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Which Type of Right Ventricular Pressure Overload Is Worse? An Echocardiographic Comparison Between Pulmonary Stenosis and Pulmonary Arterial Hypertension

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Background: Some studies have evaluated the right ventricular (RV) function in volume-overload and pressure-overload conditions and have always categorized pulmonary arterial hypertension (PAH) in the latter group. However, PAH and pulmonary stenosis (PS) are two frequent diseases, both resulting in the RV pressure overload.

Objectives: The aim of this study was to evaluate the RV response to two causes of the RV pressure overload: severe PAH and PS.

Patients and Methods: Eighteen patients with PAH at a mean age of 43 ± 12 years (66.6% female) and 16 patients with PS at a mean age of 33 ± 17 years (56.35% female) were enrolled. Standard echocardiography, tissue Doppler, and longitudinal strain imaging at the base, mid, and apical levels of the RV free wall were done.

Results: Significant tricuspid regurgitation was more prevalent in the PAH group than in the PS group (61% vs. 18.5%; $P < 0.001$). The abnormalities in the RV myocardial performance index, RV areas, and RV fractional area change were significantly more robust in the PAH group (all Ps < 0.05) despite the higher net RV systolic pressure in the PS group as compared to the PAH group (121 ± 39 vs. 88 ± 26 mmHg; $P < 0.001$).

Conclusions: It seems that severe PAH aggravates the RV function more severely.

Keywords: Stenosis; Hypertension; Pressure

1. Background

Once the right ventricle (RV) was called "the forgotten ventricle" (1); and with the progressive rate of atherosclerosis and its complications, most of the studies were focused on the left ventricle (LV). Nevertheless, the RV has a complex shape complicating the objective and precise assessment of the RV systolic function by echocardiography. The normal RV is a crescent-shaped structure wrapped around the LV and cannot be completely assessed in any single two-dimensional (2D) view. So, the assessment of the RV structure and function remains mostly qualitative and many clinicians rely on the visual assessment of the RV size and function (2, 3). Some studies have evaluated the RV function in volume-overload and pressure-overload conditions and have always tended to classify pulmonary arterial hypertension (PAH) in the latter group (4, 5). PAH and pulmonary stenosis (PS) are two frequent diseases, both resulting in the RV pressure overload.

2. Objectives

The aim of this study was to determine whether the RV function is similarly influenced by PAH and PS or whether one is more compromising than the other, keeping in mind that both conditions elevate the RV systolic pressure.

3. Patients and Methods

3.1. Patients

Eighteen patients with severe mostly idiopathic PAH, defined as the RV systolic pressure (pulmonary arterial pressure) ≥ 60 mmHg estimated by echocardiography, were enrolled. The PS group included 16 patients with severe valvular and/or subvalvular stenosis and RV systolic pressure ≥ 60 mmHg.

The exclusion criteria were comprised of:

1) Significant left-sided valvular heart disease (more than mild to moderate);

2) LV systolic dysfunction even with a mild degree (LV ejection fraction [LVEF] < 50-55%);

3) Any rhythm other than sinus rhythm;

4) Complete left or right bundle branch block;

5) Right-to-left shunt or Eisenmenger's complex;

6) Definite severe tricuspid regurgitation and/or malcoapted tricuspid valve;

7) Poor echo views.

Given the possibility of coronary artery disease in older age, all the controls > 40 years underwent exercise electrocardiography or stress echocardiography and the negative ones were enrolled.

The study protocol was approved by the institutional review board. All the subjects provided written informed consent before participation.

3.2. Transthoracic Echocardiography

All the patients underwent standard echocardiography using the American Society of Echocardiography (ASE) guidelines for transthoracic echocardiography. Tissue Doppler and Doppler-based strain imaging were done using a VIVID 7 echo machine. Three beats were stored at end expiration, and offline analysis was done for deformation studies. The LVEF was estimated by Simpson's method.

The RV fractional area change (RVFAC) was measured as:

RVFAC (%) = (RVEDA – RVESA)/RVEDA × 100

RVEDA, Right ventricular end-diastolic area; RVESA, Right ventricular end-systolic area

The RV isovolumic relaxation time (IVRTT), isovolumic contraction time (IVCT), and ejection time (ET) were measured by pulsed wave tissue Doppler from the lateral tricuspid valve annulus, and the RV myocardial performance index (RVMPI, Tei index) was calculated as: IVRTT+IVCTT/ ET

Deformation indices (RV strain and systolic and diastolic RV strain rate) were recorded from tissue Doppler imaging at the apical view with respect to minimal angle between the Doppler beam and longitudinal wall motion at base, mid, and apical levels. Tricuspid regurgitation was estimated qualitatively by visual inspection as: absent (0); mild (1);

Table 1. Demographic and Echocardiographic Data in the PAH and PS Groups and Their Age-Matched Control Groups [a, b]

Parameter	PAH (n = 18)	PS (n = 16)	P Value (PAH vs. PS)
Age, y	43 ± 12	33 ± 17	0.018
Gender			0.631
Male	6 (33)	7 (44)	
Female	12 (67)	9 (56)	
BSA, m^2	1.72 ± 0.13	1.7 ± 0.17	0.797
HR, bpm	91 ± 11	77 ± 15	0.006
LVEF, %	60 ± 6	61 ± 5	0.369
LA dimension, mm	30 ± 6	30 ± 5	0.989
IVS, mm	7.8 ± 1	7.6 ± 1	0.657
LVEDD, mm	41 ± 5	40 ± 7	0.809
LVESD, mm	25 ± 4	24 ± 6	0.837
RVD, mm	43 ± 8	37 ± 7	0.049
RV thickness, mm	9 ± 2	9.5 ± 3	0.596
RVSP, mmHg	88 ± 26	121 ± 39	< 0.001
TAPSE, mm	15 ± 5	18 ± 3	0.027
IVC, mm	18 ± 7	16 ± 4	0.263
Moderatetosevere TR, %	61	18.75	< 0.001
IVRT, ms	96.11 ± 42.18	70.13 ± 38.7	0.073
IVCT, ms	59.05 ± 18.75	62.91 ± 19.38	0.568
RVMPI	0.65 ± 0.19	0.43 ± 0.11	0.001
RVEDA, cm^2	24.82 ± 6.04	20.21 ± 6.21	0.036
RVESA, cm^2	16.41 ± 5.61	11.66 ± 5.02	0.014
RVFAC, %	36 ± 11	43 ± 9	0.039
S-Base, %	-16.50 ± 9.65	-15.72 ± 7.46	0.756
S-Mid, %	-15.55 ± 6.28	-15.01 ± 7.34	0.787
S-Apex, %	-18.15 ± 7.95	-15.86 ± 3.65	0.211
SR-Base-S	-0.99 ± 0.42	-0.93 ± 0.62	0.754
SR-Base-E	1.10 ± 0.65	0.89 ± 0.47	0.568
SR-Mid-S	-0.85 ± 0.24	-0.79 ± 0.25	0.596
SR-Mid-E	1.30 ± 0.98	1.04 ± 0.61	0.346
SR-Apex-S	-1.18 ± 0.83	-0.80 ± 0.20	0.022
SR-Apex-E	1.01 ± 0.67	1.36 ± 1.06	0.273

[a] Abbreviations: PAH, Pulmonary arterial hypertension; PS, Pulmonary stenosis; BSA, Body surface area; HR, Heart rate; LVEF, Left ventricular ejection fraction; LA, Left atrium; IVS, Interventricular septum; LVEDD, Left ventricular end-diastolic dimension; LVESD, Left ventricular end-systolic dimension; RVD, Right ventricular dimension; RV, Right ventricle; RVSP, Right ventricular systolic pressure; TAPSE, Tricuspid annular plane systolic excursion; IVC, Inferior vena cava; RVMPI, Right ventricular myocardial performance index; RVEDA, Right ventricular end-diastolic area; RVESA, Right ventricular end-systolic area; RVFAC, Right ventricular fractional area change , SR, Strain and strain rate.

[b] Data are presented as mean ± SD or No.(%).

Table 2. Associated Abnormalities in the PS Group (n= 16) [a]

Abnormality	No. (%)
Mild PI	5 (31.25)
Mild to moderate PI	5 (31.25)
Bicuspid PV	1 (6.25)
Small PFO	4 (25)
Very small VSD	1 (6.25)

[a] Abbreviations: PI, Pulmonary insufficiency; PV, Pulmonary valve; PFO, Patent foramen ovale; VSD, Ventricular septal defect.

Table 3. Results from the Multivariate Logistic Regression Analysis Performed on Patients in the PAH and PS Groups [a]

Variable	B	S.E.	Exp (B)	Sig.
Age	-3.105	469.743	0.045	0.995
HR	-0.694	1620.470	0.500	0.876
RVD	101.549	20829.753	1.265	0.996
TR	-75.246	10013.483	0.000	0.994
RVSP	1.071	272.971	2.918	0.997
TAPSE	-6.208	4761.580	0.002	0.999
RVMPI	-320.634	70109.631	0.000	0.996
RVEDA	-16.364	4128.104	0.000	0.997
RVESA	8.768	5895.249	6427.059	0.999
RVFAC	522.223	86588.136	6.288	0.995
Constant	127.440	231898.059	2.222	0.965

[a] Abbreviations: HR, Heart rate; PAH, Pulmonary arterial hypertension; PS, Pulmonary stenosis; RVD, Right ventricular dimension; RVEDA, Right ventricular end-diastolic area; RVESA, Right ventricular end-systolic area ; RVFAC, Right ventricular fractional area change; RVMPI, Right ventricular myocardial performance index; RVSP, Right ventricular systolic pressure; TAPSE, Tricuspid annular plane systolic excursion; TR, Tricuspid regurgitation.

mild to moderate (2); moderate (3); and more than moderate (4). The RV systolic pressure was estimated from tricuspid regurgitation velocity (modified Bernoulli's equation) and by adding the estimated right atrial pressure based on the ASE guideline for the assessment of the RV (5).

3.3. Statistical Analysis

All the analyses were conducted using Statistical Package for Social Sciences (SPSS) software, version 19 (SPSS Inc., Chicago, IL, USA). A descriptive analysis of the demographic and echocardiographic data of the patients was performed. The categorical variables are presented as numbers and percentages and the quantitative variables as means ± standard deviation. Comparisons were made between the groups of patients using the chi-square test for the categorical data and the independent sample T test, as appropriate. All the P values were two-tailed, and a P value of < 0.05 was considered statistically significant.

4. Results

The demographic and echocardiographic data in the PAH and PS patients are listed in Table 1.

The mean ± SD of the pulmonary valve gradient was (91.12 ± 13.76) in the PS group. The data of the most important associated abnormalities in the PS group are illustrated in Table 2.

The PAH patients were about a decade older than the PS patients, and 66.6% of the PAH patients were female versus 56.3% of the PS group. Significant tricuspid regurgitation was more prevalent in the PAH group as compared to the PS group (61% vs. 18.5%; $P < 0.001$). The RV systolic pressure was significantly higher in the PS group than in the PAH group (121 ± 39 vs. 88 ± 26 mmHg; $P < 0.001$), but it was totally discordant with the RV areas, RVFAC, and RVMPI changes between the two groups.

Among the strain and strain rate parameters (Table 1), the systolic strain rate at the RV apex was the only index which was significantly different between the patients with PAH and PS (-1.18 ± 0.83 vs. -0.80 ± 0.20; $P = 0.022$; respectively).

5. Discussion

Although there are many reports about the differences of the LV remodeling in response to various pathologies that put pressure overload on this chamber, similar studies about the RV are rare. In the present research, we sought to compare how the RV acts in the presence of pressure overload compared to normal individuals and also to find out whether there are any differences between the different pathologies that cause pressure loading on this chamber. The most important tissue Doppler imaging characteristics of PAH should be strain, systolic and diastolic SR (S, E) reduction and significant prolongation of IVRT over the tricuspid annulus. These have been confirmed by several other investigators (5-9), but this was confirmed for PS as well by a study conducted by Sutherland et al. (10). It is notable that in the ASE guideline (11), RVFAC < 35% and RVMPI > 0.55 are considered abnormal. According to our results, the PAH patients had lower RVFAC (36 ± 11% vs. 43 ± 9%; $P = 0.039$) and higher RVMPI (0.65 ± 0.19 vs. 0.43 ± 0.11; $P = 0.001$) as compared to the PS patients. Similar findings were reported in a nearly recent study by Jurcut et al. who concluded that at similar levels of pressure overload, the RV is less dilated and performs better in patients with PS compared with those with PAH (12). This suggests that the RV could activate intrinsic mechanisms that allow it to cope with increased afterload. They also noticed that although some RV functional parameters were comparable with those of healthy individuals, SR showed lower values, suggesting subclinical longitudinal dysfunction in patients with PS. However, the systolic strain rate at the apex was the only tissue-Doppler derived index which was significantly different between our PAH and PS patients. Tricuspid regurgitation severity was greater in the patients with

PAH, which can expose this group of patients to some degree of RV volume overload. This volume overload could relatively be involved in the worse condition of the RV in the PAH group, which is compatible with the study of Gondi et al. (13). The presence of some chemical mediators could also be responsible for the worse RV function in these patients.

5.1. Study Limitation

Our study has some potential limitations that should be addressed here. The main limitation of our study was its relatively small sample size, which could limit the generalizability of our results. Moreover, the use of tissue Doppler strain imaging, against 2D strain, always has the disadvantage of angle dependency (10, 14). On the other hand, myocardial strain and strain rate can be measured in all dimensions (longitudinal, radial, and circumferential), while we only quantified the longitudinal strain and SR. In addition, we considered the possibility of coronary artery disease in the controls, but the PAH patients also may be at coronary artery disease risk. The right coronary artery is the primary coronary supply to the RV and in fewer than 10% of hearts, the poster lateral branches of the left circumflex artery supply a portion of the posterior RV free wall (11). Hence, the RV myocardial ischemia, if present, would affect the strain and other RV functional parameters (10, 14). Our study demonstrated that severe PAH seems to aggravate the RV function more severely compared to PS. However, to better elucidate the role of the RV echocardiography in assessing various types of the RV pressure overload states and its application to discriminate between idiopathic primary PAH and PS patients, further studies with larger study patients are strongly encouraged.

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