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ORIGINAL ARTICLE

Right Ventricular function using Speckle Tracking Echocardiography and Reversibility Of pulmonary Hypertension in simple cardiac shunts

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ABSTRACT

Background: This study was conducted to evaluate the results of simple cardiac shunt closure using trans catheter device regarding right ventricular function using speckle tracking and reversibility of pulmonary hypertension, testing the ability of echocardiography to provide unique noninvasive information with minimal risk, we aimed to detect right ventricular function in simple cardiac shunt patients before closure using longitudinal strain and to investigate its role in predicting reversibility of pulmonary hypertension after closure

Methods: This is a prospective randomized comparative study including simple shunt patients from age 25-48 years who presented to Zagazig University hospitals, cardiology department from September 2018 to July 2019. Our patients were divided into two groups Group I: ten patients were having irreversible pulmonary hypertension. Group II: Twenty patients were having reversible pulmonary hypertension.

Results: There was statistically significant increase in group II post closure regarding LVEF, RVFAC, TAPSE, SRV, RVLS ($P< 0.05$). While PASP showed significant decrease in GII post closure ($P < 0.05$). On the other hand, RVLS was negatively correlated with the defect size ($r= -0.65$; $p = <0.001$), Qp/Qs ($r = -0.53$, $p = <0.001$), PASP ($r = -0.8$, $p = <0.001$) And significant positive correlation with S_{RV}($r = 0.37$; $p = <0.001$) RVFAC ($r=0.30$, <0.001), TAPSE($r=0.34$, <0.001).findings ($P = 0.776$), RVLS value of ≥ -20 could predict reversibility of PASP with AUC 0.9 suggesting strong accuracy ($P< 0.001$). The logistic regression analysis detected that the RVLS, RVFAC, S_{RV} were independent predictors of reversibility of pulmonary hypertension ($P< 0.05$).

Conclusion: The RVLS value of ≥-20 could predict reversibility of PASP with AUC 0.9 suggesting strong accuracy ($P< 0.001$). RVLS correctly identify simple shunt patients with increased PASP (sensitivity 80%), and it correctly reports 85 % of simple shunt patients without increased PASP as true negatives, while 15% are incorrectly identified as false positive with specificity 85%.

Keywords: Pulmonary hypertension, cardiac shunts, right ventricular strain.

1. INTRODUCTION

Pulmonary arterial hypertension in congenital heart disease (PAH CHD) is reversed by early shunt closure, but this potential is lost beyond a certain point of no return. Therefore, it is crucial assess the reversibility of this progressive pulmonary arteriopathy in an early stage. Pulmonary arterial hypertension (PAH) is a lethal syndrome characterized by increased pulmonary artery pressure (m PAP), pulmonary vascular resistance (PVR) and normal pulmonary capillary wedge pressure. The diagnosis based on assessment of these hemodynamic values, and clinical presentation predominantly comprises symptoms of resulting right heart failure [1]

PAH, have already progressed to an irreversible stage in which current targeted therapy may stabilize or decelerate progression, but cannot cure the disease [2].

However, the beneficial effects of shunt closure seem lost after a certain point of no return, after which even accelerated PAH progression may occur months to years after surgery [3]

These observations underscore the critical importance of early and accurate detection of this 'window for reversibility' in patients with PAH-CHD. The assessment of reversibility, however, is nowadays primarily based on clinical judgement and measurements of hemodynamics variables, which have limitations as surrogates for the stage of the arteriopathy [4].

Techniques able to directly assess the pulmonary vasculature are still scare from clinical practice today.

2. PATIENTS AND METHODS

Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. From September 2018 to July 2019, on 30 patients with simple cardiac shunts. Were prepared to undergo Trans catheter device closure, at echocardiographic and catheterization laboratories Cardiology Department of Zagazig University.

Inclusion criteria were: 1) Significant left-to right shunt (pulmonary-systemic flow ratio > 1.5:1).; 2) Shunt-related symptoms: Shortness of breath, especially when exercising, Fatigue, Swelling of legs, feet or abdomen, Heart palpitations or skipped beats and frequent lung infections.

Exclusion criteria were: 1) Associated congenital cardiac anomalies requiring Surgery. 2) Right-to-left shunt with a peripheral arterial saturation < 95%.

All patients were subjected to the following measures: 1) complete history taking: including age,sex, symptoms of heart failure, shunt related symptoms. 2) General and local examination: Blood pressure, pulse, neck veins, Local examination of the heart for cardiomegaly, pulsations, thrills, heart sounds and murmurs. 3) Twelve lead surface ECG: To identify evidence of chamber enlargement, abnormal axis deviation, rate, and rhythm disturbances. 4)Echocardiography: is initially performed prior to and 24 hours after percutaneous trans-catheter closure of the shunt.Conventional echocardiographic Doppler study, as well as 2D speckle tracking and tissue Doppler imaging of the RV was performed using Vivid 9, General Electric Healthcare (GE Vingmed, Norway) equipped with a harmonic M5S variable-frequency (1.7 -4 MHz) &M6S phased array transducers.Study performed from subcostal, parasternal and apical windows with the patient supine or in left lateral decubitus position connected to single lead ECG. 5)percutaneous shunt closure: In all patients after antibiotic prophylaxis, general anesthesia and sterilization, arterial and venous access were gained using the seldinger's technique, the right or left femoral artery and vein were accessed and 5-6 F sheath was introduced into the artery and 6F sheath was introduced into the vein.

After the artery was accessed 100 IU⁄ Kg heparin were administrated intravenously [5]. then device implantation was done and the patient stays in hospital overnight for post device observation and discharged home the following day. Prior to the discharge a physical examination, a TTE, ECG and a chest radiograph performed to assess the device and to look for any potential complication.

3. STATISTICAL ANALYSIS

All patients' data were collected, checked, and analyzed by using (SPSS version 20). Data were expressed as mean ± standard deviation (SD) and number with (%) according to type of variable. Chi-square test (χ^2), receiver operator curve (ROC) Correlation analysis, Regression analysis were used when appropriate. P value <0.05 was considered statistically significant.

4. RESULTS

The study included 30 patients with simple cardiac shunts the studied patients were 23 females (76.6%) and 7 males (23.4%), with average age of 37.3 ± 7 years. Fourteen patients had ASD (46.6%), 10 had VSD (33.4%) and 6 had PDA (20%), with defect size ranged from 10-22 with mean 16. 8 ± 3.6 SD. QP/QS ranged from 1.9-3.3 with mean was 2.6 ± 0.4 SD. PASP ranged from 40-69 with mean 54.5±8.8 SD. Our patients were divided into two groups according to reversibility of pulmonary hypertension post closure where Reduction of mPAP ≥10 mmHg to reach an absolute value of mPAP ≤40 mmHg is considered reversible (6): Group I: ten patients, 4 males (13.3%) and 6 females (20%) with mean age 39±6.9 years were having irreversible pulmonary hypertension. Group II: Twenty patients, 3 males (10%) and 17 females (56.7%) with mean age 36.5±7.3 years were having reversible pulmonary hypertension .There was no significant difference between both groups regarding age and sex (P> 0.05).(Table1) Defect size was 19.8±1.6 mm in group I as compared to 15.3±7.5 mm in group II with significant increase in GI (P<0.001).Also, QP/QS was 2.96±0.2 in group I as compared to 2.5±0.4 in group II with significant increase in GI (P0.003) .(Table 1)

The LVEF showed significant increase in reversible cases after catheter closure. For the RV dimensions: there is significant increase in RVFAC in reversible cases after catheter closure. TAPSE showed non-significant increase in reversible cases after closure. PASP showed significant decrease in reversible cases after interventional closure. (Table 2).Tissue Doppler tricuspid annular velocity showed insignificant increase in reversible cases post closure.(Table 2).After interventional closure of the defect, we observed a significant increase of the longitudinal RV strain.(Table 3).

RVLS was negatively correlated with the defect size (r = -0.65; p = <0.001), Qp/Qs (r = -0.53, p = <0.001), PASP (r = -0.8, p = <0.001) .On other hand, It showed significant positive correlation with S RV (r = 0.37; p = <0.001) RVFAC (r=0.30, <0.001), TAPSE (r=0.34, <0.001). (Table 4).

ROC curve analysis revealed that the RVLS value of -20 could predict reversibility of PASP with AUC 0.9 suggesting strong accuracy (P< 0.001). RVLS correctly identify simple shunt patients with increased PASP (sensitivity 80%), and it correctly reports 85 % of simple shunt patients without increased PASP as true negatives, while 15% are incorrectly identified as false positive with specificity 85 .(Table5),(Fig1).

The logistic regression analysis detected that the RVLS, RVFAC, SRV were independent predictors of reversibility of pulmonary hypertension (P< 0.05) (Table6)

Table 1: Demographic data & Shunt characteristics of the studied groups

		Group(I) η =10	Group(II) η =20	t /χ2	P-value
Age(years)	x̄±SD	39±6.9	36.5±7.3	0.89	0.32
	(Range)	29-48	25-48		
Defect size	x̄ ± SD	19.8±1.6	15.3±7.5	3.8	<0.001**
	(Range)	17-22	10-22		
Qp/Qs	x̄ ± SD	2.96±0.2	2.5±0.4	3.19	0.003*
	(Range)	2.7-3.3	1.9-3.3		
Gender (η,%)	M	4 (13.3)	3 (10.0)	0.0	0.65
	F	6 (20.0)	17 (56.7)		

Table (2): Changes in PASP& S_{RV} According To Reversibility.

		Group I	Group II	t	P-value
PASP					
Pre	x̄ ±SD	51.4 ±16.3	50.4±15.5	7.4	0.9
	(Range)	60-68	42-54		
Post	x̄± SD	48.0±4	37.3 ± 2.7	12.9	<0.01**
	(Range)	59-67	37-43		
P-value		0.8	<0.001**		
S_{RV}					
Pre	x̄ ± SD	13.4 ± 3.0	13.7 ± 2.8	8.4	0.08
	(Range)	9-13	12-16		

		Group I	Group II	t	P-value
Post	x̄ ± SD	14.1±2.6	14.0 ± 2.8	6.4	<0.001**
	(Range)	9-13	12-18		
P-value		0.9	0.8		

Table (3): Changes in RVLS according to reversibility

RVLS		**Group(I)**	**Group(II)**	**t**	**P-value**
Pre	x̄ ± SD	−20.8±8.6	24.9±2.1	3.5	<0.01**
	(Range)	15-19	23-27		
Post	x̄ ± SD	−21.3±8.5	−25.6±5.5	2.1	<0.001**
	(Range)	15-19	24-30		
P-value		0.8	0.9		

Table (4): Correlation between RVLS and Other Parameters:

	R	P-value	sign
AGE	0.26	>0.05	NS
DEFECT SIZE	-0.65	<0.001**	HS
Qp/Qs	-0.53	<0.001**	HS
EF	0.04	>0.05	NS
RVFAC	0.30	<0.001**	S
TAPSE	0.34	<0.001**	S
PASP	-0.80	<0.001**	HS
S_{RV}	0.37	<0.001**	HS

Table (5): Validity of RV Strain in Predicting Reversibility of PH:

Cutoff	Sensitivity	Specificity	PV +VE - VE	Accuracy	AUC	P-value
≥-20.0	80.0%	85.0%	72.7%89.5%	83.3%	0.9	<0.001**

Table (6): Independent predictors of Reversibility of PASP:

	B±SE	95%CL	P-value
RVFAC	0.31±0.17	0.03-0.66	0.03*
S_{RV}	0.33±0.18	0.04-0.69	0.02*
RVLS	0.28±0.006	0.11-0.44	<0.001**

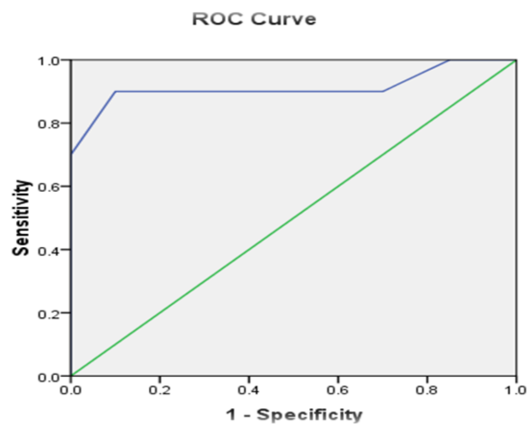

Figure (1): ROC of RV Strain in Prediction Reversibility of PH

5. DISCUSSION

Pulmonary arterial hypertension (PAH) in congenital heart disease (CHD) reversed by early shunt closure, but this potential is lost beyond a certain point of no return. Therefore, it is crucial assess the reversibility of this progressive pulmonary arteriopathy in an early stage [1]. Therefore; there is critical importance of early and accurate detection of this ‘window for reversibility’ in patients with PAH-CHD. is a crucial part in the decision for shunt closure, The assessment of reversibility however, is nowadays primarily based on clinical judgement and measurements of hemodynamics variables, which have limitations[4]

At present, no gold standard exists for the assessment of reversibility, Currently, HC is regarded the cornerstone in the diagnosis and prognostication of PAH-CHD.

Strain is a dimensionless parameter and calculated from a change in length between two points before and after movement. With some technical improvement, myocardial strain measured with echocardiographic images, and strain echocardiography introduced.

in clinical settings to offer a noninvasive and objective marker of myocardial contractility [7]

RV strain values estimated from two-dimensional speckle tracking echocardiography (2DSTE) are strong prognostic factors for several cardiovascular diseases, independent of RV ejection fraction (LVEF) Moreover; strain echocardiography can detect subclinical myocardial changes in their early stages and can be a prognostic marker for many cardiovascular diseases [8]

The studied patients showed female as a majority which agrees with Ariane et al.[9] who reported that there were significantly more females in the adult and pediatric CHD populations. In addition, our mean age was 37.3 ± 7 years, which agrees with Botto et al., [10] who reported that when all CHD lesions were considered, there have been more adults than children with CHD since 1985.

We found that majority of cases were ASD 14 (14.6%) that consists with Ariane et al. [9] who found that ASD was the most common congenital lesion in adults.

In this study the defect size mean 16.8 ± 3.6 SD which consists with Yang et al. [11] who reported that the incidence of spontaneous closure was inversely related to size of the defect, and a higher possibility of spontaneous closure can be observed in defects less than 2.85 mm. On the contrary, spontaneous closure rarely occurred in patients with defects more than 5.2 mm.

In this study, QP/QS mean 2.6 ± 0.4 SD which agrees with Yang et al. [11] who reported that spontaneous VSD closure likely to happen in patients with Qp/Qs < 1.53; conversely, spontaneous VSD closure rarely happened in patients with Qp/Qs > 2.12.

The defect size showed significant increase in GI as compared to GII (P<0.001). Which agrees with Ángel et al.[12] who found that the larger the size the defect leads to increase the severity of pulmonary hypertension that results in irreversibility But disagree with Kulik et al, [13] who found that People with a sizable ASD develop a large left-to-right shunt and occasionally develop PVO

The QP/QS showed significant increase in GI as compared to GII (p=0.003*). Which agrees with D’Alto et al. [14], who found that with increased degree of shunting are at greatest risk. But disagrees with Kulik et al. [13] who found that high pulmonary flow can be associated with normal PAP and that can be explained by that the lung is generally more flowophilic than flowphobic.

The LVEF showed significant increase in reversible cases after catheter closure. Which agrees with Kumar et al. [15] who found a significant change in LV function at each follow-up with maximum change at the end of 3 months. However, disagrees with Eroglu, et al.[16]who measured EF before closure and 24h and 1 month after closure, and found that LVEF increased immediately within 24 hours then decreased back to normal

For the RV dimensions: there is significant increase in RVFAC in reversible cases after catheter closure. Which, agrees with Islamlı1 et al.[17]that found that after closure RVFAC significantly increased comparing to before closure. But disagrees with Eroglu, et al. [16] as Right ventricular fractional area change (RVFAC) expresses the percentage change in RV area between end-diastole and end-systole so after closure of left-to-right shunt RVFAC decrease due to the decrease in RV diameters significantly

TAPSE showed non-significant increase in reversible cases after closure. Which agrees with, Balcı et al. [18] Demonstrated that TAPSE remained unchanged. They attributed that to the anatomical complexity of the right ventricle, difference in orientation of myocardial fibers, and reduced wall thickness may play a role in this result. But disagrees with Chen et al. [19] demonstrated that (TAPSE) reduced significantly after closure, which may be due to the less volume overload of the RV.

PASP showed significant decrease in reversible cases after interventional closure. Which agrees this is in agreement with Chen et al. [19] who reported similar results, and explained it that after closure, the shunt disappeared, the diastolic blood flow velocity at the tricuspid valve orifice and the systolic blood flow velocity at the pulmonary valve orifice decreased, and hemodynamic abnormalities were corrected. Our results disagree with Zwijnenburg et al. [20] who found that some patient had an increase in pulmonary pressure due to LV diastolic dysfunction.

Tissue Doppler tricuspid annular velocity showed insignificant increase in reversible cases post closure. That consists with Islamlı et al. [17] who found that in the patient group Color Tissue Doppler parameters and derivatives significantly increased after closure. However, disagrees with Akula et al. [21] reported that RV systolic velocity, tricuspid (S') decreased significantly after ASD catheter closure. Who had explained that the increased preload in right ventricle had high basal RV systolic function following Starling's law of the heart. Because the S' is, load dependent parameter, so significant decrease post-ASD device closure creating a doubt of RV systolic dysfunction.

After interventional closure of the defect, we observed a significant increase of the longitudinal RV strain. Which agrees with Moradian et al. [22] who demonstrated that peak RVLS was shown to be significantly increasing after percutaneous closure of ASD, explained by reverse remodeling effect of ASD correction on RV.But disagrees with Kumar et al.[23]who found that There was statistically significant decrease in RV global longitudinal strain after 48 h of ASD correction and decrease to near normal values at 3 months of correction.

variables correlated with RVLS strain was negatively correlated with the defect size ($r = -0.65$; $p = <0.001$), Qp/Qs ($r = -0.53$, $p = <0.001$), PASP ($r = -0.8$, $p = <0.001$) .

On other hand, It showed significant positive correlation with S RV ($r = 0.37$; $p = <0.001$) RVFAC (r=0.30, <0.001), TAPSE (r=0.34, <0.001). Which agrees with Meris et al. [24] who found that There were good correlations between global RVLS and TAPSE ($r = 0.33$, $P < .001$) and between global RVLS and RV FAC ($r = 0.43$, $P < .001$) and SRV ($r = 0.38$, $P < .001$)in the study population and this can be explained by improvement of right ventricular function and increased RVLS is associated with improvement of other RV function parameters like TAPSE,RVFAC,S_{RV}

ROC curve analysis revealed that the RVLS value of -20 could predict reversibility of PASP with AUC 0.9 suggesting strong accuracy ($P< 0.001$). RVLS correctly identify simple shunt patients with increased PASP (sensitivity 80%), and it correctly reports 85 % of simple shunt patients without increased PASP as true negatives, while 15% are incorrectly identified as false positive with specificity 85 Which agrees with Meris et al.[24] who found that RVLS cutoff value was≥ -19%, with sensitivity of 95% and specificity of 85%.

The logistic regression analysis detected that the RVLS, RVFAC, SRV were independent predictors of reversibility of pulmonary hypertension ($P< 0.05$). Which agrees with Meris et al. [24] who reported that by Using TAPSE and RV FAC as reference methods, speckle tracking–derived strain accurately identified reduced global RV function and that a global RVLS cutoff value of ≥-19% can be considered a useful means of differentiating normal and impaired right ventricles. Despite that TAPSE and RV FAC have a number of intrinsic limitations, but they are widely used in clinical practice and can be considered validated indices of global RV contractility.

6. CONCLUSION

The RVLS value of ≥-20 could predict reversibility of PASP with AUC 0.9 suggesting strong accuracy (P< 0.001). RVLS correctly identify simple shunt patients with increased PASP (sensitivity 80%), and it correctly reports 85 % of simple shunt patients without increased PASP as true negatives, while 15% are incorrectly identified as false positive with specificity 85%. The RVLS, RVFAC. SRV, were the independent variables predicting reversibility of PAH.Percutaneous closure of simple cardiac shunt results in an immediate and striking remodeling process, which shows an in homogeneous pattern and time kinesis within the RV myocardium.

Conflict of interest

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

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Ethical approval

Institutional review boards' approval was obtained.

Informed consent

Written informed consent was obtained from all patients.

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