FULL LENGTH ARTICLE

Noninvasive assessment of elevated pulmonary vascular resistance in children with pulmonary hypertension secondary to congenital heart disease: A comparative study between five different Doppler indices

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Background: **Pulmonary vascular resistance (PVR) is an important hemodynamic parameter in patients with congenital heart disease (CHD). Noninvasive estimation of PVR represents an attractive alternative to invasive measurements.**

Methods: **The study included 175 patients with pulmonary hypertension (PH) secondary to CHD. All patients underwent full echocardiographic study and invasive hemodynamic measurements. The study population was then subdivided into four subgroups. Each of the following Doppler indices was measured in one of these four subgroups: peak tricuspid regurgitant velocity (TRV), the ratio of the TRV to the velocity time integral of the right ventricular outflow tract (TRV/TVI_{RVOT}), peak velocity of tricuspid annular systolic motion (TSm), heart rate corrected acceleration time and infliction time of the proximal left pulmonary artery (ATc, InTc). The data obtained was correlated with invasive PVR measurement. An ROC curve analysis was done to generate cutoff points with the highest balanced sensitivity and specificity to predict PVR > 6WU/m^2. The receiver operating characteristics (ROC) curves were compared with each other to determine the most reliable cutoff point in predicting elevated PVR > 6WU/m^2.**

Results: **There was a significant correlation between both the TRV and TSm and invasive measurement of PVR ($r = -0.511$, 0.387 and P value = 0.0002, 0.006 respectively). The TSm and TRV cutoff values were the most reliable to predict elevated PVR > 6 WU/m^2. A TSm cutoff value of $\leqslant$16.16 cm/s provided the best balanced sensitivity (85.7%) and specificity (66.7%) to determine $PVR_{CATH} > 6$ WU/m^2. A cutoff value less than 7.62 cm/s had 100% specificity to predict $PVR_{CATH} > 6$ WU/m^2. A TRV cutoff value of >3.96 m/s provided the best balanced sensitivity (66.7%) and specificity (100%) to determine $PVR_{CATH} > 6$ WU/m^2. Both TRV and TSm had the highest area under the ROC curve among the 5 DOPPLER indices studied.**

Conclusion: **Prediction of elevated PVR in children with PH secondary to CHD could be achieved noninvasively using a number of Doppler indices. Among the five Doppler indices examined in the current study, the peak TRV and the TSm of the lateral tricuspid annulus had the highest balanced sensitivity and specificity to predict PVRI > 6 WU/m^2.**

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Abbreviations: AcT, acceleration time, AcTc, acceleration time corrected to heart rate, BSA, body surface area, CHD, congenital heart disease, DTI, Doppler tissue imaging, InT, inflection time, InTc, inflection time corrected to heart rate, MPAP, mean pulmonary artery pressure, PA, pulmonary artery, PCWP, pulmonary capillary wedge pressure, PH, pulmonary hypertension, PVR, pulmonary vascular resistance, Qp, pulmonary blood flow, ROC, receiver operating characteristics curves, RVSP, right ventricular systolic pressure, TRV, peak tricuspid regurgitant velocity, TSm, peak velocity of tricuspid annular systolic motion, TVI_{RVOT}, right ventricular outflow tract time–velocity integral.

Keywords: Pulmonary vascular resistance, Congenital heart disease, Doppler, Noninvasive

Introduction

Pulmonary vascular resistance (PVR) is a critical parameter in the assessment and treatment of patients with known or suggested pulmonary hypertension (PH), regardless of its origin. High PVR in children with congenital heart disease (CHD) can severely limit surgical repair or long term survival [17]. PVR is routinely determined using catheterization-derived measurements and calculated as the ratio of the transpulmonary pressure gradient (Δp) to flow (Qp) [19].

The invasive nature of this measurement might increase patient's risk and therefore, tends to restrict the frequency with which it is obtained. As newer therapies for PH emerge and cardiothoracic surgeons accept patients with higher and higher PVR a noninvasive method that would allow more frequent measurements of PVR may prove useful [18].

Doppler echocardiography allows for the noninvasive investigation of cardiopulmonary hemodynamics. In the last decade a number of studies has hypothesized that different Doppler indices could predict elevated PVR, however with the exception of the study by Atiq et al. [3] the rest of these indices were not tested in children with PH secondary to CHD. Moreover the comparison of these indices against each other in this important age group to determine the most clinically reliable index to predict elevated PVR was never made [1,7,10,14,15,18].

We sought to perform a prospective study to determine cutoff values of these Doppler indices that could predict elevated PVR in children with CHD compared to the invasive determination of PVR in the catheterization laboratory and to compare these values against each other as regard clinical reliability to assess elevated PVR noninvasively.

While right heart catheterization would still be the gold standard to measure PVR in children with PH secondary to CHD, using echocardiography to measure PVR in this age group would have the advantage of being able to follow patients serially as well as assess their response to treatment noninvasively and determine the suitable timing of invasively measuring PVR prior to surgical repair of their underlying CHD.

Methods

The study was approved by our institutional review board and informed consent was obtained from the parents of all the children enrolled in the study.

This was a prospective study which included 175 patients who had PH secondary to CHD and were scheduled for elective cardiac catheterization to evaluate their pulmonary circulation prior to surgical correction. Full echocardiographic study and invasive hemodynamic measurements were obtained within 6 h of each other by two different operators and the data obtained by each operator was blinded to the other. The patients' demographic and clinical characteristics are shown in Table 1.

Invasive measurements

High fidelity fluid filled catheters were used for hemodynamic measurements. Pulmonary capillary wedge pressure (PCWP), right ventricle systolic pressure (RVSP) and mean pulmonary artery pressure (MPAP) were measured. Pulmonary blood flow (Qp) was calculated using Fick's method. The oxygen consumption was obtained from estimated oxygen consumption values according to LaFarge and Miettinen [12] using standard tables with correction for age, sex, heart rate and body surface area (BSA). The PVR in Wood units (WU) was calculated using the equation: [9].

$$PVR = MPAP - PCWP/Qp$$

Echocardiography

Full echocardiographic study was done for all patients enrolled in the study using phased array transducers of different frequencies tailored according to each patient's age, body build and weight.

The study included 2D, M mode and color flow Doppler from all standard echocardiographic

Table 1. Clinical and demographic characteristics of the patients.

Characteristics	Group 1	Group 2	Group 3	Group 4	Total
Number	48	48	48	31	175
Gender (M/F)	24/24	21/27	22/26	20/11	87/88
Mean age	3.9	4.0	4.6	4.0	4.12
(range) in years	(0.5–16)	(0.5–17)	(0.4–17)	(0.6–18)	(0.4–18)
Mean of BSA	0.59	0.59	0.63	0.55	0.59
(range) in m^2	(0.3–1.7)	(0.3–1.6)	(0.3–1.45)	(0.3–1.4)	(0.3–1.7)
Mean of $MPAP_{CATH}$	54	57	57	63	57.7
(range) in mmHg	(25–91)	(25–97)	(26–100)	(25–100)	(25–100)
Mean PVR_{CATH}	9.5	12.1	11.35	15.4	12.08
(range) in WU	(0.9–24)	(1.3–23.5)	(1.4–25.3)	(1.2–45.7)	(0.9–45.7)
Referral diagnosis					
VSD	27	26	22	5	80 (45.7%)
ASD	2	1	5	2	10 (5.7%)
PDA	5	1	3	4	13 (7.4%)
Multiple shunts	14	14	6	4	38 (21.7%)
Others	0	6	12	16	34 (19.4%)

BSA = body surface area, MPAP = mean pulmonary artery pressure, PVR_{CATH} = invasive pulmonary vascular resistance, WU = woods units, VSD = ventricular septal defect, ASD = atrial septal defect, PDA = patent ductus arteriosus.

windows (i.e. subcostal, apical, parasternal and suprasternal) applying the sequential analysis to establish situs, atrioventricular and ventriculoarterial connections, level of shunt or shunts that might be causing PH with emphasis on its exact site and relation to the surrounding structure and any associated anomalies.

The study population was then subdivided into four separate groups. Each of the following Doppler indices was then measured in one of these four subgroups:

Doppler tissue imaging

After completing the conventional echocardiogram, 48 patients underwent Doppler tissue imaging (DTI) of the lateral tricuspid annulus. The DTI application of the echocardiography machine was activated. An apical four-chamber view was obtained and a pulsed tissue Doppler sample was properly positioned at the level of the lateral tricuspid valve annulus. The peak velocity of tricuspid annular systolic motion (TSm) was measured and correlated with invasive measurement of PVR [10].

Doppler measurements

Continuous wave Doppler was used to determine the peak tricuspid regurgitant velocity (TRV) (m/s) in almost all patients studied. The highest velocity obtained from multiple views was used. In another subset of patients ($n = 48$) the TRV values were correlated with invasive measurement of PVR.

The right ventricular outflow tract time–velocity integral (TVI_{RVOT}) (cm) was obtained by placing a 1- to 2-mm pulsed wave Doppler sample volume in the right ventricular outflow tract just within the pulmonary valve when imaged from the parasternal short-axis view in a third subset of 48 patients. The sample volume was placed so that the closing – but not opening – click of the pulmonary valve was visualized. 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 [1]. The ratio of the TRV to the TVI_{RVOT} was then correlated with invasive measurement of PVR.

Among the fourth and last subset of patients ($n = 31$) the proximal left pulmonary artery (PA) was visualized using standard parasternal short-axis and modified short- and long-axis views. [11]. Under guidance of color Doppler flow mapping, a sample volume of pulsed-mode Doppler was carefully positioned on the blue color-coded blood flow within the left PA approximately 5 mm to 1 cm distal to the bifurcation of the main PA. Nevertheless two more patients were excluded from this subgroup due to marked contamination of the Doppler signal from PDA flow.

The PA flow velocity profile is thought to have three stages: an accelerating stage of the curve, a peak, and a decelerating stage. In some curves, the deceleration stage consists of two stages divided by an inflection point: after rapid deceleration, one stage has a second peak in mid to late systole, and the other has a nearly horizontal flow pattern in mid to late systole. In these flow profiles, the inflection point was defined as the end of a sharp descent in mid systole [14].

From these considerations, we made the following sets of measurements: acceleration time (AcT) was the time interval in milliseconds from the onset of ejection to the peak flow velocity; inflection time (InT) was the time interval in milliseconds from the onset of ejection to an inflection point; the InT includes both the acceleration and the deceleration phases. To correct for the heart rate dependence of time intervals, InT and AcT were divided by the square root of the time interval in milliseconds between the onset of ejection in two beats, and these indices were defined as InTc and AcTc respectively. These measurements were made using a computer incorporated in the ultrasound unit.

Statistical analysis

All data were collected, tabulated, and statistically analyzed. Continuous variables were expressed as mean ± standard deviation while qualitative variables were expressed as frequencies and their related percentages. Statistical significance was assessed by analysis of variance (ANOVA) test. Linear regression analysis was used to assess correlations between the different Doppler indices and invasive hemodynamic measurements. Values were considered significantly different when *P*-values were less than 0.05.

Using receiver operating characteristics curves (ROC), PVR was analyzed based on the values of the different Doppler indices. A logistic model was generated, and a cutoff value for each of the Doppler indices studied with the highest balanced sensitivity and specificity was obtained to predict elevated PVR values indexed to the BSA (PVR > 6WU/m^2). The different ROC curves generated were then compared against each other. All statistical analyses were conducted using the MedCalc for windows statistics software program version 11.6.1 (MedCalc Software Broekstraat 52 B-9030 Mariakerke Belgium).

Results

The study included 175 patients with PH secondary to CHD who were referred for invasive assessment of PVR prior to surgical repair. The study group had a mean age of 4.12 ± 4.5 years and a mean BSA of 0.59 ± 0.31 meter square. Out of the 175 patients studied: 80 (45.7%) patients had VSD; 10 (5.7%) patients had ASD; 13 (7.4%) patients had PDA; 38 (21.7%) patients had multiple shunts; and 34 (19.4%) patients had more complex lesions like atrioventricular septal defects or double outlet right ventricle with unprotected pulmonary circulation.

The study group was subdivided into four subgroups. The distribution of cases according to their diagnosis in the four subgroups is listed in Table 1. There was no significant difference between the four subgroups in regards to age or BSA (*P* value = 0.641 and 0.882 respectively). There was also no significant difference between the four subgroups concerning the invasive measurement of PVR (*P* value = 0.271) using the ANOVA test.

There was a significant negative correlation between the TSm studied in group 1 and invasive measurement of PVR ($r = -0.511$ and *P* value = 0.0002) (Fig. 1A). There was also significant positive correlation between the TRV measured in group 2 and invasive measurement of PVR ($r = 0.387$ and *P* value = 0.0065) (Fig. 1B).

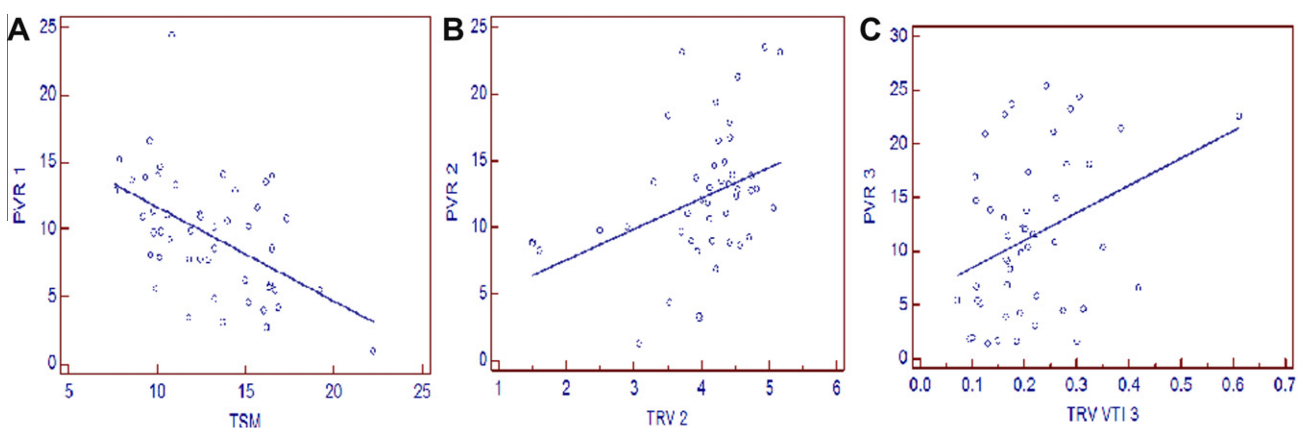

Figure 1. Linear regression analysis between invasive measurement of pulmonary vascular resistance (PVR) and (A) tissue Doppler S wave of the lateral tricuspid annulus (TSm), (B) tricuspid regurgitant velocity (TRV), and (C) the ratio of tricuspid regurgitant velocity (TRV) and velocity time integral of the right ventricular outflow tract (TVI RVOT) (TVI RVOT).

The significant positive correlation was also reported between the ratio of the TRV and TVI of the RVOT measured in group 3 and invasive PVR ($r = 0.347$ and P value = 0.015) (Fig. 1C). There was weak and non-significant correlation for either the AcTc or the InTc and the invasive measurement of PVR in group 4 ($r = -0.283$, 0.02 and p value = 0.123, 0.915 respectively) (Fig. 2A and B).

Using ROC curve analysis; a TSm cutoff value was generated to predict PVR_{CATH} > 6 WU/m^2. The area under this ROC curve was 0.778 and P-value was 0.03. A TSm cutoff value of ⩽16.16 cm/s provided the highest balanced sensitivity (85.7%) and specificity (66.7%) to determine PVR_{CATH} > 6 WU/m^2. A cutoff value less than 7.62 cm/s had 100% specificity to predict PVR_{CATH} > 6 WU/m^2 (Fig. 3).

Using ROC curve analysis; a TRV cutoff value was generated to predict PVR_{CATH} > 6 WU/m^2. The area under this ROC curve was 0.844 and P value was 0.0004. A TRV cutoff value of >3.96 m/s provided the highest balanced sensitivity (66.7%) and specificity (100%) to determine PVR_{CATH} > 6 WU/m^2 (Fig. 4).

A cutoff value for the ratio of TRV to TVI of the RVOT of >0.149 provided the highest balanced sensitivity (81.6%) and specificity (50%) to determine PVR_{CATH} > 6 WU/m^2. A cutoff value more than 0.301 had 100% specificity to predict PVR_{CATH} > 6 WU/m^2.

A cutoff value for the AcTc of ⩽4.34 provided the highest balanced sensitivity (91.3%) and specificity (50%) to determine PVR_{CATH} > 6 WU/m^2. A cutoff value less than 2.412 had 100% specificity to predict PVR_{CATH} > 6 WU/m^2. A cutoff value for the InTc of ⩽6.24 provided the highest balanced sensitivity (78.3%) and specificity (57.1%) to determine PVR_{CATH} > 6 WU/m^2. A cutoff value less than 1.108 had 100% specificity to predict PVR_{CATH} > 6 WU/m^2.

When the five Doppler indices studied were compared against each other as regard ROC curves analysis, the TSm and TRV cutoff values were the most reliable to predict elevated PVR > 6 WU/m^{2}in most of the patients studied with the highest balanced sensitivity and specificity compared to the other three Doppler indices and with the highest area under the curve among the five ROC curves studied (Table 2).

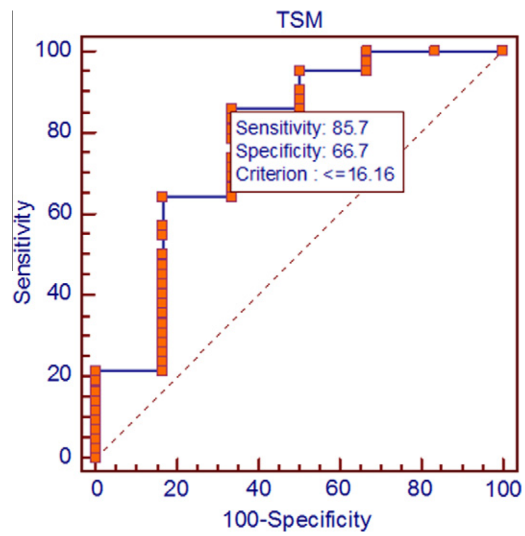

Figure 3. Receiver-operating characteristics curve. A TSm cutoff value of 16.16 provided the best-balanced sensitivity (85.7%) and specificity (66.7%) to determine patients with a PVR value > 6 WU/m^2. (Area under the curve = 0.778).

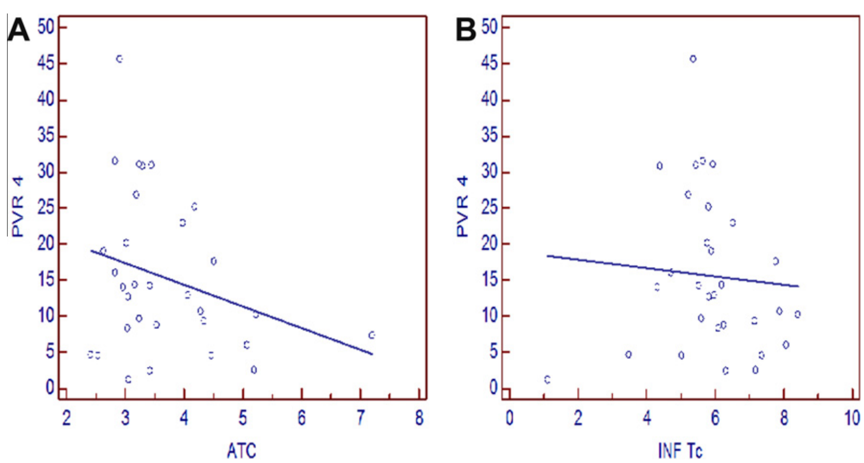

Figure 2. Linear regression analysis between invasive measurement of pulmonary vascular resistance (PVR) and (A) the heart rate corrected acceleration time (ATc), (B) the heart rate corrected inflection time (InTc).

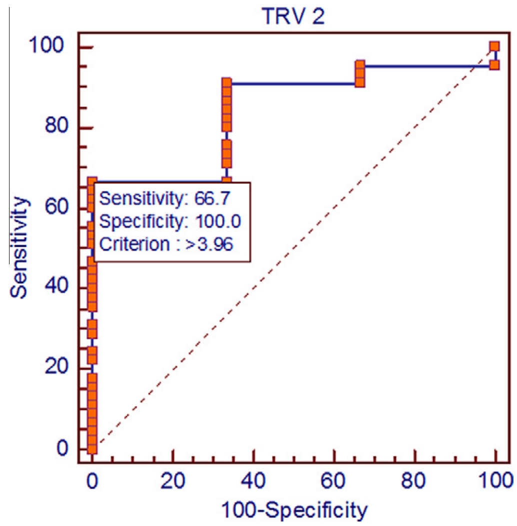

Figure 4. Receiver-operating characteristics curve. A TRV cutoff value of 3.96 m/s provided the best-balanced sensitivity (66.7%) and specificity (100%) to determine patients with a PVR value > 6 WU/m^2. (Area under the curve = 0.844.)

Discussion

PVR is an important determinant of morbidity and mortality in children with CHD. It is also a key component in determining the eligibility of patients for surgical repair. PVR is evaluated accurately by invasive measurement during cardiac catheterization, but because of its invasive nature, cardiac catheterization carries many disadvantages, including increased patients risks and discomfort, the high cost and inability to do regular follow up of PVR.

Echocardiographers continue to search for an accurate and noninvasive means of measuring PVR. Over the last decade a number of studies postulated different non-invasive means of predicting elevated PVR in patients with PH. However most of these studies did not test these hypotheses among children with PH secondary to CHD. This study tests the clinical usefulness of five of these Doppler indices in predicting elevated PVR in this important age group.

Estimation of RVSP using the Bernoulli equation to the TRV is almost a standard procedure. Most studies report a high correlation ($r = 0.57$–0.93) between trans-thoracic echocardiography and right heart catheterization measurements of RVSP [8]. Yock and Popp [20] in their study to none invasively estimate RVSP by Doppler in patients with TR found good correlation between the two measurements ($r = 0.93$). This study was published as early as 1984 and since then most of the studies dealing with the subject found variable yet good correlation between the two measurements among different patient groups. Denton et al. [5] found good correlation in patients with systemic scleroses and PH ($r = 0.83$, $P < 0.001$). Arcasoy et al. [2] found good correlation in patients with advanced lung disease ($r = 0.69$, $P < 0.0001$). We report a significant yet weaker correlation between the TRV and invasive measurement of PVR in our study ($r = 0.387$, $P = 0.0065$). It has to be noted that in case of severe PH, in fact, small variations of TRV cause large changes in RVSP value (since the modified Bernoulli equation is applied to TRV); and precise estimation of right atrial pressure may be more difficult when it is high.

Abbas et al. [1] hypothesized that since flow and pressure variables can be measured by echocardiography, a measure of PVR might be accurately obtained by Doppler-derived variables. The authors stated that since PVR is directly related to Δp and inversely related to Qp, TRV and TVI_{RVOT} can be used as correlates of Δp and Qp respectively. As PVR increases, changes in TVI_{RVOT} and TRV occur in opposite directions. The Doppler-derived ratio of TRV/TVI_{RVOT} was hence hypothesized as a good correlate of PVR. They found strong and significant correlation between this ratio and invasive measurement of PVR ($r = 0.93$, $P < 0.0001$). The authors studied 44 adult patients with wide range of diagnoses not including CHD. Many studies thereafter criticized the applicability of this hypothesis in patients with higher PVR values [7,15,16,18].

Table 2. Comparison between the different ROC curves.

ROC curve	AUC	SE	*P* value	Balanced sensitivity (%)	Balanced specificity (%)	Cutoff point
1	0.778	0.128	0.03	85.7	66.7	TSm ⩽ 16.16
2	0.844	0.098	0.0004	66.7	100	TRV > 3.96
3	0.624	0.109	0.26	81.6	50.0	TRV/TVI > 0.149
4	0.592	0.156	0.55	91.3	50	ATc ⩽ 4.34
5	0.516	0.173	0.93	78.3	57.1	InfTc ⩽ 6.24

ROC curve: receiver operating characteristics curve, AUC: area under the curve, SE: standard error, TSm: tissue Doppler S wave of the lateral tricuspid annulus, TRV: peak tricuspid regurgitant velocity, TRV/TVI: the ratio of the peak tricuspid regurgitant velocity to the velocity time integral of the right ventricular outflow tract, ATc: acceleration time corrected to heart rate, InfTc: inflection time corrected to heart rate.

In the current study the ratio of TRV/ TVI_{RVOT} had a significant yet much weaker correlation with invasive measurement of PVR ($r = 0.347$, $P = 0.015$) compared to the results obtained by Abbas et al. [1]. Our results, however, were closer to other studies which tested this ratio in patients with higher PVR [7,15,16,18]. This study, as far as we know, is the first to test this hypothesis in children with PH secondary to CHD.

Another study which tried to quantitatively assess PVR using another group of Doppler indices was that of Nakahata et al. [14]. The authors of this study selected the proximal PA branch as a sampling site to analyze the PA flow velocity curve based on the hypothesis that flow velocity profiles, as determined by AcTc and InTc in the proximal PA branch, have a greater effect on reflections from the pulmonary periphery than those in the main PA. Moreover, the authors noted that in patients with high PVR, there was a marked difference in flow velocity profiles between the left and the right PA. In this respect, they assumed that the left PA is a shorter vessel from the bifurcation of the main PA to the first branching than the right PA. This geometry, and the abnormal mechanical properties due to increased PVR, may lead to early, enhanced wave reflection in the left PA.

In the current study we measured the AcTc and InTc in the proximal left PA branch as postulated by Nakahata et al. [14]. Unlike the results obtained by Nakahata et al. [14] we found a weak and non-significant correlation between InTc in the proximal left PA branch and invasive measurement of PVR ($r = 0.02$ versus -0.8). Although the current study and that of Nakahata et al. [14] were among the few studies which tried to non-invasively assess PVR in children with PH secondary to CHD, substantial differences did exist between the two study groups that might explain these results. The mean value of PVR in group four of our study was significantly higher than that studied by Nakahata et al. [14] (14.46 ± 10.56 WU versus 8.9 ± 4.3 and 3.2 ± 0.8 WU in the high and low PVR groups studied by Nakahata et al. respectively). This might actually draw some doubts about the validity of these indices among patients with higher PVR.

In another subset of the current study (group 1, $n = 48$) we established an inverse correlation between TSm and invasive measurement of PVR with (2007) reported an inverse relationship between TSm and invasive measurement of PVR ($r = -0.710$, $P < 0.001$). Gurudevan et al. [10] studied 50 adult patients with chronic thromboembolic pulmonary vascular disease. They concluded that DTI of the lateral tricuspid annulus is a useful clinical tool that can provide a noninvasive estimate of PVR in these patients.

Our patients, unlike those of Gurudevan et al. [10], had volume overload due to intra-cardiac shunts as well as pressure overload due to progressive PH. Also our patient population had PVR values ranging from 0.9 to 24.4 WU, permitting an evaluation of TSm over a wide range of PVR. These factors might have led to the weaker negative correlation in the current study compared to that of Gurudevan et al. [10]. It is also conceivable that tricuspid annular motion increases with TR independent of RV function while the tricuspid annular motion decreases with elevated RVSP [13]. These opposite effects of TR and RVSP on the TSm might have led to the weaker correlation with PVR in the current study.

The closest study to our subset of patients in which DTI was applied concerning the study population was that of Bolca et al. [4] who examined the relationship of TSm and PVR in 28 patients with congenital or valvular disease and 10 control subjects. The r-value for this correlation was relatively low ($r = -0.47$) and was comparable to the r-value of our study ($r = -0.51$). It has to be noted however that only 14 of these 28 patients had CHD with left to right shunt versus 48 patients in our study, while the remaining patients examined by Bolca et al. [4] had mitral valve disease with pulmonary venous hypertension.

Although many cutoff points for each of the above mentioned Doppler indices were generated in the literature to predict different values of PVR, comparison of those cutoff points to the cutoff points generated in the current study is of limited value due to the fact that values postulated for PVR for which these cutoff points are generated do vary considerably from each other.

A general consensus among cardiothoracic surgeons exist that an exact value of PVR though important is not the only factor in determining the post-operative outcome after surgical repair of cardiac defects. Other factors include the type of the defect, the degree of postoperative care including the availability of extracorperal membrane oxygenation and NO, the expertise of the operating center and the co-morbid conditions of the patient. Nevertheless a PVR of 6 WU/m^2 represents a safe limit below which most of the patients can undergo surgical repair safely [6,17].

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We chose cutoff points of the five Doppler indices measured with the highest balanced sensitivity and specificity to predict PVR less than 6 WU/m^2. Unlike our study, Abbas et al. [1] chose a low PVR value of 2 WU while Nakahata et al. [14] chose PVR of 4.6 WU/m^2. Both values are lower than the safe limit for which children with CHD can undergo surgical repair safely and thus are of limited clinical usefulness. Other studies chose higher absolute values of PVR and did not index these values to the BSA of the patients which also represent a limitation in these studies [15,18].

On the other hand, the data from the different ROC curves generated in the current study were compared against each other. The highest balanced sensitivity and specificity among these five ROC curves was that of the TRV and TSm cutoff points. These two cutoff points had the highest area under the curve (0.844 and 0.788 respectively) and the only significant *P*-values (0.0004 and 0.03 respectively) among the five ROC curves generated. It should be mentioned that unlike TRV, which is dependent on proper beam alignment and on the presence of an adequate TR velocity Doppler signal (which may not be seen in all patients), the TSm of the lateral tricuspid annulus is an easy and accurate measurement that can be obtained in all patients.

Study limitations

One of the limitations of this study is the possible errors in the measurement of cardiac output using Fick's method. The accuracy of Fick's cardiac output can be affected because of its use of assumed oxygen consumption. Cardiac output measurement errors can have a significant effect on the calculated PVR and, therefore, may underestimate or overestimate the relationship between the Doppler indices studied and invasive PVR. By consensus at our institution, cardiac output is determined using Fick's method in patients with CHD as a large percentage of these patients had significant TR and the use of thermodilution method to estimate cardiac output will be subjected to significant errors in patients with CHD and significant TR.

Another limitation is that in the two subgroups where TRV measurement was required, all patients had at least mild tricuspid regurgitation, making the determination of the TRV feasible. This may not be true in the general practice in which a considerable number of patients with known or suggested PH may lack any recordable degree of TR making the calculation of these Doppler indices difficult.

Finally intra- and inter-observer variability is important since Doppler indices can be different from measure to measure among different users. Whether or not the presence of significant intra- or inter-observer variability among any of these Doppler indices will limit their use in clinical practice remains a possibility that needs to be examined in future studies.

Conclusion

Prediction of elevated PVR in children with PH secondary to CHD could be achieved non-invasively using a number of Doppler indices. Among the five Doppler indices examined in the current study, the peak tricuspid regurgitant velocity and the tissue Doppler S wave of the lateral tricuspid annulus had the highest balanced sensitivity and specificity to predict PVRI > 6 WU/m^2. A TSm cutoff value of ⩽16.16 cm/s had 85.7% sensitivity and 66.7% specificity to determine $PVR_{CATH} > 6$ WU/m^2. A cutoff value less than 7.62 cm/s had 100% specificity to predict $PVR_{CATH} > 6$ WU/m^2. A TRV cutoff value of >3.96 m/s had 66.7% sensitivity and 100% specificity to determine $PVR_{CATH} > 6$ WU/m^2. However TSm represents a technically simpler means of predicting PVR noninvasively compared to TRV.

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