Reliability of Doppler echocardiography in the assessment of high pulmonary vascular resistance in patients with severe pulmonary arterial hypertension

Srinivas Bhyravavajhala, Sreekanth Yerram, Raghukishore Galla, Venkata siva krishna Kotapati

Department of Cardiology, Nizam’s Institute of Medical Sciences, Punjagutta, Hyderabad, Telangana, 500082 India

A R T I C L E   I N F O

Article history:
Received 28 September 2018
Accepted 10 October 2018
Available online 2 November 2018

Keywords:
Doppler echocardiography
Pulmonary hypertension
Pulmonary vascular resistance
Tricuspid regurgitation velocity

A B S T R A C T

Background: The objective is to assess whether the squaring of tricuspid regurgitation velocity (TRV) gives an improved estimate of pulmonary vascular resistance (PVR) or is equivalent to the ratio of TRV and time velocity integral of right ventricular outflow tract (TVI_RVOT) (TRV/TVI_RVOT) for assessing PVR in patients with high PVR values.

Methods: Thirty patients predicted to have PVR >6 WU by Doppler were included in the present study. TRV and TVI_RVOT were measured by echo Doppler. TRV/TVI_RVOT and TRV^2/TVI_RVOT were calculated. PVR_CATH was estimated within 2 h of Doppler study. Regression equations for calculating PVR from TRV/TVI_RVOT (PVR_ECHO1) and TRV^2/TVI_RVOT (PVR_ECHO2) were developed. Bland–Altman analysis for agreement between PVR_CATH and PVR_ECHO1, PVR_ECHO2 was carried out.

Results: The mean value of PVR_CATH was found to be 15.08 ± 7.03 WU. The calculated values of PVR_ECHO1 and PVR_ECHO2 were found to be 15.08 ± 6.34 WU and 15.05 ± 6.08 WU, respectively. The linear regression analysis carried out for PVR_CATH and TRV/TVI_RVOT showed good correlation (R = 0.84). Bland–Altman analysis showed excellent agreement between the two Doppler methods and invasive PVR with negligible bias.

Conclusion: Noninvasive estimation of PVR by Doppler is reliable even in patients with high PVR (>6 WU) and, squaring TRV is not superior to TRV alone.

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1. Introduction

Pulmonary vascular resistance (PVR) is an important parameter in the assessment of patients with pulmonary arterial hypertension (PAH).1–3 PVR is also an important hemodynamic variable in the prognosis and management of patients with congenital shunt lesions and pulmonary hypertension.4,5 A risk-free noninvasive estimate of PVR is desirable. Noninvasive estimation of PVR by Doppler echocardiography has been studied in many published reports. Abbas et al have later proposed, based on their meta-analysis, that squaring TRV in the equation is more reliable in predicting higher PVR of >6 WU.8 Noninvasive estimate of PVR in this subset of patients with PAH is important as these patients require frequent monitoring of PVR to check their response to medical therapy. We aimed to study whether squaring TRV gives an improved estimate of PVR or is equivalent to the ratio of TRV/TVI_RVOT for assessing PVR in patients with high PVR values.

2. Methods

2.1. Study population

Thirty patients of PAH who had TRV/TVI_RVOT >0.275 and likely to have PVR >6 WU were included in the present study, after securing...
the permission from the Institutional Ethics Committee. A written informed consent was taken from the patients or their parents. Patients with inadequate tricuspid regurgitation (TR) jet velocity, severe right heart failure, right ventricular dysfunction, congenital aorta pulmonary shunts, and PVR <6 WU were excluded from the study.

2.2. Echocardiography

Echocardiographic study was performed using iE33 (Philips Andover, MA, USA). Procedure was performed in the left lateral decubitus position. Doppler parameters recorded were as follows: TVI_{RVOT} was obtained (in cm) by placing a pulsed wave Doppler sample volume in the RVOT just within the pulmonary valve in the parasternal short-axis view. An average of three values was taken. TRV was measured (in m/sec) in the parasternal short-axis view and apical four-chamber view. All the echo measurements were taken as per the American Society of Echocardiography guidelines. 

Suboptimal Doppler signals were augmented using agitated normal saline. Continuous-wave Doppler was used to determine the peak TRV. Care was taken to align the sample volume accurately to get the highest Doppler velocity. The highest of the velocities obtained from the above two views was taken. The TR velocity was squared; the TRV/TVI_{RVOT} and TRV^2/TVI_{RVOT} ratios were then calculated.

2.3. Cardiac catheterization

All the patients were subjected to cardiac catheterization through the femoral route within 2 h of echocardiography. For children younger than 12 years, the procedure was performed under conscious sedation at the start of the procedure. Balloon-tipped Swan-Ganz catheter was used for the hemodynamic study. Complete oximetry study and right and left heart catheterization were carried out. Pressures in the right atrium, right ventricle, pulmonary capillary wedge pressure (PCWP), pulmonary artery systolic pressure (PASP), pulmonary artery diastolic pressure and mean pressure (PAMP) were measured. Qp was calculated using the Fick method. Lafarge et al oxygen consumption tables were used in the calculation of cardiac output. PVR was calculated using the formula:

\[ \text{PVR} = \frac{\text{PAMP} - \text{PCWP}}{\text{Qp}} \]

2.4. Statistical analysis

Statistical analysis was performed using SPSS software, version 20 (La Jolla, CA, USA). Continuous variables were expressed as mean \pm standard deviation (SD) with range. Categorical variables were expressed as percentages. Pearson’s correlation coefficient was obtained between the Doppler-derived ratios and invasive PVR. Linear regression analysis was carried out between TRV/TVI_{RVOT} and PVRCATH, and the regression equation for PVR was generated (PVRECHO1). Similarly, linear regression analysis was also carried out between TRV^2/TVI_{RVOT} and PVRCATH, and regression equation for PVR was generated (PVRECHO2). Bland–Altman analysis for agreement between PVRECHO1 and PVRECHO2 with PVRCATH was performed.

3. Results

The demographic and clinical characteristics of the study population are shown in Tables 1 and 2. The study group consisted of 30 patients with age between 1 and 60 years. Males constituted 10 patients (33.33%). The most common diagnosis is primary pulmonary hypertension which constituted 10 patients (33.33%) followed by ventricular septal defect in eight patients (26.67%). PVRCATH is in the range of 8.1–40.9, the mean value being 15.08 ± 7.03. The catheterization and Doppler parameters of the study population are shown in Table 3.

![Image showing measurement of TVI_{RVOT} and TRV. TVI_{RVOT} time velocity integral of right ventricular outflow tract; TRV, tricuspid regurgitation velocity.](image-url)
Noninvasive estimation of PVR is studied by many researchers with Doppler-derived TRV and TVIRVOT as surrogates for ΔP and Qp, respectively. PVR is directly proportional to ΔP and inversely proportional to Qp. As the pulmonary artery pressure increases, TRV increases in accordance with the Bernoulli’s principle. In the absence of RVOT obstruction, TRV correlates well with PASP. As both hyperkinetic PAH and elevated PVR can increase PASP, assessment of Qp is important for PVR estimation. TVIRVOT is a surrogate for Qp. Increase in PVR is reflected by a conformational change in TVIRVOT, where mid-systolic notching and premature deceleration of pulmonary flow occur, leading to a decreased right ventricular ejection time. As PVR increases, TVIRVOT decreases. TRV/TVIRVOT has been validated in various studies as an estimate of PVR\textsubscript{CAT}.

Many studies showed good correlation of Doppler derived measurements with invasive PVR in low PVR states. Though the ROC curves showed good cut-off values for PVR there is no proper evidence of these Doppler surrogate’s use in high PVR states. Abbas et al in his meta-analysis study showed that the ratio of TRV/TVIRVOT correlated well in patients with high PVR and hypothesized that squaring TRV correlated better in high PVR states. In his study, Abbas et al hypothesized that squaring of TRV in accordance with Bernoulli’s principle (\(P = 4V^2\)) may show good correlation. But in noninvasive estimation of PVR, the absolute value of pressure is not taken, only ratio of TRV and TVIRVOT. As PVR increases, the TRV increases and TVIRVOT decreases, and the ratio maintains a linear relation with PVR.

TRV/TVIRVOT reflects the trend of PVR, and squaring TRV does not have any effect on the relation TRV/TVIRVOT has with increase in PVR. In the study by Abbas et al which is a meta-analysis, squaring TRV probably helped to maintain the homogeneity of the heterogeneous data and hence showed better correlation.

In the present study, 30 prospective patients with high PVR >6 WU were studied. Of the total population, 66.67% were females showing higher incidence of high PVR in females. The most common age group in the present study was 20–30 years constituting around 23% of the study population. Shortness of breath, which was New York Heart Association, was the most common clinical presentation of the study group. The ratio of TRV/TVIRVOT and TRV\(^2\)/TVIRVOT was calculated. Linear regression analysis showed good correlation between the two Doppler-derived parameters, and Bland–Altman analysis showed negligible bias.

### Table 2

| Diagnosis                  | Frequency, n (%) |
|----------------------------|------------------|
| OS ASD, n (%)              | 7 (23.33%)       |
| SV ASD, n (%)              | 3 (10.00%)       |
| VSD, n (%)                 | 8 (26.67%)       |
| Primary PAH, n (%)         | 10 (33.33%)      |
| PDA, n (%)                 | 2 (6.67%)        |

OS ASD, ostium secundum atrium septal defect; SV ASD, sinus venosus atrial septal defect; VSD, ventricular septal defect; PAH, pulmonary arterial hypertension; PDA, patent ductus arteriosus.

### Table 3

| Variable                  | Mean ± SD |
|---------------------------|-----------|
| TRV/TVI                   | 0.32 ± 0.05 |
| TRV\(^2\)/TVI             | 1.60 ± 0.46 |
| PVRC Ath, mean ± SD       | 15.08 ± 7.03 |
| PVRECHO1, mean ± SD       | 15.08 ± 6.34 |
| PVRECHO2, mean ± SD       | 15.05 ± 6.08 |
| PCWP, mean ± SD           | 7.6 ± 4.32  |
| RV TAPSE, mean ± SD       | 1.93 ± 0.33  |
| IVC diameter, mean ± SD   | 1.56 ± 0.29  |

SD, standard deviation; TRV, tricuspid regurgitant velocity; TVI, time velocity integral; PVR, pulmonary vascular resistance; PCWP, pulmonary capillary wedge pressure; RV TAPSE, right ventricle tricuspid annular plane systolic excursion; IVC, inferior vena cava.

The linear regression analysis carried out for PVRC\textsubscript{CAT} and TRV/TVIRVOT showed good correlation (\(R = 0.84\)), and a regression equation was derived for calculating PVRECHO1 which is as follows:

\[
PVRECHO1 = 121.439 \times \frac{TRV}{TVI} -23.886
\]

Bland–Altman analysis showed that the bias between the two methods is negligible (–0.0002) with 95% limits of agreement being –5.41 and 5.41.

Similarly, another linear regression analysis was carried out for PVRC\textsubscript{CAT} and TRV\(^2\)/TVIRVOT which showed good correlation (\(R = 0.775\)) (Fig. 2), and regression equation for calculating PVRECHO2 was derived which is as follows:

\[
PVRECHO2 = 13.237 \times \frac{TRV^2}{TVI} - 6.014
\]

Bland–Altman analysis showed that the bias between these methods is negligible (–0.0101) with 95% limits of agreement being –6.595 and 6.45 (Fig. 3).

### 4. Discussion

Assessment of PVR is important in the prognostication and management of patients with congenital and acquired PAH and also for monitoring the response to newer modalities of treatment. Many studies showed good correlation of Doppler derived measurements with invasive PVR in low PVR states. Though the ROC curves showed good cut-off values for PVR there is no proper evidence of these Doppler surrogate’s use in high PVR states. Abbas et al hypothesized that squaring of TRV in accordance with Bernoulli’s principle (\(P = 4V^2\)) may show good correlation. But in noninvasive estimation of PVR, the absolute value of pressure is not taken, only ratio of TRV and TVIRVOT. As PVR increases, the TRV increases and TVIRVOT decreases, and the ratio maintains a linear relation with PVR.

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Fischer’s R to Z transformation test showed no superiority of one over the other. Although the reliability of Doppler in high PVR is still debated and studies showed conflicting results, in our study, there was a good correlation. This is in contrast to previous studies by Bhatt et al and Rajagopalan et al. In our study, we found no added advantage of the TRV² as hypothesized previously for better correlation in high PVR.

4.1. Limitations

Limitations inherent to the Doppler technique are related to proper alignment of the ultrasound beam, and the error is minimized by taking average of three values and using agitated saline to augment the Doppler signals. In addition, the peak TRV may vary with respiration, so using an average of multiple beats, rather than the maximum velocity obtained during sinus rhythm, may be a more appropriate representation of this parameter.

In addition, all the patients included in the study did not undergo right heart catheterization and Doppler echocardiography simultaneously, so an error of different hemodynamic states may have confounded the results. The sample is small in our present study. The patients with high PVR are prospectively studied, so this sample size may be adequate for statistical analysis, but still larger population may be required. Another limitation is we did not study the follow-up PVR estimation in these patients after starting therapy to track PVR changes.

5. Conclusion

We conclude that the ratio of TRV/TRVTI is a good noninvasive parameter for assessing PVR, even in patients with high PVR value.

Conflict of interest

All authors have none to declare.

Funding

No financial support was received for this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijhj.2018.10.031.