Comparative Evaluation of Different Echocardiographic Doppler Measurements of Pulmonary Vascular Resistance in Acyanotic Congenital Heart Disease with Pulmonary Artery Hypertension

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Background --- Current evaluation of pulmonary hypertension in children involves measurement of pulmonary vascular resistance. This study determines the accuracy of Doppler echocardiographic measurements in assessing pulmonary vascular resistance in patients diagnosed with acyanotic congenital heart disease with pulmonary arterial hypertension.

Methods --- This is a cross-sectional study involving 19 pediatric acyanotic congenital heart disease patients with pulmonary hypertension, who are admitted for hemodynamic study. Hemodynamic findings were compared with Doppler parameters such as RVPEP/VTI and TRV/ VTIRVOT. Measures of validity as well as correlation were determined with the invasive measurements as gold standard.

Results --- The ratio of TRV/VTIRVOT showed a significant correlation with pulmonary vascular resistance (r= 0.98, p-value of 0.0001) while the ratio of RVPEP/ VTIRVOT showed no significant correlation (r = 0.42, p-value of 0.06).

Conclusion --- The ratio of TRV/ VTIRVOT is recommended for estimating the degree of pulmonary vascular resistance. ***Phil Heart Center J 2008; 14(1):20-25.***

Key Words: Pulmonary Hypertension, Congenital Heart Disease, Echocardiography, Cardiac Catheterization, Pulmonary Vascular Resistance ■

Pulmonary vascular resistance is an important he modynamic variable used in the management of patients with congenital heart disease with pulmonary artery hypertension. It is used to evaluate the response to pharmacologic therapy in patients with congestive heart failure. It is an essential component of heart-and-liver transplant candidate evaluation and in predicting early and late clinical outcome. Accurate evaluation of pulmonary vascular resistance is a key component in evaluating operability and surgical outcome of congenital heart disease with increased pulmonary vascular resistance. Most Doppler echocardiographic studies attempting to assess pulmonary artery hypertension did not address whether the pulmonary hypertension was the result of increased pulmonary blood flow or increased pulmonary vascular resistance. Thus invasive procedures usually are required to resolve that issue.

Several studies have applied Doppler echocardiographic technique to estimate pulmonary artery pressure. Kosturakis et.al. noted that the ratio of acceleration time (Act) to right ventricular ejection time (RVET), Act/RVET correlated well with the mean pulmonary artery pressure, but it cannot distinguish between patients with pulmonary hypertension secondary to increased blood flow or increased pulmonary vascular resistance.[1]

In a study done by Ebeid et.al. on doppler echocardiographic evaluation of pulmonary vascular resistance in children with congenital heart disease, invasive measurement of pulmonary vascular resistance of 33 patients (mean age 1.4 years) were compared with Doppler echocardiographic parameters. The right ventricular pre-ejection period (RVPEP), ejection time (RVET), and ratio RVPEP/RVET correlated better with pulmonary vascular resistance than with pulmonary artery pressure. A highly significant correlation was demonstrated between pulmonary vascular

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resistance and a newly derived parameter RVPEP/ VTIRVOT with r=0.87 and p value of < 0.0001. An RVPEP/ VTIRVOT value of <0.4 seconds/meter was able to select patients with pulmonary vascular resistance of <3 Wood units with 97% accuracy (100% sensitivity, and 92% specificity), even in the presence of pulmonary hypertension caused by increased pulmonary blood flow. An RVPEP/ VTIRVOT value of 0.4 to 0.6 seconds/m identified patients with pulmonary vascular resistance between 3 to 7.5 Wood units with 91% accuracy, while a value of > 0.6 seconds/m selected patients with total pulmonary vascular resistance > 7.5 Wood units with 94% accuracy.[2]

In 1998, a local study by Acosta et.al. compared different Doppler ratios such as RVPEP/RVET and RVPEP/ VTIRVOT. The study demonstrated that the ratio of RVPEP/ VTIRVOT measured by Doppler echocardiography was a better way of estimating noninvasive measurement of pulmonary vascular resistance with an interclass correlation coefficient (r) of 0.808 and a p-value of 0.000 as compared to RVPEP/RVET ratio with r=0.581 and a p-value of 0.023.

Abbas et.al in 2003 demonstrated that the ratio of peak tricuspid regurgitation velocity (TRV, ms) to the RVOT velocity time integral (VTIRVOT, cm) correlated well with invasive pulmonary vascular resistance measurements (r = 0.929, 95% confidence interval 0.87 to 0.96). The Bland-Altman analysis between PVR obtained invasively and that by echocardiography using the equation: PVR = TRV/TVIRVOT x 10 + 0.16, showed satisfactory limits of agreement (mean 0 + 0.41). A TRV/TVI cutoff value of 0.175 had a sensitivity of 77% and a specificity of 81% to determine PVR >2WU.[4]

In the study done by Vanaja et.al, TRV/ VTIRVOT correlated well with invasive pulmonary vascular resistance measurements (r=0.93, 90% confidence interval 0.90-0.95). Invasive pulmonary vascular resistance measurement correlated well with echocardiographic Doppler measurements if PVR was < 6.0 wood units, whereas no correlation was found when PVR was >6.0 wood units. [5]

This study was done to correlate the Doppler echocardiographic measurements, such as ratios of RVPEP/VTI and TRV/TVIRVOT, to actual measurements of pulmonary vascular resistance in cardiac catheterization. Also, the sensitivity and specificity of these two Doppler ratio measurements would be determined using invasive measurements as the gold standard.

Methods

This is a cross-sectional study involving patients under 19 years of age with a diagnosis of acyanotic shunt lesions (Atrial Septal Defect, Ventricular Septal Defect and Patent Ductus Arteriosus) with pulmonary artery hypertension who were admitted for hemodynamic studies for determination of pulmonary vascular resistance and assessment of operability. Patients with pulmonary acceleration time of less than or equal to 90ms by Doppler measurement (with pulmonary artery systolic pressure equivalence of >40mmHg) and moderate to severe tricuspid regurgitation with estimated right ventricular systolic pressure of >40mmHg were included in the study.

Patients with RVOT obstruction, arrhythmia, patients with organic pathology of the tricuspid valve causing tricuspid regurgitation and patients with cyanotic congenital heart disease were excluded in the study.

Doppler echocardiographic measurements were done within 24 hours before hemodynamic study using Phillips IE33 ultrasound system. Measurements included were right ventricular pre-ejection period (RVPEP), velocity time integral (VTIRVOT), and tricuspid regurgitation velocity (TRV). Doppler parameters such as velocity in cm/s for RVPEP and m/s for TRV and velocity time integral in centimeters. Example of Doppler spectral display is illustrated with figure 1.

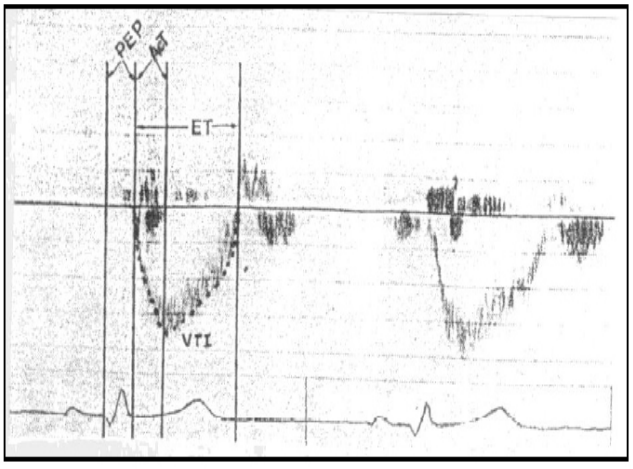

Figure 1: The RVPEP is measured from the beginning of the QRS wave to the opening of the pulmonic valve expressed in cm/s. The VTI in cm is obtained by digitalizing the signal envelope with the aid of the computer program expressed in cm.

RATIO:	PVR (WU):
< 0.4	< 3 wood units
0.4 – 0.6	3 – 7.5 wood units
>0.6	> 7.5 wood units

In figure 1, the right ventricular pre-ejection period (RVPEP) was measured from the beginning of the QRS wave to the opening of the pulmonic valve expressed in cm/s. The right ventricular outflow tract-velocity time integral (VTIRVOT) (cm) was obtained by placing a 1 to 2 mm pulsed wave Doppler sample volume in the proximal right ventricular outflow tract just within the pulmonary valve when imaged from the parasternal short-axis view. Pulsed wave Doppler was used rather than continuous wave Doppler to eliminate cases with increased pulmonary velocities secondary to either pulmonary valve or peripheral pulmonary artery stenosis. The velocity time integral at the right ventricular outflow tract (VTIRVOT) was obtained by digitalizing the signal envelope with the aid of the computer program expressed in cm. We computed for the ratio RVPEP/ VTIRVOT, which has a corresponding measurement of pulmonary vascular resistance in Wood units. Ratio equivalent to <0.4 corresponds to PVR of < 3 Wood units, 0.4 – 0.6 corresponds to 3 – 7.5 Wood units, and >0.6 corresponds to >7.5 Wood units.

Continuous wave Doppler was used to determine the peak tricuspid regurgitation velocity (TRV) (m/s). The highest velocity was obtained from multiple views. The TRV/VTIRVOT ratio was then calculated. (Figure 2 & 3)

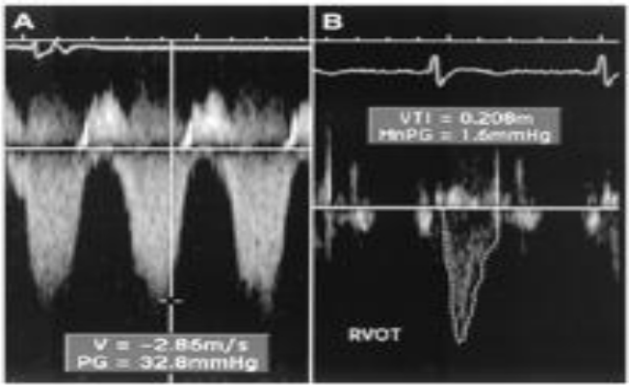

Figure 2: Images showing peak tricuspid regurgitant velocity (TRV) and right ventricular outflow velocity time integral (VTIRVOT) in a patient with normal pulmonary vascular resistance (PVR). (A) TRV is 2.86 m/s. (B) VTIRVOT is 20.8 cm. The ratio of TRV/ VTIRVOT = 2.86/20.8 = 0.1375. This patient's invasive PVR measurement was within 0.4 WU of the echocardiographic value (PVRCATH = 1.3 WU). PVRECHO = PVR in WU calculated based on the linear regression equation in which a value for PVR in WU was modeled based on TRV/ VTIRVOT . PVRCATH = invasive PVR

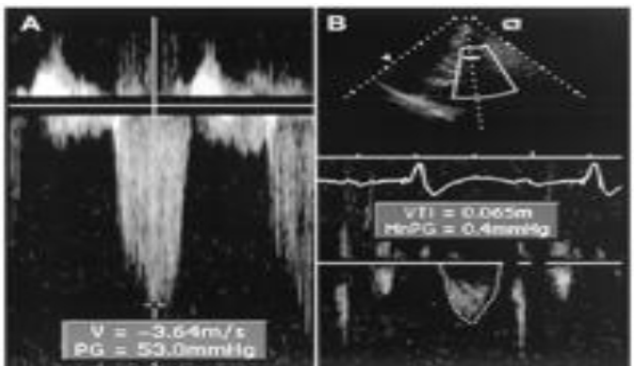

Figure 3: Images showing TRV and VTIRVOT in a patient with elevated PVR. (A) TRV is 3.64 m/s. (B) VTIRVOT shows a clear deceleration of pulmonary flow before the pulmonic valve closure click and is calculated at 6.5 cm. The ratio of TRV/VTIRVOT = 3.64/6.5 = 0.56.
PVR = 0.56 x 10 + 0.16 = 5.76 WU
This patient's invasive PVR measurement is also within 0.4 WU of the echocardiographic value (PVRCATH = 6.0 WU)

The peak tricuspid regurgitation was expressed in m/s and was divided by the velocity time integral at the right ventricular outflow tract in cm (VTIRVOT). Using the formula in figure 3, the TRV/ VTIRVOT ratio was multiplied by 10 and 0.16 was added to get the pulmonary vascular resistance in Wood units. Sample of the computation is illustrated in figure 3.

To increase intraobserver reliability, Doppler measurement was done by principal author only and 3 repeated measurements were taken with all the parameters needed.

Doppler echocardiographic measurements of pulmonary vascular resistance were compared with invasive hemodynamic measurements. Right and left heart catheterization were done to all patients. Oximetry and pressure recordings were taken in order to compute for the cardiac output, pulmonary blood flow and pulmonary vascular resistance. The oxygen consumption was obtained from the table of LaFarge using the Fick's principle. The pulmonary vascular resistance was calculated as follows: mean pulmonary artery pressure minus the left atrial pressure divided by the pulmonary blood flow. Pulmonary artery wedge pressure or left ventricular end diastolic pressure were either used if left atrial pressure was not available. Pulmonary vascular resistance was expressed in Wood units.

Patients were labeled as follows: pulmonary artery hypertension with normal pulmonary vascular resistance (PVR <3 w.u) or pulmonary artery hypertension with increased pulmonary vascular resistance (PVR >3 w.u).

Sample Size:

At least sixty patients (n= >60) were needed for

the study to assure sensitivity of 81%, relative error of 20% and confidence level of 95% ($\alpha = 0.05$). However, only nineteen patients (n=19) were recruited.

Data analysis

Pearson's Correlation coefficient was obtained between Doppler echocardiographic ratio measurements and invasive pulmonary vascular resistance. It is expressed by mean standard deviation. A p value of <0.05 was considered significant.

T-test was done to determine significant difference and agreement between pulmonary vascular resistance measured by cardiac catheterization and pulmonary vascular resistance by Doppler technique TRV/VTIRVOT ratio. A p value of <0.05 was considered significant.

Sensitivity and specificity were computed for both ratio RVPEP/ VTIRVOT and TRV/VTIRVOT in comparison with invasive pulmonary vascular resistance to predict whether the patient had normal or elevated pulmonary vascular resistance.

Results

Demographic Data

A total of 19 patients (8 males and 11 females) who underwent echocardiographic and cardiac catheterization evaluation during the study period were included. The frequency of cardiac lesions were as follows: 8 ventricular septal defect, 5 patent ductus arteriosus, 4 atrial septal defect, 1 aortopulmonary window and a case of a double shunt with ASD and VSD.

Pulmonary vascular resistance by invasive measurements were expressed in Wood units and patients were labeled either with normal (<3 Wu) or with elevated pulmonary vascular resistance (>3 Wu). Of the 19 patients who had undergone cardiac catheterization, seventeen of them had elevated pulmonary vascular resistance and two had normal pulmonary vascular resistance. In comparison with the two Doppler ratios, using the ratio TRV/VTIRVOT, seventeen patients had elevated pulmonary vascular resistance. On the other hand, using RVPEP/VTIRVOT, only two of the patients demonstrated elevated pulmonary vascular resistance (Table 1).

Table 1.a. Correlation between RVPEP/VTIRVOT ratio and Invasive Pulmonary Vascular Resistance Measurement.

PVR	Invasive (n=19)	Percent (%)	RVPEP VTI (n=19)	Percent (%)
Normal (<3 wu)	2	10	17	90
Elevated (≥3 wu)	17	90	2	10
Total	19	100	19	100
r		0.42		
p value		0.06		

Table 1.b. Correlation between TRV/VTIRVOT ratio and Invasive Pulmonary Vascular Resistance Measurement.

PVR	Invasive (n=19)	Percent (%)	TRV VTI (n=19)	Percent (%)
Normal (<3 wu)	2	10	2	10
Elevated (≥3 wu)	17	90	17	90
Total	19	100	19	100
r		0.98		
p value		0.0001		

The correlation of the pulmonary vascular resistance computed using RVPEP/ VTIRVOT ratio to invasive measurement was not statistically significant (r = 0.42, p-value of 0.06). However, a statistically significant correlation of the pulmonary vascular resistance computed by the ratio TRV/ VTIRVOT to invasive measurement was noted. (r=0.98, p-value of 0.0001). Furthermore, the scatter plot (graph 1) illustrates good correlation between the Doppler ratio TRV/ VTIRVOT to invasive measurement, however, the trend demonstrated that as pulmonary vascular resistance increases or elevates, the difference obtained between the two measurements likewise increases.

Further paired sample statistics using the T-test revealed significant difference between the pulmonary vascular resistance computed by cardiac catheterization and Doppler measurement by TRV/ VTIRVOT ratio with a mean difference of 4.8 Wood units (SD= 7.64 Wood units) and p value of 0.014 as shown in Table 2.

Graph 1. Correlation between PVR measured Invasively & Doppler Ratio TRV/ VTIRVOT

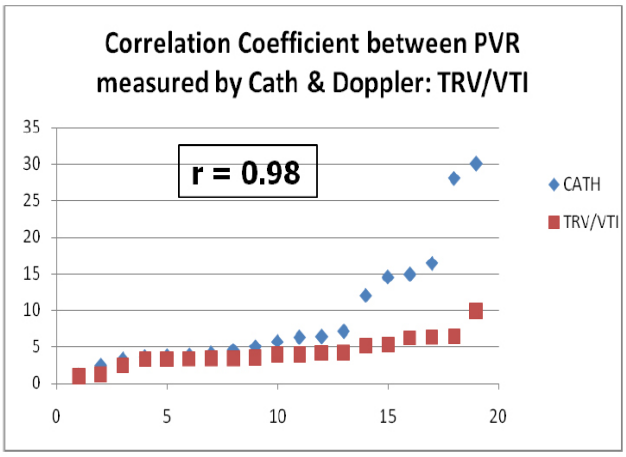

Table 2. Mean Difference between PVR measured Invasively by Cardiac Catheterization & Doppler Ratio TRV/ VTIRVOT

Procedure	Paired Differences (PVR in Wood units) mean	S D
Invasive (Cardiac Cath)	9.1	8.31
Echo: TRV/ VTI_{RVOT}	4.3	2.05
mean difference	4.8 (SD 7.64)	
p value	0.014 (S)	

However with the data collected, the trend that pulmonary vascular resistance obtained invasively with that of Doppler TRV/ VTIRVOT ratio still had significant mean difference though it was minimal value of 0.78 Wood units (SD = 0.52 Wood units; p value = 0.001) if pulmonary vascular resistance was < to 6 Wood units. Whereas, if pulmonary vascular resistance was > 6 Wood units the mean difference was higher at 9.26 Wood units (SD = 7.17) with a p value of 0.005 as shown in Table 3.

Table 3. Comparison of Mean Difference between PVR < 6 W.u. and > 6 W.u. measured Invasively by Cardiac Cath & Doppler Ratio TRV/ VTIRVOT

Procedure	PVR ≤ 6 W.u. mean	S D	PVR > 6 W.u. mean	S D
Invasive (Cardiac Cath)	3.72	1.29	15.06	8.8
Echo: TRV/ VTI_{RVOT}	2.9	1.01	5.8	1.8
mean difference	0.78	0.52	9.26	7.17
p value	0.001(S)		0.005(S)	

Further T-test was not applied with the ratio RVPEP/VTI and invasive PVR measurements because it only predicted a range of pulmonary vascular resistance in Wood units.

For the computation of the sensitivity and specificity of TRV/ VTIRVOT ratio to invasive PVR measurement, a cut-off value of <3 Wood units was considered normal while >3 wood units was considered elevated pulmonary vascular resistance. This cut-off provided sensitivity of 94% and specificity of 100% with 95% confidence interval. For the RVPEP/ VTIRVOT ratio a sensitivity of 12% and specificity of 100% was obtained as shown in Table 4a and 4b. Although the pulmonary vascular resistance derived from TRV/ VTIRVOT ratio is in agreement with the pulmonary vascular resistance by cardiac catheterization, the pulmonary vascular resistance by RVPEP/VTIRVOT ratio is not significant with the pulmonary vascular resistance by cardiac catheterization.

Table 4a. Sensitivity and Specificity of RVPEP/ VTIRVOT to Invasive PVR Measurement

		Pulmonary Vascular Resistance Invasive (Cardiac Cath) Elevated	Normal	Total
Pulmonary Vascular Resistance by ECHO (RVPEP/ VTI_{RVOT})	Elevated	2	0	2
	Normal	15	2	17
	Total	17	2	19

Sensitivity 12; Specificity 100%

Table 4b. Sensitivity and Specificity of TRV/ VTIRVOT to Invasive PVR Measurement

		Pulmonary Vascular Resistance Invasive (Cardiac Cath) Elevated	Normal	Total
Pulmonary Vascular Resistance by ECHO (TRV/ VTI_{RVOT})	Elevated	16	0	16
	Normal	1	2	3
	Total	17	2	19

Sensitivity 94; Specificity 100%

Discussion

Pulmonary vascular resistance is directly related to change in pressure (Δp) and inversely related to pulmonary blood flow (Qp). Thus, TRV and VTIRVOT can be used as correlates to Δp and Qp respectively. As pulmonary vascular resistance increases, there is earlier and enhanced reflection of the pressure wave propagated from the right ventricular outflow tract into

the pulmonary trunk. This is reflected by a confrontational change in VTIRVOT leading to a decrease right ventricular ejection time (RVET).

Our results showed that the TRV/ VTIRVOT ratio gives us the exact pulmonary vascular resistance in Wood units that previous studies did not demonstrate. Such that, acyanotic shunts with pulmonary arterial hypertension can be labeled whether it is secondary to increased pulmonary blood flow or increased pulmonary vascular resistance non-invasively by Doppler echocardiography. The correlation coefficient of the Doppler ratio TRV/ VTIRVOT with invasive PVR measurements was significant with r = 0.98(p- value of 0.0001) as compared to the RVPEP/ VTIRVOT ratio to invasive PVR measurements which was not significant with r = 0.42 (p-value of 0.06). The Doppler ratio TRV/ VTIRVOT with invasive PVR measurements showed satisfactory limits of agreement especially if pulmonary vascular resistance was < 6 Wood units, however, the mean difference was still significant.

Recommendation

Doppler echocardiography using the TRV/ VTIRVOT ratio may provide reliable non-invasive method measurement of pulmonary vascular resistance, which is a useful parameter in monitoring patients with congenital heart disease with pulmonary artery hypertension preoperatively and post-operative follow-up. Furthermore, it could be used as a non-invasive parameter to test pulmonary bed vasoreactivity to certain drugs which has a pulmonary dilating effect. Since we were limited by our sample size, a follow-up study is recommended to further establish the correlation and agreement of Doppler measurement TRV/ VTIRVOT ratio with invasive measurement especially in cases where pulmonary vascular resistance < or > 6 wood units.

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