

Correlation between Pulmonary Vascular Resistance and Some Cardiac Indices

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Abstract

Background: The Pulmonary Vascular Resistance (PVR) index is an important hemodynamic variable in making determinations regarding cardiopulmonary diseases and can be measured echocardiographically. The objective of this report is to examine the relationship between echocardiographic parameters of ventricular function using PVR measurements.

Materials and Methods: This study included 40 patients. PVR and left ventricular function indexes (left ventricle diastolic function and Systolic Pulmonary Arterial Pressure (SPAP)) were measured echocardiographically and analyzed using a linear regression test. The relationship between the right ventricular Tricuspid Annular Plane Systolic Excursion (TAPSE) index and the mean PVR index was assessed with the Mann-Whitney test using SPSS Ver. 15.

Results: A comparison between PVR and TAPSE showed that the mean PVR was significantly reduced when TAPSE increased, with a cut-off point of 1.8 ($P=0.026$). Examination of the relationship between SPAP and PVR made it clear that increased SPAP (mean PAP > 25 mmHg) caused PVR to significantly increase ($P < 0.0001$). Analysis of the relationship between LVEF and PVR showed that PVR decreased significantly in parallel with an increasing ejection fraction ($P=0.004$). Determination of the mean PVR in the LV Diastolic dysfunction group showed that the mean difference between the PVR indexes of the LV diastolic dysfunction group and the restrictive pattern group was significantly higher than the mean difference between the PVR indexes of the LV diastolic dysfunction group and the normal group ($P < 0.0001$).

Conclusion: Considering the significance of PVR measurement in treating cardiovascular diseases, we recommend echocardiography as a simple, accessible and noninvasive method for determining this metric. In this study, we demonstrated that the strongest relationship between echocardiographically determined measurements exists for the correlation between PVR and diastolic dysfunction and the grades thereof. This method can be used as an accessible method for determining PVR and as an index for assessing prognosis.

Keywords: Pulmonary Vascular Resistance; Left Ventricular Ejection Fraction; Systolic Pulmonary Arterial Pressure; Left Ventricle Diastolic Function; Echocardiography

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Introduction

In healthy adults, the pulmonary vascular bed is a low pressure and resistance system that receives a high volume of blood. Vascular resistance is measured in terms of a pressure gradient. As Doppler echocardiography is capable of measuring this gradient as well as blood circulation flow, it is possible to conduct a variety of vascular resistance measurements in several organs using both two-dimensional and Doppler echocardiography. Pulmonary Vascular

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Resistance (PVR) is an important parameter in terms of treating cardiopulmonary patients. It is therefore necessary to obtain PVR measurements from patients with diseases that result in an elevated PVR index (e.g., chronic heart failure, valvular diseases, primary pulmonary hypertension and congenital diseases accompanied by a cardiovascular shunt) to effectively assist clinicians in treating patients and in assessing disease prognosis

Left ventricle ejection fraction (LVEF) index for the assessment of left ventricular systolic function

The LVEF is one of the most recognized and ac-

Table 1: Diastolic dysfunction classification

1. Mild dysfunction	Impaired relaxation with normal filling pressure
2. Moderate dysfunction	Pseudonormalized mitral inflow pattern
3. Severe reversible dysfunction	Reversible restrictiveness (high filling pressure)
4. Severe irreversible dysfunction	Irreversible restrictiveness (high filling pressure)

ceptable indexes of left ventricular systolic function. Normal LVEF values as measured by echocardiography and angiography are in the range of 55% to 75%. However, measurements performed using nuclide angiography generally produces lower values (45% to 65%). A value below 45%, aside from other loading conditions, is illustrative of a ventricular dysfunction.

Examination of LV diastolic function

Determination of left ventricular diastolic function is an important component of the cardiac evaluation. Patients are classified into four classes, depending on the degree of diastolic dysfunction (Table 1). Presently, echocardiography is the best means of making this assessment.

Pulmonary Artery Pressure (PAP) index

Pulmonary artery hypertension (PAH) refers to chronic elevated PAP and PVR indexes and leads to enlargement and hypertrophy of the right ventricle and right cardiac failure.²⁻⁹ In patients with early-stage of pulmonary hypertension (PH), the PAP is normal at rest. However, PAP increases pathologically during exercise. In more severe form of pulmonary hypertension, PAP is high even at rest. Doppler echocardiography is noninvasive methods for measuring PAP and pulmonary hypertension is defined when mean PAP is more than 25 mmHg. This value may also be measured invasively via catheterization. PAH has three primary causes: (1) remodeling of vascular walls, (2) thrombosis, and (3) vasoconstriction. Increases in PVR may be either reversible or irreversible. Remodeling occlusion is the cause of irreversible pulmonary hypertension, and an increase of vascular tone is among the reversible causes of pulmonary hypertension, which comprises more than half of pulmonary hypertension cases.

Tricuspid Annular Plane Systolic Excursion (TAPSE)

Echocardiography is the most accessible method for examining right ventricular function. The results of echocardiographic tests for estimating right ven-

tricle function (RVEF) completely agree with results based on radionuclide methods, despite the fact that echocardiography generally and systemically ignores right ventricle trabeculations; therefore, determining RVEF tests via echocardiography may occasionally underestimate some measures of ventricular dysfunction when compared to measurements made using the radionuclide method. One of the indexes measured using echocardiography by non-geometric methods is Tricuspid Annular Plane Systolic Excursion (TAPSE). This is a simple measurement for estimation of right ventricular function. Previous studies have established that the use of TAPSE for estimation of RVEF provides results that are both highly satisfactory and in significant agreement with measurements obtained using the radionuclide method. The sensitivity of TAPSE measurements in diagnosis of initial stage of right ventricle failure is even higher than that of the radionuclide method. It appears that systolic deceleration of tricuspid valve annulus represents a very accurate index for predicting right ventricle dysfunction. Alternatively, in patients suffering from cardiac failure, a reduction in the TAPSE index is directly related to the intensity of right ventricular failure. TAPSE index values range from 1.5 to 2 in normal individuals.

The present research is designed to assess whether Doppler echocardiography can be a suitable and non-invasive method for estimating PVR by measuring indexes of left and right ventricular function and to study the relationship between these parameters.

Methods and Materials

This cross-sectional prospective study addressed a cohort of 40 consecutively referred outpatients or hospitalized patients at Taleghani Hospital, Tehran, from July 2009 to October 2009. Patients suffering from severe PAH (PASP > 60 mmHg), cor-pulmonale, Chronic Obstructive Pulmonary Disease (COPD), valvular diseases, pulmonary thromboembolism or acute heart failure were excluded.

All patients underwent two-dimensional Doppler echocardiography using a Vivid 3 Echo-Doppler sys-

Table 2: Variables Measured in Echocardiography by Sex

Sex	PVR	EF	SPAP	TAPSE
Female	1.7±0.36	0.52±0.06	30.15±13.22	2.25±0.32
Male	1.86±0.66	0.46±0.12	35±18.43	1.99±0.52

Table 2: Mean PVR in Various LV Diastolic Function Groups

LVS	PVR Mean \pm SD	P Value
Normal	1.75 \pm 0.56	-
Impaired relaxation	1.68 \pm 0.35	0.09
Pseudo-normal	1.75	0.9
Restrictive pattern	3.1 \pm 0.57	< 0.05

tem (GE). The patients' LV diastolic function, LVEF, SPAP, TAPSE, and PVR in respective exponents were determined and recorded in the echocardiography report. The variable parameters investigated in this study were determined via echocardiography, and hence, their reliability depended on the accuracy of the echocardiography conducted by the respective physician, the preciseness of the set used, and the inherent limitations of trans-thoracic echocardiography (TTE). We attempted to overcome these limitations by selecting accurate patient data sets, and to have a highly attentive and experienced physician performing all of the TTE measurements. The data were entered into a database and analyzed using SPSS Ver. 15 software. Quantitative results are presented as the mean \pm SD, and qualitative results are presented as percentages. We applied Mann–Whitney statistical tests and linear regression analyses to examine the relationship between PVR and each variable. $P < 0.05$ was considered significant. To verify the accuracy of the measurements, another specialist remeasured all echocardiographic variables obtained from the first 5 patients and used the respective results to standardize the echocardiography readings. All patients taking part in this study gave written consent to participate in the project.

Results

Forty patients entered this study. Of these, 19 (47.5%) were female, and 21 (52%) were male. The average age of the female patients was 50.1 ± 16.90 years and that of the male patients was 55.09 ± 19.51 years (Table 2). The male and female patients did not differ statistically in age ($P = 0.3$). The means of the ejection fraction (EF), PVR, SPAP, and TAPSE values for the groups of male and female patients are presented in Table 2.

To determine a cut-off point for the TAPSE and PVR measurements, patients were divided into two groups: those presenting TAPSE index ≥ 1.8 and those exhibiting TAPSE index < 1.8 . The patients' PVR indexes were then assessed under these classifications. The Mann–Whitney test was used to make comparisons at $\alpha = 0.05$. The resulting mean PVR indexes were significantly higher in the TAPSE index < 1.8 group than that in the TAPSE index ≥ 1.8 group

($P = 0.026$).

To determine the mean PVR in patients with varying degrees of LV diastolic function, the patients were classified into four groups: normal, impaired relaxation, pseudo-normal and restrictive pattern. The PVR in each of these groups was then assessed using a simple linear regression model. Linear regression analysis of the mean PVR index related to the above classifications of LV diastolic function showed that there was no significant difference between the mean PVR index of the impaired relaxation and pseudo-normal groups. The analysis also showed that the mean PVR in restrictive pattern group was 4.215 units higher than that of the normal group (Table 3).

It should be noted that this model is adjusted for age and sex; i.e., these variables had no definite effect on PVR.

We determined the relationship between LVEF and PVR by applying a linear regression model. The model was adopted for sex and age, i.e., these variables had no definite effect on either PVR or LVEF. The analysis indicated that increases in PVR were significantly correlated with reductions in LVEF ($P = 0.004$). The linear regression model indicates that PVR changes are in significant agreement with SPAP changes. That is, for each 1-unit increase in SPAP, PVR increases by 0.024 units ($P < 0.0001$). Age and sex were not significant variables in this model, i.e., they had no effect on the measured PVR.

Discussion

Pulmonary blood circulation determines right ventricular output and modifies left ventricular venous return. Consequently, an increase in pulmonary vascular tone may aggravate myocardial dysfunction. The pulmonary vascular bed in healthy adults is a low pressure, low resistance system that receives a high volume of blood. Among other properties, this vascular bed is highly capable of adapting to extremely large volumes of blood and of maintaining desirable pulmonary artery pressure. The PVR index is an important hemodynamic variable used to evaluate a patient's response to cardiac congestive failure. Determination of the PVR index is also a necessary component in examinations of candidates for heart and liver transplantation and plays a significant role in the prediction of both short- and long-term outcomes in these patients. Additionally, the PVR index is used to determine the surgical outcome in patients with congenital heart diseases. Previously, invasive methods, such as catheterization, were primarily used to measure PVR. However, recent studies have shown that noninvasive methods, such as bidimensional echocardiography, may be satisfactory substitutes for PVR measurement.

The relationship between TAPSE and PVR

Our decision to classify the patients in this cohort

into groups of individuals presenting TAPSE indexes ≥ 1.8 and TAPSE indexes < 1.8 was based on a study performed by Forfia et al. in which the same classification scheme was used. Forfia et al. reported that right ventricle function is important for risk stratification of patients suffering from pulmonary hypertension and that the TAPSE index correlation with those of PVR measurements. Consequently, the TAPSE index may be used to estimate the degree of PVR.¹

Additionally, McLean et al. determined that changes in the TAPSE index in patients suspected of pulmonary hypertension were decisive in confirming this diagnosis. These researchers also found that the presence of pulmonary hypertension can be confirmed by blind measurements of the TAPSE index.²

Furthermore, Gurudevan et al. determined that PVR measurements made by either catheterization or echocardiography were strongly and significantly related.³

Kouzu found that PVR measurements made via catheterization and those made by determining the tricuspid regurgitant pressure gradient to time-velocity integral (TRPG/ TVI) ratio (the component values which are echocardiographic) were significantly and linearly related ($P < 0.0001$).⁵

Based on the results of the Mann–Whitney test, our results indicate that the mean PVRs of the two groups (TAPSE indexes ≥ 1.8 and TAPSE indexes < 1.8) are significantly different, i.e., the mean PVR in the lower TAPSE index group is higher than that of the higher TAPSE index group ($P = 0.026$).

Relationship between PVR and SPAP

In a study performed by Sablotzki et al., PVR and PAP were measured prior to and following Iloprost inhalation in patients with high PVR indices. The results of this study indicated that PVR measurements were significantly reduced in those patients receiving an inhalation of Iloprost ($P < 0.05$). However, the reduction in PAP was not significant.⁶

Other studies have confirmed the relationship regarding the simultaneous and significant lowering of PAP and PVR in patients suffering from pulmonary hypertension by treatments such as nitric oxide.⁷

Corte et al. reported a significant correlation between PVR and PAP. In lung transplant candidates, a PVR value higher than 6.23 was found to be independently predictive of post-transplant mortality.⁸ A number of other studies have also found a significant relationship between PVR and PAP.^{9, 10, 11, 12, 13}

Shandas et al. conducted a study on patients suffering from pulmonary hypertension and proposed the following formula to determine the PVR index:

$$\text{PVR} = 1.55 \text{ Vel prop (Velocity Propagation Slope)} + 24.¹⁴$$

A study by Nath et al. demonstrated that in patients suffering from high PAP who had been treated with

epoprostenol, the pulmonary total resistance index improved significantly, indicating that this index may be used to evaluate the degree of epoprostenol effect on PVR.¹²

In patients suffering from pulmonary hypertension, Loogen et al. showed that the use of vasodilators, such as adenosine, epoprostenol, or nitric oxide was significantly effective in reducing PVR and PAP.¹⁵

The results of the regression model used in the present study to examine the relationship between SPAP and PVR (as adopted for the respective ages and sexes of the patients) indicated a statistically significant correlation ($P < 0.0001$), such that there was an increase of 0.024 units in the PVR index per unit increase in SPAP. The relationship between PVR and PAP can be described by the following formula:

$$\text{PVR} = 0.921 + (0.024 \times \text{SPAP}).$$

Neither age nor sex was a significant variable in the model described in the present study, i.e., they had no significant effect on the PVR index.

Relationship between PVR and LV Diastolic Dysfunction Grade and LVEF

In Rajagopalan et al. concluded that the degree of LV dysfunction plays an important role in pulmonary hypertension pathophysiology.¹⁶

Additionally, Chang et al. found that as their patients' pulmonary hypertension became more severe, LVEF decreased, and LV diastolic dysfunction significantly increased.¹⁷

Hayward et al. did not observe a significant relationship between PVR and normal LVEF following inhalation of nitric oxide.¹⁸

However, the conclusions reached by other researchers indicate that in patients suffering from PH, irrespective of the etiology of the illness, LVEF improves significantly, and PVR is reduced.^{19, 20}

In a review article, Ehtisham et al. stated that pulmonary artery thromboendarterectomy results in a significant and effective reduction in PVR and an increase in cardiac output and right ventricle function.²¹

Scapellato arrived at the conclusion that in patients suffering from chronic cardiac failure, the PVR indexes measured by both catheterizations and Doppler echocardiography were similar.²²

In the present study, the mean PVR in the impaired relaxation and pseudo-normal groups did not vary significantly from that of the normal group. However, the mean difference between the normal group and the restrictive pattern group was significant ($P < 0.0001$). This relationship explains the correlation between severe left diastolic dysfunction and increased PVR. The mean PVR in the restrictive pattern group was found to be higher than that in the Normal group by an average of 4.215 Wood units. This model was adopted for age and sex; however, these variables did not significantly affect the model, i.e., they had no discernable effect

on PVR.

Conclusion

Echocardiography is a simple, inexpensive and noninvasive method for monitoring hemodynamic variables in patients with cardiac diseases. Measurement of PVR via right ventricular catheterization is invasive, but knowledge of this value is required in many patients (e.g., those suffering from pulmonary hypertension or heart failure and those waiting to receive heart or lung transplants). Based on the results of linear regression analysis, we determined that indexes of right and left ventricular function (e.g., LVEF, SPAP, TAPSE, and LV Diastolic Dysfunction) were significantly correlated with PVR measurement. Additionally, we demonstrated that the strongest echocardiographic correlation was between PVR and severe diastolic dysfunction. Considering the significant correlations identified for this index in the present study and in previous researches, echocardiography-based PVR measurement can begin to be used with a high degree of confidence.

References

- Forfia PR, Fisher MR, Mathai SC, Harris T, Hemnes AR, Borlaug BA, et al. Tricuspid annular displacement predicts survival in pulmonary hypertension. *Am J Respir Crit Care Med* 2006;**174**:1034-41. [PMID:16888289]
- Mc Lean AS, Ting I, Huang SJ, Wesley S. The use of the right ventricular diameter and tricuspid annular tissue Doppler velocity parameter to predict the presence of pulmonary hypertension. *Eur J Echocardiogr* 2007;**8**:128-36. [PMID:16672193]
- Gurudevan SV, Malouf P, Kahn A, Auger WR, Waltman TJ, Madani M, et al. Noninvasive assessment of pulmonary vascular resistance using Doppler tissue imaging of the tricuspid annulus. *J Am Soc Echocardiogr* 2007;**20**:1167-71. [PMID:17566699]
- Vlahos AP, Feinstein JA, Schiller NB, Silverman NH. Extension of Doppler-derived echocardiographic measures of pulmonary vascular resistance to patients with moderate to severe pulmonary vascular disease. *J Am Soc Echocardiogr* 2008;**21**:711-4. [PMID:18187297]
- Kouzu H, Nakatani S, Kyotani S, Kanzaki H, Nakanishi N, Kitakaze M. Noninvasive estimation of pulmonary vascular resistance by Doppler echocardiography in patients with pulmonary arterial hypertension. *Am J Cardiol* 2009;**103**:872-6. [PMID:19268748]
- Sablutzki A, Czeslick E, Gruenig E, Friedrich I, Schubert S, Börgermann J, et al. First experiences with the stable prostacyclin analog Iloprost in the evaluation of heart transplant candidates with increased pulmonary vascular resistance. *J Thorac Cardiovasc Surg* 2003;**125**:960-2. [PMID:12698166]
- Sitbon O, Brenot F, Denjean A, Bergeron A, Parent F, Azarian R, et al. Inhaled nitric oxide as a screening vasodilator agent in primary pulmonary hypertension: a dose-response study and comparison with prostacyclin. *Am J Respir Crit Care Med* 1995;**151**:384-9. [PMID:7842196]
- Corte TJ, Wort SJ, Gatzoulis MA, Macdonald P, Hansell DM, Wells AU. Pulmonary vascular resistance predicts early mortality in patients with diffuse fibrotic lung disease and suspected pulmonary hypertension. *Thorax* 2009;**64**:883-8. [PMID:19546096]
- Nadrous HF, Pellikka PA, Krowka MJ, Swanson KL, Chaowalit N, Decker PA, et al. The impact of pulmonary hypertension on survival in patients with idiopathic pulmonary fibrosis. *Chest* 2005;**128**:616-7S. [PMID:16373870]
- Hamada K, Nagai S, Tanaka S, Handa T, Shigematsu M, Nagao T, et al. Significance of pulmonary arterial pressure and diffusion capacity of the lung as prognosticator in patients with idiopathic pulmonary fibrosis. *Chest* 2007;**131**:650-6. [PMID:17317730]
- Lettieri CJ, Nathan SD, Barnett SD, Ahmad S, Shorr AF. Prevalence and outcomes of pulmonary arterial hypertension in advanced idiopathic pulmonary fibrosis. *Chest* 2006;**129**:746-52. [PMID:16537877]
- Nath J, Demarco T, Hourigan L, Heidenreich PA, Foster E. Correlation between right ventricular indices and clinical improvement in epoprostenol treated pulmonary hypertension patients. *Echocardiography* 2006;**22**:374-9. [PMID:15901287]
- Shorr AF, Wainright JL, Cors CS, Lettieri CJ, Nathan SD. Pulmonary hypertension in patients with pulmonary fibrosis awaiting lung transplant. *Eur Respir J* 2007;**30**:715-21. [PMID:17626111]
- Shandas R, Weinberg C, Ivy DD, Nicol E, DeGroff CG, Hertzberg J, et al. Development of a noninvasive ultrasound color M-mode means of estimating pulmonary vascular resistance in pediatric pulmonary hypertension: mathematical analysis, in vitro validation, and preliminary clinical studies. *Circulation* 2001;**104**:908-13. [PMID:11514378]
- Loogen F, Worth H, Schwan G, Goeckenjan G, Losse B, Horstkotte D. Long-term follow-up of pulmonary hypertension in patients with and without anorectic drug intake. *Cor Vasa* 1985;**27**:111-24. [PMID:4028729]
- Rajagopalan N, Simon MA, Edelman K, Mathier MA, López-Candales A. Identifying left ventricular dysfunction in pulmonary hypertension. *Congest Heart Fail* 2009;**15**:218-21. [PMID:19751422]
- Chang SM, Lin CC, Hsiao SH, Lee CY, Yang SH, Lin SK, et al. Pulmonary hypertension and left heart function: insights from tissue Doppler imaging and myocardial performance index. *Echocardiography* 2007;**24**:366-73. [PMID:17381645]
- Hayward CS, Kalnins WV, Rogers P, Feneley MP, MacDonald PS, Kelly RP. Effect of inhaled nitric oxide on normal human left ventricular function. *J Am Coll Cardiol* 1997;**30**:49-56. [PMID:9207620]
- Balligand JL, Ungureanu D, Kelly RA, Kobzik L, Pimental D, Michel T, et al. Abnormal contractile function due to induction of nitric oxide synthesis in rat cardiac myocytes follows exposure to activated macrophage-conditioned medium. *J Clin Invest* 1993;**91**:2314-9. [PMID:8486792]
- Finkel MS, Oddis CV, Jacob TD, Watkins SC, Hattler BG, Simmons RL. Negative inotropic effects of cytokines on the heart mediated by nitric oxide. *Science* 1992;**257**:387-9. [PMID:1631560]
- Mahmud E, Raisinghani A, Hassankhani A, Sadeghi HM, Strachan GM, Auger W, et al. Correlation of left ventricular diastolic filling characteristics with right ventricular overload and pulmonary artery pressure in chronic thromboembolic pulmonary hypertension. *J Am Coll Cardiol* 2002;**40**:318-24. [PMID:12106938]
- Scapellato F, Temporelli PL, Eleuteri E, Corrà U, Imparato A, Giannuzzi P. Accurate noninvasive estimation of pulmonary vascular resistance by Doppler echocardiography in patients with chronic heart failure. *J Am Coll Cardiol* 2001;**37**:1813-9.