via extensive extracellular matrix deposition and wall thickening (4), all factors playing major roles in the PVR shift. In CTEPH, the thromboembolic process direct leads to vessel narrowing followed by secondary vascular remodeling due to neurohumoral activation (7, 8, 9) both increase PVR. The extent and homogeneity of vascular remodeling vary in these subgroups of precapillary PH. In the everyday clinical practice there are few options to characterize the degree of pathological alterations in pulmonary arteries. Pulmonary angiography can be used to examine the narrowing or occlusion of arterial lumen, while PVR is a routinely used hemodynamic parameter to characterize the total vascular resistance of the pulmonary circulation. RVSWI measured by right heart catheterization represents a promising index for right ventricular function.

Other parameters such as reduced pulmonary arterial compliance (PAC), elevated pulmonary arterial stiffness (4, 10, 11) increased pulse pressure (PP), fractional pulse pressure (PPf) (12) could provide additional insights that may further characterize pulmonary arterial function.

Furthermore, it can be speculated that vascular remodeling due to various underlying mechanisms may result in different patterns of right ventricular adaptation in the PH subgroups. In addition, the varying age of patients, the different course of the disease and the difference in neurohumoral and metabolic processes in the groups can also influence PH characteristics (13, 14). HPH and CTEPH patients are generally older and have more comorbidities than the PAH population. Indeed in CTEPH and in idiopathic PAH (IPAH) in the study of *Reesink et al.* (8) and *van Wolferen et al.* (15) there was no reduction in right ventricular ejection fraction and stroke volume as assessed by MRI. A metaanalysis form *Delcroix et al.* (12) confirmed that PAP and cardiac index were lower, but PVR was similar in CTEPH and IPAH. On the contrary, Wang et al. proved a less pronounced elevation in PVR and less obvious RV morphological changes in HPH when compared to PAH because of higher degree of adaptation (16).

Thus, in the current study, our aim was to investigate the differences in indicative parameters of pulmonary vascular remodeling and right ventricular adaptation in subgroups of precapillary PH of different etiologies and to explore the correlation of PVR as the main parameter relating to the severity of PH to other parameters and to determine the role of RVSWI as measure of right ventricular function in characterization the severity of vascular remodeling and right ventricular dysfunctions in PH.

Materials and Methods

Subjects and study design

Fifty-one patients with precapillary PH were enrolled into the study who underwent right heart catheterization (RHC) for diagnosing PH or repeated RHC for re-evaluation the severity at the Cardiopulmonary Unit, Department of Pulmonology, Semmelweis University, Budapest Hungary, between January 2020 and December 2021. Patients underwent detailed examinations (recording of medical history, echocardiography, lung function test, pulmonary HRCT, angio-CT, lung perfusion scans, blood tests, and determination of functional class). The classic PAH definition was used (mPAP ≥25 mmHg). We could classify them to clinical subgroups according to current guideline (2): 18 patients into PAH group (IPAH N=15, PH associated to portal hypertension N=1, drug-induced N=1, hereditary N=1), 15 patients had CTEPH and 18 cases corresponded to HPH (interstitial lung disease N=10, chronic obstructive pulmonary disease N=8). We retrospectively analyzed results of RHC, echocardiography and laboratory tests. RHC was performed in all of our

TABLE 1. Patient characteristics

	All PH	PAH	CTEPH	HPH	p-value
Number	51	18	15	18	
Sex, male/female N	23/28	7/11	8/7	8/10	0.59
Age, years	57±15	48±15	61±13	64±11*	<0.05
BSA, kg/m^2	1.9±0.2	1.9±0.2	2.0±0.3	1.9±0.2	0.26
Blood tests					
pH	7.42±0.04	7.41±0.03	7.43±0.07	7.41±0.04	0.40
PaO_2, mmHg	59.9±11.8	65.2±12.9	63.7±8.7	50,3±5,1$^{\#\#\#***}$	<0.001
$PaCO_2$, mmHg	33.5±5.9	32.6±3.9	30.1±5.1	50.3±5.137,1±6,6$^{\#\#***}$	<0.01
NTproBNP, pg/ml	1655 (591–3331)	1119 (202–1992)	1665 (789–3460)	2647 (703–3838)	0.09
Functional class					
I	1	1	0	0	0.18
II	17	8	7	2	
III	30	9	8	13	
IV	3	0	0	3	
Major comorbidity (more than one per patient)					
Number	20	5	9	12	
Hypertension (syst)	13	2	5	6	
Lives cirrhosis	1	1	0	0	
Neurofibromatosis	1	1	0	0	
Diabetes mellitus	6	0	3	3	
Atrial fibrillation	4	0	2	2	
Malignancy	1	0	1	1	
Chronic renal failure	5	0	3	2	

Data are presented as mean ± standard deviation or median (IQR). PH subgroups were analysed using ANOVA, Kruskal-Wallis, Chi-square and Fisher-exact tests. WHO functional classes were grouped as I-II and III-IV before analysis. *p<0.05, ***p<0.0001 vs. PAH; $^{\#\#}$p<0.01, $^{\#\#\#}$p<0.0001 vs. CTEPH. BSA: body surface area CTEPH: chronic thromboembolic PH, HPH: PH due to lung disease, N: number, NT-proBNP: N-terminal pro B-type natriuretic peptide, , PaO_2/CO_2: arterial partial pressure of O_2/CO_2, PAH: pulmonary arterial hypertension, PH: pulmonary hypertension

cases. In 39 new patients, diagnostic catheterization was used during evaluation. In 12 other cases (PAH N=8, HPH N=3, CTEPH N=1) the condition, the potential PAH-progression was monitored through repeated hemodynamic test. This latter group was on specific vasodilator treatment. PAH patients received specific pulmonary vasodilator monotherapy or combination therapy (2 patients with oral combination therapy as phosphodiesterase-5 inhibitor, endothelin receptor antagonist, 6 patients with triple combination of phosphodiesterase-5 inhibitor, endothelin receptor antagonist and prostacyclin analogue). Specific pulmonary vasodilator drugs were taken for an off-label use in patients with HPH with severe hemodynamic alteration and out-of-proportion exercise limitation as bridge to lung transplantation. The single CTEPH patient in the re-evaluation group was on pulmonary vasodilator monotherapy (phosphodiesterase-5 inhibitor) due to inoperable CTEPH.

Comorbidities were common, occurring in 5 cases in the PAH group, in 9 cases in the CTEPH group and in 12 cases in the HPH group *(Table 1).*

Measurements of invasive and non-invasive parameters

Right heart catheterization: During RHC the routine parameters were registered including right atrial pressure, right ventricular pressure, PAP, PCWP. Cardiac output (CO) was measured with thermodilution method, mixed venous oxygen saturation (SvO_2) was determined from pulmonary artery blood sample. In PAH, vasoreactivity tests were done with intravenous iloprost for 15 minutes in 4 ng/kg/min dosage. Furthermore, the stroke volume (SV=CO/heart rate), stroke volume index (SVI=SV/body surface area), pulmonary vascular resistance (PVR=(mean PAP-PCWP)/CO) and the cardiac index (CI=CO/body surface area) were calculated (2). Additional parameters were determined to assess the severity of pulmonary arterial remodeling and systolic right ventricle function including pulmonary arterial compliance (PAC=SV/[systolic PAP – diastolic PAP];) (11), pulse pressure (PP=sPAP-dPAP), fractional pulse pressure (PPf=PP/mPAP) (17), right ventricular stroke work index (RVSWI= (mean PAP – right atrial pressure) x SVI x 0.0136) (18).

TABLE 2. Hemodynamic and echocardiographic parameters in PH groups

	All PH (N=51)	PAH (N=18)	CTEPH (N=15)	HPH (N=18)	P-value
Hemodynamic parameters					
sPAP, mmHg	76.9±14.8	80.7±16.8	78.9±12.5	71.5±13.5	0.11
mPAP, mmHg	50.2±9.6	54.4±11.2	49.7±7.6	46.6±8	0.06
dPAP, mmHg	34±9	38.6±8.8	31.5±6.7*	31.5±9.5*	<0.05
RAP, mmHg	10 (6–16)	9.5 (8–15)	9 (6–18)	12 (4–17)	0.89
PCWP, mmHg	10.6±3.9	10.4±3.5	9.8±6.4	11.5±4.6	0.56
PP, mmHg	42.6±12.1	42.2±12.9	47.4±11.3	39.3±11.5	0.20
PPf	0.87±0.22	0.77±0.2	0.96±0.2	0.87±0.22	0.06
SV, mL/beat	28.1±8.4	57.1±14.5	56.3±17.2	48.1±16.6	0.80
CI, L/min/m^2	2.1 (1.9–2.6)	2.2 (2.0–2.6)	2.0 (1.9–2.9)	2.1 (1.9–2.6)	0.70
PVR, Wood Unit	10.2±4.2	10.3±4	10.6±4.2	9.6±4.6	0.64
PAC, mL/mmHg	1.3 (1.0–1.6)	1.3 (1.1–1.8)	1.2 (1.0–1.5)	1.2 (0.9–1.7)	0.48
RVSWI, g/m^2/beat	14.9±6.4	18.2±7.3	14.5±5.4	12.1±4.9*	<0.05
Echocardiographic parameters					
sPAP, mmHg	72±19	73.6±23.4	74.2±16	69.4±17.8	0.67
Pgr, mmHg	62.1±19.4	69.5±29	64.5±15.5	58.7±18.4	0.51
RV, mm	38 (34–47)	40.5 (33–49)	36 (34–42)	39 (35–47)	0.64
TAPSE, mm	17.9±4.8	18±5.5	18.7±4.9	17.1±4	0.70
RA area, cm^2	24.6 (18.2–32.0)	24.3 (17.6–36.0)	29.5 (20.8–41.0)	23.0 (19.9–32.0)	0.43
RVOT VTI, cm	10.9±3.7	12.2±3.8	10.9±2.7	9.5±4.2*	<0.05
RVOT AT, msec	81.5±30.8	87.4±36.7	74.5±23.5	81.9±30.8	0.55

Data are presented as mean ± standard deviation or median (IQR). Groups were compared with ANOVA and Kruskal–Wallis test. *p<0.05 vs. PAH
CI: cardiac index, CTEPH: chronic thromboembolic PH, HPH: PH due to lung disease, PH: pulmonary hypertension, PAH: pulmonary arterial hypertension, PAC: pulmonary artery compliance, PH: pulmonary hypertension, s/m/dPAP: systolic/mean/diastolic pulmonary artery pressure, PCWP: pulmonary capillary wedge pressure, Pgr: pressure gradient, PP: pulse pressure, PPf: fractional pulse pressure, PVR: pulmonary vascular resistance, RA: right atrium, RAP: right atrial pressure, RV: right ventricle, RV: right ventricular, RVOT AT/VTI: right ventricular outflow tract acceleration time/velocity time integral, RVSWI: right ventricular stroke work index, SV: stroke volume, TAPSE: tricuspid annular plane systolic excursion

Echocardiography

Echocardiography was performed with Mindray DC-70 X-Insight instrument (Shenzhen Mindray Bio-Medical Electronics Co., Shenzen, China). RA measurements were assessed in the apical 4-chamber view. RA area was estimated by planimetry at the end of ventricular systole (largest volume), tracing from the lateral aspect of the tricuspid annulus to the septal aspect, excluding the area between the leaflets and annulus, after the RA endocardium. The RV dimension was measured from a right ventricle-focused apical four-chamber view at the end of the diastole. TAPSE was acquired by placing an M-mode cursor through the tricuspid lateral annulus and measuring the amount of longitudinal motion of the annulus at peak systole in the apical 4 chamber view. Right ventricular outflow tract velocity time integral (RVOT VTI), right ventricular outflow tract acceleration time (RVOT AT) and ejection time (RVOT ET) was measured on pulsed wave tracings in parasternal short axis view at the aortic level. From the apical 4 chamber peak velocity TR tracings we calculated the right atrial-right ventricular pressure gradient to better characterize the hemodynamic state. To calculate the pulmonary arterial systolic pressure, we added the right atrial pressure to the pressure gradient according to the ASE recommendation based on the size and the change in respiration of the inferior vena cava (2, 19).

Blood tests

N-terminal pro B-type natriuretic peptide (NTproBNP) concentration and arterial blood gases were measured.

Statistical analysis

Subject characteristics are expressed as mean ± standard deviation (SD) or median (interquartile range, IQR), and were assessed using ANOVA or *Kruskal-Wallis* tests, depending on the distribution of the variable. For multiple comparisons, the significance values were adjusted by the Bonferroni correction. Categorical variables were compared with Chi-square or Fisher-exact test as appropriate. We used Spearman correlation to examine the relationship between hemodynamic and echocardiographic parameters. Probability values <0.05 were considered significant. Data analysis was carried out by IBM SPSS Statistics software system for Windows, version 27 (IBM Corp., Armonk, NY, USA).

TABLE 3. Correlation analysis between PVR and echocardiographic parameters

	All PH		PAH		CTEPH		HPH	
	R	p	R	p	R	p	R	p
RVOT VTI, cm	–0.25	0.07	–0.61	<0.05	–0.31	0.26	0.16	0.53
RVOT AT, msec	–0.37	<0.05	–0.52	<0.05	–0.12	0.66	–0.58	0.01
RV, mm	0.14	0.30	–0.58	<0.05	–0.40	0.13	0.11	0.65
RAA, cm^2	0.24	–0.34	0.71	<0.05	0.26	0.35	0.22	0.35
TAPSE, mm	–0.34	<0.05	–0.72	<0.05	–0.44	0.13	–0.06	0.78

Data were analyzed with Spearman correlation, and correlation coefficients are shown. Significant correlations are highlighted in bold. CTEPH: chronic thromboembolic pulmonary hypertension, HPH: pulmonary hypertension due to lung disease, PAH: pulmonary arterial hypertension, RAA: right atrial area, RV: right ventricular, RVOT AT: right ventricular outflow tract acceleration time, RVOT VTI: right ventricular outflow tract velocity time integral, TAPSE: tricuspid annular plain systolic excursion

Results

Subject characteristics

There was no difference in gender ratio, body surface area among PH subgroups, but patients with PAH were younger than HPH patients. Hypoxemia was more pronounced in patient with HPH, who also presented hypercapnia with unchanged pH vs. the other groups. There was no difference in NTproBNP level or functional capacity among the groups *(Table 1)*. RHC indicated moderate to-severe increases of mPAP and PVR parallel with decreased cardiac index in the whole population *(Table 2)*. Vasoreactivity was not observed in any PAH patient.

Comparison of hemodynamic and right ventricular parameters in different PH subgroups

Hemodynamic parameters characterizing the severity of pulmonary hypertension such as PVR, mPAP and CI did not show a difference among the 3 subgroups *(Table 2)* but dPAP was significantly higher in PAH than in CTEPH and HPH (p<0.05). Hemodynamic parameters as PAC and PPf, which characterize the degree of pulmonary arterial remodeling did not differ either among in different PH subgroups (all p>0.05). Interestingly, RVOT VTI and RVSWI, measures of RV function and adaptation, were reduced in HPH compared to patients with PAH or CTEPH (p<0.05), but other right heart parameters (RV diameter, RA area, TAPSE, RVOT AT) remained similar in the subgroups.

The relationship between PVR and hemodynamic parameters of arterial remodeling

We examined the relationship between the severity of pulmonary circulation damage i.e. PVR and other parameters which characterize the degree of arterial remodeling such as PAC and PPf. PVR showed an inverse, hyperbolic correlation to PAC in the total cohort (p<0.05, r=–0.661). A significant relationship was also detected in the separate subgroups (PAH p<0.05, r=–0.7; CTEPH p<0.05, r=–0.525; HPH p<0.05, r=–0.793). PPf, which is related to the severity of arterial remodeling and pulse wave propagation, did not show relationship with PVR (p=0.22, r=–0.171) *(Figure 1)*.

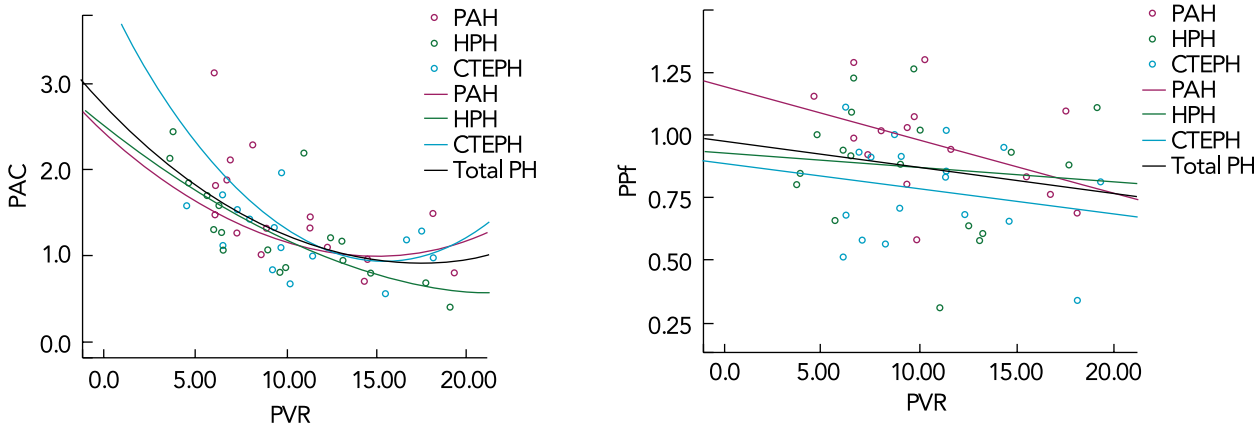

FIGURE 1. Left: inverse, hyperbolic correlation between PAC and PVR (p<0.05, r=–0.661). Correlation data for the subgroups are in the results. Right: no correlation between PPf and PVR in precapillary PH groups (p=0.22, r=–0.171
CTEPH: chronic thromboembolic pulmonary hypertension, HPH: pulmonary hypertension due to lung disease, PAH: pulmonary arterial hypertension, PAC: pulmonary arterial compliance, PPf: fractional pulse pressure, PVR: pulmonary vascular resistance

The relationship between PVR and echocardiographic parameters of right ventricular adaptation

In the whole population, PVR showed a significant correlation to RVOT AT, TAPSE and Pgr, but there was no relationship with RVOT VTI, RV diameter or RA area. Examining PH subgroups of different etiologies separately, in PAH all parameters including RVOT VTI, AT, TAPSE, RV diameter and RA area showed correlations with PVR. In the HPH group, only RVOT AT had a significant correlation with PVR, but no parameters in the CTEPH group showed a significant relationship *(Table 3)*.

Discussion

Pulmonary vasculopathy

Precapillary PH is a progressive disease. Progression is primarily determined by the degree of vascular pathological disorders, such as arterial remodeling, obstruction of arterial branches and damage of the vascular bed. In different precapillary PH groups the vascular alterations can be evaluated more accurately by PVR, as well as by the use of some further calculated invasive parameters, such as PAC (12). Changes in PAC in PH depend on a number of factors, including pressure in pulmonary arteries and elasticity of the arterial wall. The amount of elastin fibers and collagen, pathological disorders in the distal and proximal pulmonary arteries (4, 11), the presence of thrombi and the total cross-sectional diameter of arteries influence the elasticity. An inverse, hyperbolic relationship between PVR and total PAC in PAH and CTEPH is well-known, but relatively little is known about HPH in this regard (20, 21). Raui-Caro and coworkers previously described this hyperbolic relationship between PVR and PAC in PAH and CTEPH patients and they found that CTEPH enhanced RV afterload, as compared to PAH, by increasing the hemodynamic parameters related to the pulsatile load (22).

In the current study, we describe how PVR correlates with the invasively measured PAC in a mixed group of patients with precapillary PH. PVR showed in our data also an inverse, hyperbolic correlation to PAC in the total cohort, but as a new result, our data also confirmed a significant relationship in all the subgroups, including HPH *(Figure 1)*. However, we did not find a significant difference in PAC between PH subgroups. Thus it appears to be a good indicator of the severity of vascular remodeling, but not a valuable enough parameter to assess specific etiological differences of vascular abnormalities. We also calculated the correlation between PVR and some echocardiographic parameters of right ventricular functions in different PH groups. Such a link could only be justified in the PAH group.

Pressure wave propagation and RV adaptation

In pulmonary arteries, pressure wave propagation and wave reflection also vary in accordance with different pathological backgrounds. In CTEPH, the presence of proximal thrombi causes early pulse reflection and increased pulmonary pressure waves. The function and stiffening of large pulmonary arteries can be characterized by PP and PPf (12). PPf is known to be significantly higher in CTEPH than in PAH (17). In HPH, due to chronic hypoxia, remodeling and stiffening can be detected in both distal and proximal pulmonary arteries. It can be presumed that this causes a difference in wave propagation in pulmonary arteries in the different subgroups but there are limited data on the hemodynamic effects of the involvement of large pulmonary arteries in HPH. In our study, PPf values were higher in CTEPH and HPH than in PAH with a trend for significance due to limited sample size. Hence, RV adaptation varies from patient to patient, depending not only from the severity of PVR increase, but also being influenced by several other factors, including etiology. Understanding these mechanisms is crucial, as this significantly determines the life expectancy of patients. Evaluation of RV adaptation is not a simple task. Although the gold standard for measuring volumetric and functional right ventricular Parameters is cardiac MRI, this test requires specialized equipment and medical staff, consequently limiting the access. On the other hand, the widely available echocardiographic parameters can routinely be used – even bedside – to follow right ventricular dysfunction. Some of these parameters play significant role in the risk stratification and management of therapy (2, 23, 24) and have a correlation with hemodynamic parameters (25). Little has been known about the differences in certain echocardiographic parameters in right ventricular adaptation in PH groups of various etiologies.

In this regard we could not prove any alterations in the routinely used parameters among different pre-capillary PH groups *(Table 2)*. Analyzing the relationship between right ventricular parameters and the severity of PH in the total patient population and in all subgroups, the ventriculo-atrial pressure gradient (Pgr) calculated from TR maximal velocity showed a significant correlation with PVR. Interestingly only in PAH but not in CTEPH and HPH. Several further right heart parameters also presented a significant correlation with PVR. This discrepancy can be explained by the presence of other factors in CTEPH and HPH including age and comorbidities, which can also affect right heart function. Based on all of this, Pgr may well characterize the severity of PVR in precapillary PH in general, while in PAH, on the other hand, changes in the right ventricular parameters can follow the progression of the disease much better than in other subgroups.

Right ventricle stroke work index (RVSWI)

In addition to imaging studies, certain measured and calculated hemodynamic parameters are also used for the evaluation of right ventricular adaptation. RVSWI is

a hemodynamic index for characterization of RV systolic function and RV work, which depend not only from RV morphology, but is also influenced by hemodynamic changes and the metabolic state of myocardium. Early studies confirmed the prognostic value of this parameter i.e. lower RVSWI was significantly associated with death or readmission due to heart failure (HF) in patients with PAH and CTEPH (18).

Within our PH group with similar hemodynamic severity and with similar right ventricular function and volumes, RVSWI was significantly lower in HPH than in PAH. We were able to state a new finding that low RVSWI in the HPH group was a sign of a worse prognosis. Between CTEPH and HPH RVSWI difference did not reach the level of significance. The true clinical relevance of this difference is questionable, but based on these findings, differences in right ventricular functional adaptation in HPH can be assumed. However, the long-term prognostic role of RVSWI in the different subgroups of precapillary PH needs further evaluation.

Conclusion

Most hemodynamic and echocardiographic parameters were similar in PH subgroups with different etiologies. The severity of PH as measured by PVR is related to the calculated pulmonary arterial compliance not only in PAH and CTEPH, but also in HPH, thus, this association is independent of the pathomechanism of vascular abnormalities. Furthermore, PVR shows an association to right ventricular functional parameters as measured by echocardiography only in patients with PAH. The different degree of right ventricular adaptation in the various subgroups of PH is shown by an invasive parameter, RVSWI.

Declaration of interest

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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