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Salah Yassin Abood Medical City, Baghdad, Iraq Right ventricular assessment by transthoracic echocardiography in patients with pulmonary hypertension in relation with functional and hemodynamic data

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Abstract

Background: Transthoracic echocardiography is a noninvasive method commonly used to assess the right ventricular function in patients with pulmonary hypertension.

Aim of study: To determine the role of transthoracic echocardiography parameters (GLSRV, TAPSE, RVs, FAC & RIMP) to assess the right ventricular function in patients with pulmonary hypertension in correlation with functional capacity (six-min walk distance) and trans-catheter mean PAP.

Patients and methods: This is a cross sectional study including patients with pulmonary hypertension aged more than18 years at Baghdad Heart Center and Ibn Al-Baitar Heart Center from May 2019 to May 2020. All patients underwent echocardiography examination with estimation of following parameters (LVEF, FAC, TAPSE, RVs, RIMP, PASP, TR velocity, mean PAP, GLSRV) and all patients underwent six-minute walking distance test and Right heart catheterization to assess the functional capacity and pulmonary artery pressure respectively.

Results: 40 patients with varied WHO classifications of pulmonary hypertension (mean age 41.58 ± 15.49 years) and male to female ratio were included in the research (1:1.2). GLSRV had a negative linear connection with TAPSE (P=0.015) and RVs' (P=0.017) but not FAC or RIMP. The 6-MWD correlated positively with GLSRV (P = 0.011). Echo and right heart catheterization mean PAP measurements correlated (P value <0.0001). Right heart catheterization severity of pulmonary hypertension correlated with RV function echo parameters like FAC (p=0.020).

Conclusion: Global longitudinal strain of right ventricle showed high ability to detect early stage of RV failure in patients with pulmonary hypertension with high agreement of RV failure detection with 6-MWD& echocardiography parameters like RIMP & FAC.

Keywords: Pulmonary hypertension, echocardiography, six-min walk distance, right heart catheterization, strain

Introduction

Right heart catheterization (RHC) defines pulmonary hypertension (PH) as a hemodynamic and pathophysiological condition with a resting mean arterial pressure (mPAP) higher than 25 mmHg ^[1]. According to statistics, the normal mean PAP at rest is 14+3 mmHg, with an upper limit of 20 mmHg ^[2]. It is split into pre-capillary and post-capillary pulmonary hypertension. Increased pulmonary vascular resistance causes pulmonary hypertension ^[3]. Echocardiographic evaluation of pulmonary hypertension (PH) must consider the relationship between the ventricle's load from the pulmonary arteries' higher resistance and the right ventricle's contractile force (RV). Right ventricular and pulmonary artery pressures depend on these two parameters ^[4]. Traditional echocardiography estimates pulmonary artery systolic pressure (PASP) by deriving right ventricular pressure from tricuspid regurgitation (TR) velocity and qualitatively assessing right atrial pressure (RAP). Earlier investigations have shown high correlation across patient groups but modest accuracy of TR velocity-based absolute PASP values ^[5]. Clinically, RV function is assessed by 2D echocardiography. Numerous studies used echocardiographic measures to assess RV function, including TAPSE, RVs', FAC, and RIMP. Systolic velocities s' at the lateral tricuspid annulus are

Corresponding Author: Zoubaida Ali Mardan Mohammed Medical City, Baghdad, Iraq recommended for right heart function assessment by the 2010 echocardiographic recommendations for adults ^[6]. RV dysfunction is 90% sensitive and 85% specific for tricuspid annular systolic velocity s' ≤ 11.5 cm/s ^[7]. Strain is a dimensionless metric determined from the length difference between two places before and after movement. Strain echocardiography, a noninvasive and objective marker of cardiac contractility, was adopted in clinical settings after certain technological improvements. Myocardial strains indicate regional and global systolic function [8]. Strain echocardiography may also identify early myocardial changes ^[9] and be a prognostic sign for several cardiovascular diseases [10] Research on strain echocardiography increased once RV systolic function was measured. RV strain measures, specifically RV global longitudinal strain (GLSRV), outperform other traditional echocardiographic indicators of RV systolic function [11-12]. RV strain is measured using just apical-4 chamber images, unlike LV strain. Current recommendations favor focused RV or modified apical 4 chamber view [13]. Recent guidelines advocate concentrated RV perspective to decrease RV structural foreshortening ^[14]. RV strain analysis uses RVGLS total and RVGLS free wall longitudinal strain. RVGLS total value comprises ventricular septum and free wall strain values. Vendor strain value estimations vary [15]. The six-MWD is the most frequent exercise capacity test and a main endpoint in many therapeutic clinical studies. Most PAH prognostic indicators RV include resting function measurement by echocardiography or right heart catheterization (RHC)^[16]. Standard testing seldom measures exercise-induced dynamic changes. The lung's ability to recruit and distend the pulmonary vasculature lowers pulmonary vascular resistance (PVR) and raises pulmonary blood flow, increasing pulmonary artery pressure (PAP) somewhat during maximum activity. PAH pulmonary arteries are pathologically altered with decreased distensibility, making them less sensitive to exercise-induced blood flow. Exercise may drastically raise PAP, impairing RV function, increasing dead space, and decreasing blood oxygenation ^[17]. The aim of study is to determining the role of transthoracic echocardiography parameters (GLSRV, TAPSE, RVs', FAC& RIMP) in assessment of right ventricular function in patients with pulmonary hypertension in correlation with functional capacity (six-min walk distance) and trans catheter mean PAP.

Method

This cross-sectional study included patients with pulmonary hypertension from different WHO classes, aged >18 years, conducted at Baghdad Heart Center & Ibn AL-Baitar Heart Center from May 2019 to May 2020. Exclusion criteria were poor image quality, atrial fibrillation or flutter, pregnancy, and inability to walk. Echocardiographic studies were performed using a GE Vivid E9 ultrasound machine. Various parameters were estimated, including peak TR velocity, PASP, RAP, mean PAP, FAC, TAPSE, RIMP, RVs', and LVEF. Global longitudinal strain of the right ventricle (GLSRV) and time-to peak strain were calculated. GLSRV was evaluated from an RV-focused apical 4chamber view, and the endocardial borders were automatically tracked throughout the cardiac cycle. Sixminute walk distance (6-MWD) was measured following the American Thoracic Society's guideline on the standardization of 6-MWD. Pulse rate, blood pressure, and oxygen saturation (SpO2) were measured at rest, and the level of tiredness and dyspnea were determined according to the Borg scale before and after the test. Right heart catheterization (RHC) was performed using the Allura Xper FD10 system to measure pulmonary artery pressures (mean PAP). Statistical analysis was conducted using SPSS for Windows software (version 23, 2018). Continuous data were expressed as mean values (\pm standard deviation). Comparisons between two means in the group were performed using the student's test for paired samples. Pearson Correlation Coefficient (r) was calculated for Y and X continuous variables. Associated receiver operating characteristic (ROC) curves for predicted probabilities were drawn for a diagnostic model, and corresponding areas under the curve with their 95% CIs were calculated. Twotailed P-values were considered significant if below 0.05.

Results

A total of 40 patients, included different WHO classes of pulmonary hypertension (mean age 41.58 ± 15.49 years), consisting of 22 (55%) female (mean age 38.41 ± 14.90 years) & 18 (45%) male (mean age 45.44 ± 15.74 years). The baseline characteristic of echocardiographic parameters, Right heart catheterization & six- min walking distance are shown in (table 1).

Variables	Mean ± SD	Min	Max	
	ECHO parameters			
LV EF (%)	59.45 (9.75)	29.00	76.00	
FAC (%)	35.70 (9.97)	12.00	52.00	
TAPSE(mm)	18.32 (5.28)	7.00	31.00	
RV s`(cm/s)	10.05 (2.81)	5.00	15.00	
RIMP index	0.58 (0.14)	0.41	0.91 -4.50	
GLSRV (%)	-15.01 (6.08)	-29.00		
PASP (mmHg)	69.03 (20.35)	39.00	112.00	
TR velocity(m/s)	3.88 (0.67)	2.80	5.20	
Mean PAP (mmHg)	44.07(12.43)	25.79	70.32	
	RHC			
Mean PAP (mmHg)	58.80(23.53)	35.00	120.00	
	6MWD			
6MWD (m)	315.9 (127.9)	93.00	610.00	

LVEF=left ventricular ejection fraction, FAC=fractional area change, TAPSE=tricuspid annular plane systolic excursion, RVs`=tricuspid lateral annular systolic velocity, RIMP=right ventricular index of myocardial performance, GLSRV=global longitudinal strain of right ventricle, PASP=pulmonary artery systolic pressure, TR velocity= maximum velocity of tricuspid regurgitation, mean PAP=mean pulmonary artery pressure, RHC=right heart catheterization, 6MWD=6 min walking distance.

The mean (\pm SD) 6MWD was 315.9 (127.9) & demonstrated significant correlation with GLSRV ((r=0.366, p-value =0.011). However, it did not have a significant correlation with other Echocardiographic parameters like TAPSE, FAC, RIMP & RVs` as shown in (table 2).

 Table 2: Correlation between 6MWD in meter & echocardiographic parameters

6MWD*	Echo parameters	r	P value
6MWD(m)	GLSRV (%)	0.399	0.011
	TAPSE(mm)	0.233	0.149
	FAC (%)	0.260	0.105
	RIMP index	-0.186	0.251
	RV s'(cm/s)	0.241	0.134

*6MWD=6min walking distance.

The mean PAP measurement by echocardiography found significant correlation with the mean PAP measurement by right heart catheterization (P value =0.0001) as shown in (Table 3).

 Table 3: Correlation between Echo Doppler estimated mean PAP

 & trans-catheter estimated mean PAP

Parameters	Mean ± SD	Diff Mean ± SD	P value	
Mean PAP by RHC*	58.80 (23.53)	14.73 (19.51)	0.0001	
Mean PAP by Echo	44.07 (12.43)	14.75 (19.51)	0.0001	
*RHC=Right heart ca	theterization.			

The mean PAP calculated by Right heart catheterization had

good correlation with echocardiographic parameter like FAC (r = -0.365, p=0.020) but no statistical significant correlation with GLSRV, TAPSE, RIMP& RVs` as shown in (table 4).

 Table 4: Correlation between trans-catheter estimated mean PAP

 & different right Ventricular echocardiographic variables.

RHC*	parameters	r	P value
	GLSRV (%)	0.218	0.176
Mean PAP (mmHg)	TAPSE(mm)	-0.300	0.060
	FAC (%)	-0.365	0.020
	RIMP index	0.148	0.364
	RV s(cm/s)`	-0.177	0.275

* RHC=right heart catheterization.

ROC curves were used to obtain area under the curve (AUC) values found that there was significant ability of the PASP (Area =0.827. p=0.001) &TR velocity (Area=0.797, p=0.002) to detect severe PH (meanPAP \geq 45mmHg), but it did not significant for the ability of LV EF, FAC, TAPSE, RIMP index, GLSRV to detection severe PH (meanPAP \geq 45mmHg) as shown in (table 5 and fig 1)

 Table 5: AUC analysis for echocardiographic variables to detect severe PHT

Test Result	Area	Р	95% CI		
Variable(s)	Area	value	Lower Bound	Upper Bound	
LV EF %	0.621	0.199	0.425	0.817	
FAC %	0.415	0.370	0.236	0.595	
TAPSE(mm)	0.406	0.320	0.219	0.593	
RV s(cm/s)`	0.413	0.355	0.223	0.603	
RIMP index	0.493	0.945	0.310	0.677	
GLSRV (%)	0.633	0.159	0.458	0.808	
PASP(mmHg)	0.827	0.001	0.698	0.956	
TR velocity	0.797	0.002	0.658	0.936	

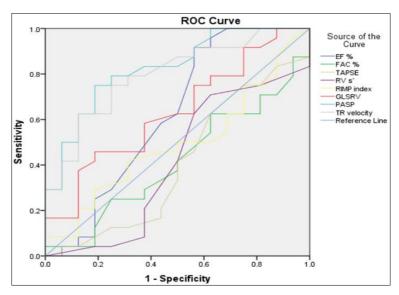


Fig 1: ROC area of echocardiographic variable regarding detection of severe PH. EF=left ventricular ejection fraction

The point (61mmHg) had considered the best one to be selected as a cut-off point of PASP to detect severe PH (meanPAP \geq 45 mmHg) as it revealed a (79%) sensitivity & (75%) specificity. The point (3.57) had considered the best one to be selected as a cut off point for TR velocity to detect severe PH (meanPAP \geq 45 mmHg) as it revealed a (80%) sensitivity & (70%) specificity. The point (-17.20) had considered the best one to be selected as a cut off point for GLSRV to detect severe PH (meanPAP \geq 45 mmHg) as it

revealed a high (75%) sensitivity & lower (44%) specificity as shown in (table 6).

Table 6: The cut –off point to detect severe PH (meanPAP ≥45 mmHg) with their correspondent sensitivity and specificity for PASP, TR velocity &GLSRV.

	Cut- off point	Sensitivity	specificity
PASP	61 mmHg	0.79	0.75
TR velocity	3.57	0.80	0.70
GLSRV	- 17.20	0.75	0.44

Agreement in RV failure detection between GLSRV and TAPSE is (43.75%), normal detection is (87.50%)& total Agreement is ((14 + 7)/40 = 52.5%) with P value (0.102). Agreement in RV failure detection between GLSRV and RVs'is (43.75%), normal detection is (75%) & total Agreement `is (14+6/40=50%) with (Pvalue=0.333). Agreement in RV failure detection between GLSRV and RIMP is 59.38%, normal detection is (87.50%) & total

Agreement is (19+7/40=65%) with significant P value (0.018). Agreement in RV failure detection between GLSRV and FAC is (43.75%), normal detection is (100%) & total Agreement between is (14+8/40=55%) with significant P value (0.020). Agreement in RV failure detection between GLSRV & 6MWD is (71.88), normal detection is (75%) & total Agreement is (23+6/40=73%) with significant P value (0.014).as shown in (table 7).

capacity and invasive hemodynamic parameters. Treatment

Table 7: Agreement of ECHO parameters &6MWD with GLSRV

GLSRV	TAPSE N	TAPSE No (%) FNRV s No (%) FN		RIMP No (%) F N		FAC % No (%) F N		6 MWD No (%) F N		
Failure n=32	14 (43.75)	18 (56.25)	14 (43.75)	18 (56.25)	19 (59.38)	13 (40.62)	14 (43.75)	18 (43.75)	23 (71.88)	9 (28.13)
Normal n=8	1 (12.50)	7 (87.50)	2 (25.00)	6 (75.00)	1 (12.50)	7 (87.50)	0 (0.00)	8 (100.0)	2 (25.00)	6 (75.00)
Total	15	25	16	24	20	20	14	26	25	15
P value	0.1	.02	0.333		0.018		0.020		0.014	

Discussion

Vasoconstriction and vascular remodeling cause pulmonary vascular resistance to slowly grow in pulmonary hypertension. Despite PH's initial clinical alterations in the pulmonary vasculature, RV function was linked to prognosis ¹⁸. Strain was originally developed to quantify LV mechanics; however, speckle strain has been used to assess the RV in several diseases categories ^[19]. We used GLSRV and other RV echocardiographic measures to assess RV function in PH patients in connection to functional and hemodynamic state, including 6-MWD and transcatheter determined meanPAP. The present research found that GLSRV was highly linked with other conventional RV systolic function indicators including TAPSE and RVs' on routine transthoracic echocardiography. These findings are consistent with (Li Y et al.) [20] who found that right ventricular free wall longitudinal peak systolic strain was obtained by echocardiographic parameter and correlated well with other conventional indices of RV systolic function on routine transthoracic echocardiography examination like (TAPSE&RV s`) and could reflect the range of right heart function reduction in PH patients. In addition, Park Jh et al. ^[21] found that GLSRV had a significant link with traditional echocardiographic markers of RV systolic performance such TAPSE and lower supreme GLSRV was associated with worse clinical events and deaths in PAH patients. In addition, (Li Y, Xie M et al)²² found that speckle tracking echocardiography (STE) may detect abnormalities in RV reginal and global systolic function in PAH patients with different degrees. Modern, easy, substantial, and repeatable STE assesses RV systolic function using routine pictures. We then examine RV longitudinal systolic function. RV function parameters like TAPSE and RV s are widely used in clinical practice and may be regarded global RV contractility files ^[6]. Myocardial strain may detect early myocardial dysfunction and improve chronic heart failure management ^[23]. Our investigation found no significant correlation between GLSRV and other echocardiographic measures like FAC and RIMP. These results contradict Li Y et al. ^[20] and Park Jh et al. ^[21]. While imaging quality has improved, 2DE marker assessment of the sick RV remains difficult. The RV chamber's complicated structure and systolic mechanics may explain it ^[6]. We discovered that GLSRV was substantially linked with 6-MWD in metres, meaning that individuals with impaired GLSRV had shorter 6-MWD. This supports Park JH et al. [24]. In PAH patients, strain echocardiography measures right ventricular longitudinal strain (RVLS), which correlates with functional

reduced meanPAP and PVR and increased RVLS. Our findings also agree with (Sunbul et al.) [34], who showed decreased RV strain in chronic thromboembolic pulmonary hypertension patients with shorter 6-MWD and a good association between 6-MWD and RV myocardial deformation (mid &basal-RV lateral strain). Nonetheless, the 6-MWD might be a helpful and widely used instrument (test) for assessing the functional capacity of patients with cardiac or pulmonary dysfunction and predicting the feasibility of therapeutic approaches for pulmonary arterial hypertension and patient survival and advancement. Poor exercise capacity (6MWD<332m) correlated strongly with poor prognosis ^[26]. The present research indicated that echocardiograms were beneficial for measuring mean PAP and correlated with RHC measurements. This supported (Oxley C et al.) ^[27] WHO found that conventional echocardiogram calculations for mean PAP and PASP correlated well with RHC data, whereas transthoracic echocardiography for RAP measurements did not. Transthoracic echocardiography can assess pulmonary artery pressure in PH ^[28] patients noninvasively. Our findings disagreed with Constantinescu T et al. [29], who said research supports the use of novel that the echocardiographic parameters for non-invasive right heart evaluation in PAH patients. Cardiac ultrasonography is less reliable for assessing assessment pressure in severe PAH but seems to provide correct information for cardiac index and PVR. RHC provides a more complete hemodynamic picture of the PAH patient and is required for the final diagnosis. They showed that multiple studies suggest that echocardiography lacks essential accuracy in measuring both systolic and mean pulmonary artery pressure, with diagnostic errors in up to 20% of cases, making RHC necessary for the final decision and treatment recommendations [30]. Our investigation found that RHC meanPAP was substantially linked with RV echocardiography FAC (Li Y et al.) ^[20]. Right heart catheterization is the "gold standard" for diagnosing pulmonary hypertension ^[31]. Thus, it cannot be conducted in all patients without definite sign. Transthoracic echocardiography is non-invasive, affordable, and widely available, making it an intriguing screening tool for pulmonary hypertension and a method for tracking disease development over time [32] PASP &TR velocity outperformed GLSRV, TAPSE, FAC, RIMP&RVs` for identifying severe PH (45mmHg). & this conclusion is inconsistent with (Li Y et al.) [20] Who stated that RV free

wall strain is better than RIMP, TAPSE, FAC, and RVs for detecting severe PH < 45mmHg. Our work employed GLSRV (3-segment free wall + 3-segment interventricular) to estimate RV strain, which may explain this difference. Nevertheless, IkedaS et al. [33] found that the area under the curve for RV dysfunction in patients with severe PH (meanPAP>35mmHg) and RV free wall strain was better than tricuspid regurgitation pressure gradient for PH identification. Nevertheless, GLSRV had the strongest prognostic power ^[34]. In individuals with suspected right ventricular cardiomyopathy, heart transplantation candidates, or left ventricular assist device recipients, RV free wall strain may be more important. In this research, echocardiographic Doppler estimated PASP's cut-off value is (61mmH) with sensitivity (79%) and specificity (75%) and TR velocity's cut-off value is (3.57 m/s) with sensitivity (80%) and specificity (70%) to diagnose severe PH (mean PAP>45mmHg). although the GLSRV's cut-off value (-17.20%) has high sensitivity (75%) and poor specificity (44%). compare our results to Park Jh et al. [30], who discovered the cutoff value of GLSRV was -15.5% with sensitivity of 70% and specificity of 77%. (Li Y et al.) [20] discovered the RV free wall strain cutoff value for severe PH (meanPAP>45mmHg) was -19.26% with sensitivity (83.9%) and specificity (73.4%). (Motoji et al.) [35] They discovered RV free wall strain (-19.4) had 90% sensitivity and 69% specificity for cardiovascular event identification, whereas TAPSE (<16mm) had 90% sensitivity and 75% specificity. We assessed RV strain using the RV free wall and interventricular septum combined. The interventricular septum comprises LV and RV mechanical components, making strain evaluation difficult. Nonetheless, prolonged RV pressure overload may affect ventricular shape, and the interventricular septum is crucial to RV systolic mechanics [19]

Conclusion

The current study found that GLSRV has high ability in detecting RV dysfunction in patients with pulmonary hypertension & and also showed it is agreement with others echo parameters like (RIMP&FAC) & in addition to 6MWD. The GLSRV is well correlated with functional capacity (6-MWD) and showed significant negative linear correlation with TAPSE & RVs[°]. Moreover, there was agreement between mean PAP estimated by both echo Doppler & transcatheter measurement. There is superiority of PASP &TR velocity to detect severe pulmonary hypertension than others traditional echocardiographic parameters.

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