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Non-invasive Estimation of Pulmonary Vascular Resistance in Patients of Pulmonary Hypertension in Congenital Heart Disease with Unobstructed Pulmonary Flow

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Abstract

Background: Pulmonary vascular resistance (PVR) plays a pivotal role in determining operability and prognosis in patients with congenital heart disease (CHD) complicated by pulmonary hypertension (PH). Right heart catheterization (RHC) is the gold standard for assessing PVR, but its invasive nature limits its frequent use, particularly in pediatric populations. Non-invasive echocardiographic methods have emerged as promising alternatives.

Objective: To evaluate the accuracy and clinical utility of Doppler-derived echocardiographic indices for estimating PVR in patients with CHD-associated PH and unobstructed pulmonary flow.

Methods: This prospective observational study was conducted at a tertiary care center in South India and included 80 patients with CHD and PH. Doppler echocardiography was used to measure tricuspid regurgitation velocity (TRV), right ventricular outflow tract velocity-time integral (VTIRVOT), and pulmonary artery acceleration time (PAAT). The TRV/VTIRVOT ratio and PAAT were analyzed in relation to invasive PVR data available in a subset of patients undergoing cardiac catheterization.

Results: TRV/VTIRVOT ratio correlated strongly with invasive PVR ($r = 0.78$, $p < 0.001$). A ratio >0.2 demonstrated a sensitivity of 86% and specificity of 81% for detecting elevated PVR (>3 Wood units). PAAT <90 ms was also significantly associated with high PVR. Bland-Altman analysis showed good agreement between non-invasive and invasive PVR measurements.

Conclusion: Non-invasive estimation of PVR using echocardiographic parameters, especially TRV/VTIRVOT and PAAT, provides a reliable and practical alternative to invasive catheterization in selected patients with CHD and unobstructed pulmonary flow. These

measures can support early diagnosis, risk stratification, and decision-making in operability assessment.

Introduction

Pulmonary hypertension (PH) is a significant complication in patients with congenital heart disease (CHD), particularly those with left-to-right shunt lesions such as atrial septal defect (ASD), ventricular septal defect (VSD), and patent ductus arteriosus (PDA) (1,2). Persistent elevation of pulmonary blood flow in these conditions can lead to pulmonary vascular remodelling, increased pulmonary vascular resistance (PVR), and eventual right heart failure if left unaddressed. Accurate assessment of PVR is crucial in determining the operability of these patients and predicting postoperative outcomes.

Right heart catheterization (RHC) remains the gold standard for measuring PVR (3,4). However, its invasive nature, associated risks, and limited availability, especially in resource-constrained settings, necessitate the exploration of non-invasive alternatives. Echocardiography, a widely accessible and non-invasive imaging modality, has emerged as a potential tool for estimating PVR.

Several echocardiographic parameters have been proposed for non-invasive estimation of PVR. Among these, the ratio of tricuspid regurgitation velocity (TRV) to the right ventricular outflow tract time-velocity integral (VTIRVOT) has shown promise (5). This ratio reflects the relationship between pressure and flow across the pulmonary circulation, providing an indirect measure of PVR. Studies have demonstrated a significant correlation between TRV/VTIRVOT ratio and invasively measured PVR, suggesting its utility in clinical practice (6,7).

Another parameter, the pulmonary artery acceleration time (PAAT), defined as the interval from the onset of systolic flow to peak flow velocity in the pulmonary artery, has been inversely correlated with PVR. Shorter PAAT values indicate higher PVR, making it a useful non-invasive marker (8,9).

Despite these advancements, the application of echocardiographic parameters for PVR estimation in patients with CHD and unobstructed pulmonary flow remains underexplored. Most existing studies have focused on heterogeneous populations, including those with pulmonary venous hypertension or obstructive lesions, which may confound the accuracy of echocardiographic measurements. Therefore, there is a need for focused research on this specific subset of patients.

This study aims to evaluate the accuracy and clinical utility of Doppler-derived echocardiographic indices, specifically the TRV/VTIRVOT ratio and PAAT, for estimating PVR in patients with CHD-associated PH and unobstructed pulmonary flow. By correlating these non-invasive measures with invasively obtained PVR values, we seek to validate their applicability in routine clinical practice, potentially reducing the reliance on invasive procedures.

Methods

Study Design and Setting

This was a prospective cross-sectional observational study conducted in the Department of Pediatric Cardiology at a tertiary care center in South India over a period of 10 months, from January to October 2024. The study aimed to evaluate the reliability of echocardiographic indices for estimating pulmonary vascular resistance (PVR) in children with congenital heart disease (CHD) and pulmonary hypertension (PH) with unobstructed pulmonary flow.

Study Population

Inclusion Criteria:

- Children aged 1 to 18 years.
- Diagnosed with acyanotic CHD with left-to-right shunt (e.g., ASD, VSD, PDA).
- Evidence of pulmonary hypertension defined by tricuspid regurgitation velocity (TRV) > 2.8 m/s on echocardiography.
- Unobstructed pulmonary venous return and right ventricular outflow tract (RVOT).

Exclusion Criteria:

- Cyanotic CHD.
- CHD with right or left ventricular outflow obstruction or significant valvular stenosis.

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- Chronic lung disease, airway anomalies, or known interstitial lung disease.
- Poor echocardiographic window or inadequate Doppler signal.
- Hemodynamically unstable patients or those already receiving PH-specific therapy.

Echocardiographic Assessment

All patients underwent a detailed transthoracic echocardiogram using a Philips Affiniti 70 or equivalent machine. The echocardiograms were performed by experienced pediatric cardiologists blinded to the clinical and catheterization data.

Key Doppler Measurements:

1. **Tricuspid Regurgitation Velocity (TRV)** – Measured via continuous-wave Doppler from the apical four-chamber or parasternal long axis view.
2. **Right Ventricular Outflow Tract Velocity Time Integral (VTIRVOT)** – Measured using pulsed-wave Doppler at the proximal RVOT in the parasternal short-axis view.
3. **TRV/VTIRVOT Ratio** – Calculated to serve as a surrogate marker for PVR.
4. **Pulmonary Artery Acceleration Time (PAAT)** – Defined as the interval from onset to peak of pulmonary systolic flow, measured in the main pulmonary artery.
5. **Systolic Pulmonary Artery Pressure (sPAP)** – Estimated using the Bernoulli equation from TRV and adding right atrial pressure.

Each parameter was measured in triplicate and averaged for analysis.

Invasive Hemodynamic Measurement

A subset of 30 patients underwent cardiac catheterization for operability assessment. Right heart pressures and pulmonary artery pressures were recorded. PVR was calculated using the Fick principle as:

PVR (WU)=Mean PAP - PCWPCardiac Output (L/min)\text{PVR (WU)} = \frac{\text{Mean PAP - PCWP}}{\text{Cardiac Output (L/min)}}PVR (WU)=Cardiac Output (L/min)Mean PAP - PCWP

Where pulmonary capillary wedge pressure (PCWP) was assumed to be 5 mmHg in the absence of left heart disease and measured if necessary.

Data Collection

Demographic details, clinical diagnosis, body surface area, and oxygen saturation were collected from medical records. All patients were evaluated for operability based on standard hemodynamic cut-offs (PVR < 4 WU considered operable).

Statistical Analysis

Statistical analysis was performed using SPSS version 26.0. Continuous variables were presented as mean ± standard deviation (SD) or median with interquartile range (IQR). Categorical variables were expressed as percentages. Pearson's correlation coefficient was used to evaluate the association between echocardiographic and catheter-derived PVR values.

Receiver Operating Characteristic (ROC) curve analysis was used to determine the predictive ability and optimal cut-offs for TRV/VTIRVOT ratio and PAAT in identifying elevated PVR (>3 Wood units). Bland-Altman analysis was performed to assess agreement between non-invasive and invasive methods. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from the parents or guardians of all participating children. Confidentiality was maintained throughout the study.

Results

A total of **80 children** with congenital heart disease and echocardiographic evidence of pulmonary hypertension were enrolled. The mean age of the participants was **9.2 ± 3.1 years**, and 56% were male. Among the cohort, **30 patients** underwent right heart catheterization for invasive PVR measurement, enabling validation of non-invasive indices.

Table 1: Baseline Demographic and Clinical Characteristics

Characterstics	**n = 80 (mean ± SD)**
Mean Age (years)	9.2 ± 3.1

Male : Female	1.3 : 1
Common CHD Diagnoses	VSD (40%), ASD (35%), PDA (25%)
Mean Body Surface Area (m^2)	0.95 ± 0.14
Mean Oxygen Saturation (%)	95.6 ± 1.8
Patients undergoing catheterization	30

The study population primarily consisted of children with common acyanotic CHDs. A representative subset underwent invasive pressure measurement for correlation analysis.

Table 2: Doppler Echocardiographic Measurements

Parameter	**Mean ± SD (n = 80)**
TRV (m/s)	3.5 ± 0.4
VTIRVOT (cm)	14.2 ± 2.1
TRV/VTIRVOT Ratio	0.25 ± 0.07
Pulmonary Artery Acceleration Time (PAAT) (ms)	81 ± 15
Estimated sPAP (mmHg)	56.7 ± 8.9

Doppler-derived measurements were consistent across the population. The TRV/VTIRVOT ratio and PAAT were used as surrogate markers for non-invasive PVR estimation.

Table 3: Invasive vs Non-Invasive PVR Correlation (n = 30)

Parameter	**Correlation with Invasive PVR**	**p-value**
TRV/VTIRVOT Ratio	r = 0.78	< 0.001
PAAT	r = -0.65	< 0.01

Estimated sPAP	r = 0.61	0.02

The TRV/VTIRVOT ratio showed a strong positive correlation with catheter-derived PVR, while PAAT showed a moderate negative correlation. These findings support their diagnostic utility in non-invasive PVR assessment.

Table 4: ROC Curve Analysis for Elevated PVR (>3 Wood Units)

Parameter	**AUC**	**Sensitivity**	**Specificity**	**Optimal Cut-off**
TRV/VTIRVOT Ratio	0.89	86%	81%	> 0.20
PAAT	0.84	80%	75%	< 90 ms

Both TRV/VTIRVOT ratio and PAAT had high diagnostic accuracy for detecting elevated PVR. A TRV/VTIRVOT ratio > 0.20 had the highest predictive power for PVR >3 WU.

Table 5: Bland-Altman Analysis – Invasive vs Non-Invasive PVR

Statistic	**Value**
Mean Difference (Non-invasive – Invasive)	0.3 Wood Units
Limits of Agreement (95% CI)	–1.2 to +1.8 WU

The Bland-Altman plot indicated good agreement between non-invasive and invasive methods for estimating PVR, with a small bias and acceptable limits of agreement.

Discussion

This study aimed to evaluate the accuracy and clinical utility of Doppler-derived echocardiographic indices, specifically the TRV/VTIRVOT ratio and PAAT, for estimating PVR in patients with CHD-associated PH and unobstructed pulmonary flow. By correlating these non-invasive measures with invasively obtained PVR values, we sought to validate their

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applicability in routine clinical practice, potentially reducing the reliance on invasive procedures.

Our findings demonstrated a strong positive correlation between the TRV/VTIRVOT ratio and catheter-derived PVR ($r = 0.78$, $p < 0.001$). A TRV/VTIRVOT ratio > 0.20 was identified as an optimal cutoff for predicting elevated PVR (>3 Wood units), with a sensitivity of 86% and specificity of 81%. These results align with previous studies that have reported similar correlations and cutoff values, reinforcing the utility of this ratio as a reliable non-invasive marker for PVR estimation (10–12).

Similarly, PAAT demonstrated a moderate negative correlation with invasive PVR measurements ($r = -0.65$, $p < 0.01$). A PAAT value < 90 ms was associated with elevated PVR, exhibiting a sensitivity of 80% and specificity of 75%. These findings are consistent with existing literature that highlights the inverse relationship between PAAT and PVR, further supporting its role as a non-invasive surrogate for PVR assessment (13,14).

The Bland-Altman analysis in our study revealed good agreement between non-invasive and invasive PVR measurements, with a mean difference of 0.3 Wood units and limits of agreement ranging from -1.2 to +1.8 WU. This suggests that echocardiographic estimates of PVR can reliably approximate invasive measurements, particularly in patients with CHD and unobstructed pulmonary flow.

While our study reinforces the potential of echocardiographic parameters in non-invasive PVR estimation, it is essential to acknowledge certain limitations. The sample size, particularly the subset undergoing catheterization, was relatively small, which may affect the generalizability of the findings. Additionally, echocardiographic measurements can be operator-dependent, and factors such as image quality and patient cooperation can influence the accuracy of the assessments. Future studies with larger cohorts and standardized measurement protocols are warranted to validate and refine these non-invasive techniques.

Conclusion

Our study demonstrates that echocardiographic parameters, specifically the TRV/VTIRVOT ratio and PAAT, are valuable non-invasive tools for estimating PVR in patients with CHD-associated PH and unobstructed pulmonary flow. These measures can aid in the early identification of elevated PVR, guide clinical decision-making regarding operability, and potentially reduce the need for invasive procedures. Incorporating these non-invasive assessments into routine clinical practice could enhance the management and outcomes of patients with CHD and PH.

Recommendations

Based on our findings, we recommend the routine use of Doppler echocardiographic parameters—particularly the TRV/VTIRVOT ratio and PAAT—for non-invasive estimation of pulmonary vascular resistance in children with congenital heart disease and unobstructed pulmonary flow. These indices offer reliable screening tools in outpatient settings, especially where catheterization is not readily available or feasible. Incorporating these measures into initial evaluations and follow-up assessments may enhance early detection of elevated PVR and guide timely referral for invasive testing or surgical decision-making. Future research should focus on multicenter validation and incorporation into operability scoring systems.

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