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Original Article

Comparisons Between the Effects of Right Ventricular Pressure and Volume Overload on Ventricular-Arterial Coupling

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ABSTRACT

Background: In congenital heart disease, the right ventricle (RV) has been the forgotten chamber for many decades. Congenital atrial septal defect (ASD) leads to volume overload on the RV, while pulmonary hypertension (PH) results in pressure overload. Three-dimensional echocardiography is noninvasive and has become a readily available method for assessing the RV-PA coupling ratio through the division of the RV stroke volume (SV) by RV end-systolic volume (ESV), correlating with RV function. We sought to compare this ratio between ASD (RV volume overload) and PH (RV pressure overload) groups.

Methods: Ninety patients were divided into 3 equal groups: congenital ASD, PH, and control. Electrocardiography-gated 2D and 3D echocardiographic studies were performed on the study population.

Results: The ASD and PH groups showed statistically significant differences regarding RV volume and the RV-PA coupling ratio compared with the control group. However, the PH group was affected more than the ASD group concerning the RV-PA coupling ratio, with the mean coupling ratio being 1.14 in the ASD group, 0.77 in the PH group, and 1.25 in the control group. The *P* value between the ASD and control groups was 0.054, while the *P* value between the PH and control groups was below 0.0001.

Conclusions: The RV-PA coupling ratio, measured by 3D echocardiography (RVSV/RVESV), was markedly reduced (uncoupling) in the PH group and to a lesser extent in the ASD group compared with the control group. ***(Iranian Heart Journal 2023; 24(3): 54-61)***

KEYWORDS: ASD, PH, 3D ECHO, RV-PA coupling

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In congenital heart disease, the right ventricle (RV) has often been forgotten. However, the last decade has witnessed an increasing focus on the RV to avoid the adverse outcomes possibly associated with RV dysfunction and fibrosis. These outcomes include not only exercise limitation and RV failure but also, more importantly, lethal ventricular arrhythmias. [1]

Atrial septal defect (ASD) leads to volume overload on the RV. The hallmarks of such cases are RV dilatation, hypertrophy, and a predominantly diastolic leftward shift of the septum. RV dilatation leads to increased wall tension and afterload. RV contractility remains preserved for a long time. Nonetheless, the contractile reserve may be compromised. Chronic volume overload may finally result in RV systolic dysfunction, increasing morbidity and mortality. [2]

Pulmonary hypertension (PH) is defined as a mean pulmonary artery pressure of ≥ 25 mm Hg. PH has many etiologies and is classified into 5 groups. Group I is pulmonary arterial hypertension (PAH). In this group, idiopathic PAH is considered the most common etiology. Group II involves PH due to left heart disease and is considered to be the most common cause of PH. Group III PH is due to lung diseases. Group IV is caused by chronic pulmonary thromboembolism, and Group V PH is created by miscellaneous causes. [3]

Three-dimensional echocardiography (3DE) is readily available and is a noninvasive method for assessing RV volume and ejection fraction (EF), correlating strongly with cardiac magnetic resonance evaluation. Both RV contractility and RV afterload must be determined to assess RV function. RV function can be evaluated noninvasively through the RV-pulmonary artery (PA) coupling ratio, which can be calculated by dividing stroke volume (SV) by end-systolic volume (SV/ESV) obtained from the 3DE of the RV. [4]

The use of echo-derived RV-PA coupling ratio has been growing over the past years in multiple aspects. Nevertheless, to our knowledge, no studies have to date applied the RV-PA coupling ratio derived from 3DE to assess the RV in pediatric patients with ASD (volume overload). Accordingly, we aimed to study the effects of volume overload as represented in patients with congenital ASD on the RV-PA coupling ratio and compare them with PH and control groups.

METHODS

The study protocol received approval from the Ethics Committee of Ain Shams University, Cairo, Egypt. The present prospective cross-sectional study was conducted on 90 subjects, comprising both males and females, who were distributed equally among 3 groups: the ASD group (30 patients with congenital ASD), the PH group (30 patients with Group I PH), and the control group (30 subjects). Subjects were randomly selected via convenience sampling from those referred to the Echocardiography Unit in the Cardiology Department at Ain Shams University Hospital between August 2020 and January 2022. The exclusion criteria consisted of categorization in the other groups of PH, prior surgical operations requiring the operative manipulation of the RV, arrhythmias, comorbidities (hepatic or renal), and insufficient ultrasound image quality.

Height in centimeters and weight in kilograms were measured to estimate the body surface area in the square meter (the Haycock formula).

Full electrocardiography (ECG)-gated echocardiographic studies in the left lateral position were performed by a pediatric echocardiographer using the GE Vivid E95 echocardiography machine with an M4S matrix sector array probe at a frequency of 2.5 MHz (General Electric Vingmed Ultrasound, Horten, Norway). The echocardiographic study included situs, atrioventricular (AV) and ventricular-arterial (VA) connections, the relationships and abnormalities of the great vessels, ventricular dimensions and functions, the state of the cardiac valves, venous connections, and PA pressure.

For the evaluation of RV systolic function, fractional area change was calculated using the following equation:

$$\frac{(End\ Diastolic\ area) - (End\ Systolic\ area)}{(End\ Diastolic\ area)}\ x100$$

In the RV-focused apical 4-chamber view, the RV area was obtained by tracing the endocardial tissue border from the tricuspid annulus to the apex and back to the annulus again. Measurements were obtained at end-diastole and end-systole; then, the fractional area change of the RV was calculated. Within the area measured, the papillary muscles, trabeculations, and moderator bands were included. RV dysfunction was defined by a fractional area change of less than 35%.[5]

Tricuspid annular plane systolic excursion (TAPSE) was evaluated in the anterior 4-chamber view with the M-mode along the lateral tricuspid annulus. The total tricuspid annular displacement (mm) was measured from end-systole to end-diastole. RV systolic dysfunction was determined if values were less than 16 mm. [5]

Tissue Doppler imaging was performed in the anterior 4-chamber view with the tissue Doppler mode. The pulsed Doppler cursor was placed at the tricuspid annulus of the RV free wall. The velocity (S') was defined as the highest systolic velocity, with the result considered abnormal if values were less than 9.5 cm/s. [5]

For the measurement of the right ventricular systolic pressure (RVSP), the simplified Bernoulli equation (RVSP = 4 × tricuspid regurgitation velocity max^2 + right atrial pressure) was used. RVSP and right atrial pressure were calculated according to the size and collapsibility of the inferior vena cava. [6]

Next, 3DE-derived parameters were obtained using a wide-angle broadband 4V (GE E95) matrix-array transducer. The subjects were examined in the left lateral position, and all the studies were ECG-gated. The RV cavity volume measurement during the cardiac cycle was done using a semi-automated segmentation algorithm. An initial 3D deformable model of the RV endocardium, the tricuspid valve plane, and the RV outflow tract was located and scaled using user-defined landmarks to initialize the algorithm. The extended Kalman filter, which integrates RV geometry, is a motion model that involves tissue tracking and edge-detection techniques, determining the deformation of the 3D model. [7-9] The fully integrated 4D Auto RVQ Workflow tool was used to analyze and obtain the results, including RV end-diastolic volume (EDV), ESV, SV, 3D-estimated RVEF, and the 3D model of the RV. The RV-PA coupling ratio was then obtained through the division of RVSV by RVESV. [4]

Statistical Analysis

IBM SPSS Statistics, version 25, was used to gather, code, tabulate, and finally statistically analyze the data (IBM Corporation, Armonk, NY, USA). Categorical variables were presented as percentages and numbers using the χ^2 test. Mean and standard deviation (SD) were utilized to evaluate continuous variables. The Student *t* and Mann-Whitney *U* tests were applied to determine whether the above variables passed or failed normality tests, respectively. The Pearson correlation coefficient (*r*) and the Spearman correlation were employed to examine correlations. A *P* value of less than 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

The present study recruited 90 patients divided into 3 equal groups: the congenital

ASD group, consisting of patients with right-sided volume overload, the PH group, composed of patients with right-sided pressure overload, and the control group. The baseline clinical characteristics of the patients are summarized in Table 1. The study population was comprised of 37 males and 53 females. There were no statistically significant differences between the 3 groups regarding sex or age.

Comparisons between the ASD and control groups

The echocardiographic characteristics in the ASD and control groups are summarized in Table 2, which shows that the ASD group had a significantly higher EDV index, ESV index, and SV index, indicating volume overload. However, no significant differences existed between the 2 groups regarding EF and RVSP.

The coupling ratio obtained from 3DE data through the division of SV by ESV was less in the ASD group than in the control group (1.14 +/- 0.2 vs 1.25 +/- 0.22, respectively; *P* =0.054).

Comparisons between the PH and control groups

The echocardiographic characteristics of the PH and control groups are summarized in Table 3, which demonstrates statistically significant differences apropos of the EDV index, the ESV index, the SV index, and RVSP indicating RV pressure overload. EF was significantly reduced in the PH group compared with the control group (*P* <.00001). The coupling ratio was significantly less in the PH group than in the control group (0.77 +/- 0.22 vs 1.25 +/- 0.22 respectively; *P* <0.0001).

Comparisons between the ASD and PH groups

The comparisons between the ASD and PH groups are summarized in Table 4. There were statistically significant differences between the 2 groups vis-à-vis the ESV index, RVSP, and EF. A significant increase was reported in the ESV index and RVSP in the PH group compared with the ASD group (*P* =0.0009 and *P* <0.0001, respectively). There was also a significant reduction in EF in the PH group (*P* <0.0001). The coupling ratio was significantly reduced in the PH group compared with the ASD group (*P* <0.0001). The coupling ratio in the ASD group showed a trend toward the control group, unlike the PH group, in which the coupling ratio was markedly reduced. This showed that the ASD group, as a surrogate for volume overload, had less effect on the coupling ratio than pressure overload.

Table 1: Baseline clinical characteristics of the study population

Variable	The Atrial Septal Defect Group (n =30) Mean (SD)	The Pulmonary Hypertension Group (n =30) Mean (SD)	The Control Group (n =30) Mean (SD)	N	*P* value
Age, y	11.4 (7.71)	13.6 (5.75)	11.3 (2.17)	90	0.057
BSA, m^2	1.04 (0.4)	1.39 (0.454)	1.12 (0.211)	90	<0.01
Sex male female	 13 (43%) 17 (57%)	 10 (33%) 20 (67%)	 14 (47%) 16 (53%)	 37 53	0.55

BSA, Body surface area

Table 2: Comparisons between the atrial septal defect and control groups

Variable	The Atrial Septal Defect Group (n =30)			The Control Group (n =30)			
	n	Mean	SD	n	Mean	SD	*P* value [a]
2DE							
FAC	30	45.6667	5.7854	30	50.2667	8.8002	0.0200
RVSP	30	24.2000	3.1666	30	23.7667	2.5146	0.5595
S'	30	12.7000	1.4657	30	13.6333	2.8945	0.1205
TAPSE	30	21.5667	2.7877	30	24.2667	5.8187	0.0255
3DE							
EDVI	30	67.4000	17.5864	30	40.0000	8.9558	<0.0001
EF	30	52.4000	4.6875	30	53.7667	7.5461	0.4029
ESVI	30	32.0333	7.4347	30	19.1667	6.7471	<0.0001
SVI	30	36.3000	9.6137	30	22.2333	4.2238	<0.0001
Coupling	30	1.1470	0.2094	30	1.2557	0.2192	0.0544

2DE, Two-dimensional echocardiography; FAC, Fractional area change; RVSP, Right ventricular systolic pressure; TAPSE, Tricuspid annular plane systolic excursion; S', Systolic excursion velocity; 3DE, Three-dimensional echocardiography; EDVI, End-diastolic volume index; EF, Ejection fraction; ESVI, End-systolic volume index; SVI, Stroke volume index

Table 3: Comparisons between the pulmonary hypertension and control groups

Variable	The Pulmonary Hypertension Group (n =30)			The Control Group (n =30)			
	n	Mean	SD	n	Mean	SD	*P* value [a]
2DE							
FAC	30	39.7767	6.8907	30	50.2667	8.8002	<0.0001
RVSP	30	72.3333	29.5872	30	23.7667	2.5146	<0.0001
S'	30	10.2333	1.0726	30	13.6333	2.8945	<0.0001
TAPSE	30	19.0333	3.9869	30	24.2667	5.8187	0.0001
3DE							
EDVI	30	73.4333	21.6663	30	40.0000	8.9558	<0.0001
EF	30	42.7867	7.9094	30	53.7667	7.5461	<0.0001
ESVI	30	41.7000	13.1625	30	19.1667	6.7471	<0.0001
SVI	30	31.6333	10.9497	30	22.2333	4.2238	<0.0001
Coupling	30	0.775	0.2234	30	1.2557	0.2192	<0.0001

2DE, Two-dimensional echocardiography; FAC, Fractional area change; RVSP, Right ventricular systolic pressure; TAPSE: Tricuspid annular plane systolic excursion; S', Systolic excursion velocity; 3DE, Three-dimensional echocardiography; EDVI, End-diastolic volume index; EF, Ejection fraction; ESVI, End-systolic volume index; SVI, Stroke volume index

Table 4: Comparisons between the atrial septal defect and pulmonary hypertension groups

Variable	The Atrial Septal Defect Group (n =30)			The Pulmonary Hypertension Group (n =30)			
	n	Mean	SD	n	Mean	SD	*P* value [a]
2DE							
FAC	30	45.6667	5.7854	30	39.7767	6.8907	0.0007
RVSP	30	24.2000	3.1666	30	72.3333	29.5872	<0.0001
S'	30	12.7000	1.4657	30	10.2333	1.0726	<0.0001
TAPSE	30	21.5667	2.7877	30	19.0333	3.9869	0.0060
3DE							
EDVI	30	67.4000	17.5864	30	73.4333	21.6663	0.2412
EF	30	52.4000	4.6875	30	42.7867	7.9094	<0.0001
ESVI	30	32.0333	7.4347	30	41.7000	13.1625	0.0009
SVI	30	36.3000	9.6137	30	31.6333	10.9497	0.0847
Coupling	30	1.1470	0.2094	30	0.7753	0.2234	<0.0001

2DE, Two-dimensional echocardiography; FAC, Fractional area change; RVSP, Right ventricular systolic pressure; TAPSE: Tricuspid annular plane systolic excursion; S', Systolic excursion velocity; 3DE, Three-dimensional echocardiography; EDVI, End-diastolic volume index; EF, Ejection fraction; ESVI, End-systolic volume index; SVI, Stroke volume index

DISCUSSION

The use of echo-derived RV-PA coupling has been growing over the past 3 years. The gold standard for the evaluation of RV-PA coupling is the invasive assessment of the ratio of RV end-systolic elastance (Ees) to pulmonary arterial elastance (Ea). RV contractility is obtained through the division of ESP by ESV, the result of which is termed "Ees". RV afterload can be obtained from the pressure-volume relation through the division of ESP by SV, whose result is termed "arterial elastance (Ea)". Ees/Ea represents the ventricular-arterial coupling ratio and is simplified as SV/ESV. [4] Different noninvasive methods have been proposed to calculate the RV-PA coupling ratio. For instance, Tello et al [10] (2019) compared the invasive and noninvasive assessments of RV-PA coupling and found that 2DE-derived TAPSE/PA systolic pressure was a straightforward noninvasive measure of RV-arterial coupling. On the other hand, Pei-Ni Jone et al [4] used 3DE-derived RVSV/ESV as a predictor of RV- PA coupling.

Recently, there has been growing support for the use of RV-PA coupling as a novel prognostic marker for a wide spectrum of diseases affecting the RV or the left ventricle. Pei-Ni Jone et al [4] (2019) used RV-PA coupling as a predictor of the outcome in pediatric PH. Kazimierczyk et al [11] (2021) noninvasively assessed RV-PA coupling in adult patients with PAH. In the same year, Arora et al [12] showed promising results for the use of RV-PA coupling as a predictor of mortality after transcatheter aortic valve implantation. Sandeep et al [13] studied RV-PA coupling in patients following tetralogy of Fallot repair.

To the best of our knowledge, the current study is the first investigation to compare the effects of volume overload with those of pressure overload on the RV-PA coupling using 3DE. In the current study, the RV-PA coupling ratio as measured by 3DE through the division of SV by ESV was markedly reduced (uncoupling) in patients with pressure overload (the PH group) and to a lesser extent in patients with volume overload (the ASD group) compared with the control group.

Pei-Ni Jone et al [4] studied the prognostic impact of RV-PA coupling in pediatric PH using parameters derived from 3DE and the same formula as ours where the RV-PA coupling ratio is RV (SV/ESV). They recruited 125 patients with Group I PH and 65 controls. They also included patients with idiopathic PAH and those with PAH associated with congenital heart disease. In their study, the mean age of both PH and control groups was very close to ours (9 vs 13 y and 8 vs 11 y, respectively). Moreover, RV volume indexed to the body surface area was greater in the PH group, whereas the RV-PA coupling ratio measured by 3DE was lower in the PH group, which is similar to our results.
Kazimierczyk et al [11] compared RV-PA coupling between PH and controls at a mean age of 40 years and found a significantly lower RV-PA coupling ratio in the PH group than in the control group. Their findings chime with our results except that our patients were much younger and our coupling was based on 3DE measurements rather than 2D.

In our study, we observed a difference between the ASD and control groups regarding the coupling ratio in that RV-PA coupling was less in the ASD group (*P* =0.054).
Suzuki et al [14] studied the impact of the preoperative coupling ratio on residual symptoms after ASD closure in 120 adults with ASD. There was a statistically significant difference between the ASD and control groups regarding the RV coupling ratio measured as TAPSE/PA systolic pressure. The values were lower in the ASD group than in the control group and improved 6 months after percutaneous closure. Their findings are in line with our results insofar as the coupling ratio was less in the ASD group (yet with a *P* value =0.054). However, Suzuki and colleagues used the 2DE-derived coupling ratio, whereas we utilized the 3DE-derived coupling ratio via the SV/ESV equation.
In a study by Öykü Tosun et al, [15] the results were similar to ours inasmuch as TAPSE was lower in the ASD group than in the control group. Dehong Kong et al [16] showed that 3DE-derived RV volume was significantly higher in the ASD group than in the control group, which agrees with our results.

CONCLUSIONS

To the best of our knowledge, the current study is the first study to compare the effects of volume overload with those of pressure overload on the RV-PA coupling ratio using 3DE in pediatric age. The clinical significance of the present investigation is that coupling can be used as a simpler method to assess RV function and is affected by both volume and pressure overload on the RV. Our results should be tested by future studies on larger sample sizes.

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