ORIGINAL ARTICLE

Accuracy of Doppler-Derived Indices in Predicting Pulmonary Vascular Resistance in Children With Pulmonary Hypertension Secondary to Congenital Heart Disease With Left-to-Right Shunting

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Abstract This study aimed to evaluate the accuracy of Doppler echocardiography-derived indices in children with pulmonary hypertension secondary to congenital heart disease with left-to-right shunting. Doppler-derived indices including the acceleration time corrected (AcTc), deceleration time corrected, deceleration index, peak velocity, heart-rate-corrected inflection time (InTc), and a new index (the acceleration slope [Acc = peak flow velocity/AcTc]) were measured from the pulmonary artery (PA) systolic flow curve before and after 100 % oxygen administration in the main, left, and right PAs of 33 children. The acquired data were compared between low and high pulmonary vascular resistance (PVR) groups and between responders and nonresponders to the vasoreactivity test. The AcTc values differed significantly between the low and high PVR groups before and after oxygen administration in the main ($P = 0.032$ and <0.001, respectively), right ($P = 0.011$ and <0.001, respectively), and left ($P < 0.001$ and <0.001, respectively) PAs. The AcTc cutoff point in the main PA was 3.44 before oxygen administration (81 % sensitivity and 91 % specificity). The InTc in the main PA and its changes differed significantly between the low and high PVR groups before and after oxygen administration and between the responders and nonresponders ($P = 0.016$, 0.046, and 0.021, respectively). The velocity changes of the

PA in the main PA differed significantly between the responders and nonresponders to oxygen administration ($P < 0.001$). The Acc and its changes differed significantly between the low and high PVR groups after oxygen administration and between the responders and nonresponders to oxygen administration ($P = 0.044$ and 0.006, respectively). Doppler echocardiographic examination using PA systolic flow indices in addition to PA reactivity testing is a promising technique for assessing PVR in children with congenital heart disease.

Keywords Pulmonary hypertension · Congenital heart disease · Echocardiography · Pulmonary vascular resistance

Introduction

The pulmonary blood flow plays a vital role in gas exchange, oxygen transfer, and heart function. In children with congenital heart disease, left-to-right shunting raises the pulmonary blood flow and thus causes significant structural and functional changes in the pulmonary vessels. Pulmonary artery (PA) hypertension is a major determinant of mortality in this group of patients.

The current gold standard for the prediction of pulmonary vascular resistance (PVR) and PA reactivity is cardiac catheterization [2]. However, the invasive nature of this technique limits its use in routine follow-up evaluation for patients under treatment for PA hypertension. Therefore, a noninvasive method would be a clinical advance in the evaluation of PVR and PA reactivity in this group of patients.

Doppler echocardiography is the most extensive and portable technology among other noninvasive methods. It

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also is reliable for the evaluation of PA pressure and PVR [11].

Application of Doppler echocardiography for the estimation of systolic PA pressure, with the recording of tricuspid regurgitation jets, was first reported by Yock and Popp [14] in 1984. Kitabatake et al. [7] also studied and compared PA flow velocity between patients with PA hypertension and normal individuals with the aid of Doppler echocardiography. Also, a good correlation exists between PVR and Doppler-derived TRV/VTI RVOT (tricuspid regurgitation velocity to the velocity time integral of the right ventricular outflow tract; [1, 13]).

In patients with PA hypertension, the characteristics of the pulmonary flow velocity curve are affected by the vascular impedance condition. The variation in time and severity of the reflected wave in the main PA and its branches may have different effects on the PA velocity curve [3, 4, 8].

Nakahata et al. [9] assessed the usefulness of Doppler-derived indices to differentiate between high and low PVR and PA reactivity in patients with congenital heart disease (as determined by cardiac catheterization) and concluded that Doppler-derived indices, especially the heart-rate-corrected inflection time (InTc) obtained from the left PA, separated patients in the high and low PVR groups significantly. In addition, the Nakahata et al. [9] study demonstrated that changes in InTc during oxygen administration in the high PVR group indicated good PA reactivity in this group of patients.

The reports from studies using the acceleration time corrected (AcTc), deceleration time corrected (DcTc), and InTc in children with congenital heart disease and left-to-right shunting have been conflicting. We therefore aimed to evaluate the Doppler-derived indices and the Doppler-derived systolic PA velocity curve in the main, left, and right PAs in this group of patients.

In this report, we also introduce a new index, namely, the acceleration slope (Acc = peak flow velocity/AcTc). This index was primarily inspired by the Shandas et al. [12] study, which evaluated the relationship between velocity propagation in ultrasound color M-mode and PVR as determined by cardiac catheterization. The Acc is the ratio of PA peak velocity (PV) to the AcTc (m/s^2).

We also evaluated the PA reactivity to oxygen with the aid of Doppler echocardiography and cardiac catheterization to assess their relationships. The current study had two major hypotheses: (1) that in a low-PVR group, the values of AcTc, DcTc, InTc, Acc, and PA velocity are higher and the value of DT is lower than in a high-PVR group, and (2) that the values of AcTc, DcTc, Acc, and PA velocity increases significantly if the high-PVR patients respond to the vasoreactivity test.

Materials and Methods

After the Institutional Review Board approved the study protocol, and written informed consent was obtained from the parents of the minors who met our inclusion criteria, we studied 33 congenital heart disease patients who had left-to-right shunting and pulmonary hypertension (mean PA pressure, ≥25 mmHg) when cardiac catheterization was performed at the Rajaie Cardiovascular, Medical and Research Center between April 2011 and May 2012.

The patients who experienced right ventricular outflow tract stenosis, significant arrhythmia, and severe heart failure (which may interfere with cardiac disease) were excluded from the study. The study population was composed of 18 girls and 15 boys who ranged in age from 4 months to 14 years (mean 4.36 years).

The patients were divided into two groups according to the Cooper et al. [6] study: those with a baseline PVR of 4.5 WU/m^2 or lower (low PVR) and those with a baseline PVR of 4.6 WU/m^2 or higher (high PVR). Also, the patients confirmed as having high PVR were classified into two subgroups (responders and nonresponders) on the basis of changes in catheter-derived PVR with 100 % oxygen administration. The patients whose PVR decreased to 4.5 WU/m^2 or lower were defined as responders, and those whose PVR remained at 4.6 WU/m^2 or higher were defined as nonresponders to the vasoreactivity test. Changes in the Doppler-derived indices were compared between the responders and nonresponders.

With respect to the patients' cardiac defects, ventricular septal defects were detected in 21 children, atrioventricular septal defects in 2 children, patent ductus arteriosus in 2 children, atrial septum defects in 2 children, and ventricular septal defects plus atrioventricular septal defects in 6 children. The heart rate ranged from 90 to 127 beats/min (mean 107 beats/min).

Cardiac Catheterization

Cardiac catheterization was performed in the standard manner. Pressures were measured with a fluid-filled catheter system. The PVR was calculated using the method of Fick, with assumed oxygen consumption as shown by the ratio of the difference between pulmonary arterial pressure and left atrial pressure or pulmonary arterial wedge pressure to the mean flow in the PA indexed to the body surface area (WU/m^2). These parameters also were obtained before and after PA reactivity testing using 100 % oxygen for 5 min with face masks on all the patients. Afterward, all the patients were sedated with intravenous midazolam (0.1 mg/kg) for cardiac catheterization.

Transthoracic Doppler Echocardiographic Examinations

All the patients underwent echocardiographic examinations 24 h before cardiac catheterization by a single operator, and all the echocardiographic examinations were performed using the cardiovascular ultrasound GE Vivid 7 system (Vingmed 7; GE Medical System, Inc., Horten, Norway) with a 3- to 5-MHz broad-band transducer. Sedation was achieved with chloral hydrate (25–50 mg/kg) if required.

The main PA and the proximal left and right PAs were visualized with the patient in the supine or left lateral position using the standard parasternal short-axis view. The appropriate position for the sample site was determined via two-dimensional and color Doppler echocardiography with a disc-shaped sample volume of 3–4 mm. The Doppler was carefully positioned on the blue color-coded blood flow within the main PA (approximately 5 mm–1 cm distal to the center of the pulmonary valve) and within the right and left PAs (approximately 5 mm–1 cm distal to the bifurcation of the main PA).

All the patients also underwent PA reactivity testing via the administration of 100 % oxygen through a face mask for 5 min, and the required parameters were collected. Interobserver error vis-à-vis the Doppler echocardiographic indices was prevented by measuring the mean of three consecutive PA systolic flows in each position.

Pulmonary Flow Velocity Measurements

The acceleration time (AcT) was the interval in microseconds from the onset of ejection to the peak flow velocity. The inflection time (InT) was the interval in μs from the onset of ejection to an inflection point. The deceleration time (DcT) was measured from PV to the end of ejection, and the deceleration index (DI) was the ratio of peak flow velocity (i.e., flow velocity at the time of an inflection point) to peak flow velocity. To correct for the heart rate dependence of time intervals, the AcT, DcT, and InT were divided by the square root of the interval in μs between the onset of ejection into two beats, and these indices were defined as the AcTc, DcTc, and InTc, respectively.

The Acc was another index measured in the main PA and its branches before and after oxygen administration. The Acc was the ratio of the PA PV to the AcTc (m/s^2). The InT, the inflection point, and the AcT and DcT in the PA velocity profile are demonstrated in Figs. 1 and 2.

Statistical Analysis

The statistical analyses were performed with SPSS software, version 15 (SPSS, Chicago, IL, USA). The clinical
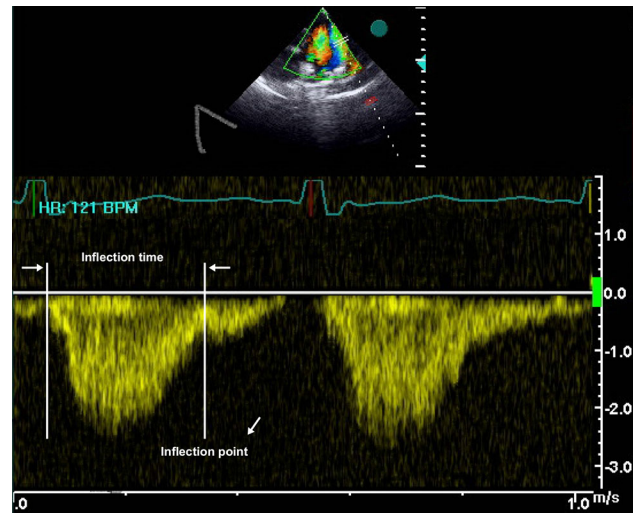
Fig. 1 Inflection time and inflection point in pulmonary artery flow velocity profile in the main pulmonary artery of a patient with pulmonary hypertension. Inflection time was the interval in μs from the onset of ejection to an inflection point
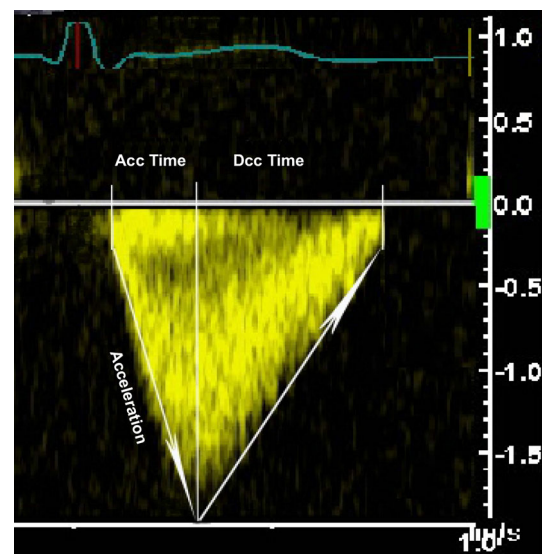
Fig. 2 Acceleration and deceleration times in pulmonary artery velocity profile. Acceleration time was the interval in μs from the onset of ejection to peak flow velocity. Deceleration time was measured from peak velocity to the end of ejection. Acc was the ratio of peak velocity in the pulmonary artery (PA) to the heart-rate-corrected acceleration time (m/s^2)

data are expressed as mean values ± standard deviations. Differences were analyzed with the paired and the independent Student's t test for the values of a scaling term and the Pearson χ^2 test for the nominal values. The Mann–Whitney U test was used to compare the values without normal distribution between the two groups. A P value lower than 0.05 was considered statistically significant. Receiver operating curve (ROC) analysis was performed to

determine a cutoff value for the Doppler-derived indices with the highest balanced sensitivity and specificity.

Results

Before oxygen administration, the 33 enrolled patients had a mean PVR value of 8.29 ± 6.17 WU/m^2 (range 1.5–26 WU/m^2): 13 patients (39.4 %) with a low PVR (mean 3 ± 1 WU/m^2) and 20 patients (60.6 %) with a high PVR (mean 11.69 ± 5.7 WU/m^2). After oxygen administration, the 33 patients had a mean PVR value of 5.67 ± 5.122 WU/m^2 (range 1–23 WU/m^2): 22 patients (66.7 %) with a low PVR (mean 2.9 ± 1.48 WU/m^2) and 11 (33.3 %) patients with a high PVR (mean 11.07 ± 5.7 WU/m^2).

The data acquired from cardiac catheterization before and after oxygen administration were evaluated and compared between the low and high PVR groups before and after oxygen administration. The results are depicted in Table 1. Before oxygen administration, the mean value of AcTc in the main PA was 3.90 ± 0.63 in the low PVR group and 3.18 ± 0.63 in the high PVR group ($P = 0.032$). After oxygen administration, the mean value of AcTc in the main PA was 4.26 ± 0.62 in the low PVR group and 3.2 ± 0.46 in the high PVR group ($P < 0.001$; Fig. 3).

Before oxygen administration, the mean value of InTc in the main PA was 7.90 ± 0.0 in the low PVR group and 5.61 ± 0.75 in the high PVR group ($P = 0.016$). After oxygen administration, the mean value of InTc in the main PA was 7.48 ± 1.85 in the low PVR group and 5.8 ± 0.68 in the high PVR group ($P = 0.046$).

Before oxygen administration, the mean value of PV in the main PA was 143 ± 29 in the low PVR group and 110 ± 30 in the high PVR group ($P = 0.005$). After oxygen administration, the mean value of PV in the main PA was 172 ± 31 in the low PVR group and 107 ± 22 in the high PVR group ($P < 0.00$; Fig. 4).

Before oxygen administration to the 33 patients, 12 of the patients had an inflection point on the PA systolic velocity curve (1 patient with low PVR and 11 patients with high PVR), and both InTc and DI were calculated. After oxygen administration, this ratio changed to five patients with high PVR and seven patients with low PVR.

Before oxygen administration, the mean value of the Acc in the main PA was 37.5 ± 9.5 in the low PVR group and 37.2 ± 10 in the high PVR group ($P = 0.841$). After oxygen administration, the mean value of the Acc in the main PA was 42.2 ± 12 in the low PVR group and 33 ± 7.3 in the high PVR group ($P = 0.042$). The Doppler-derived quantitative data in the main PA and its
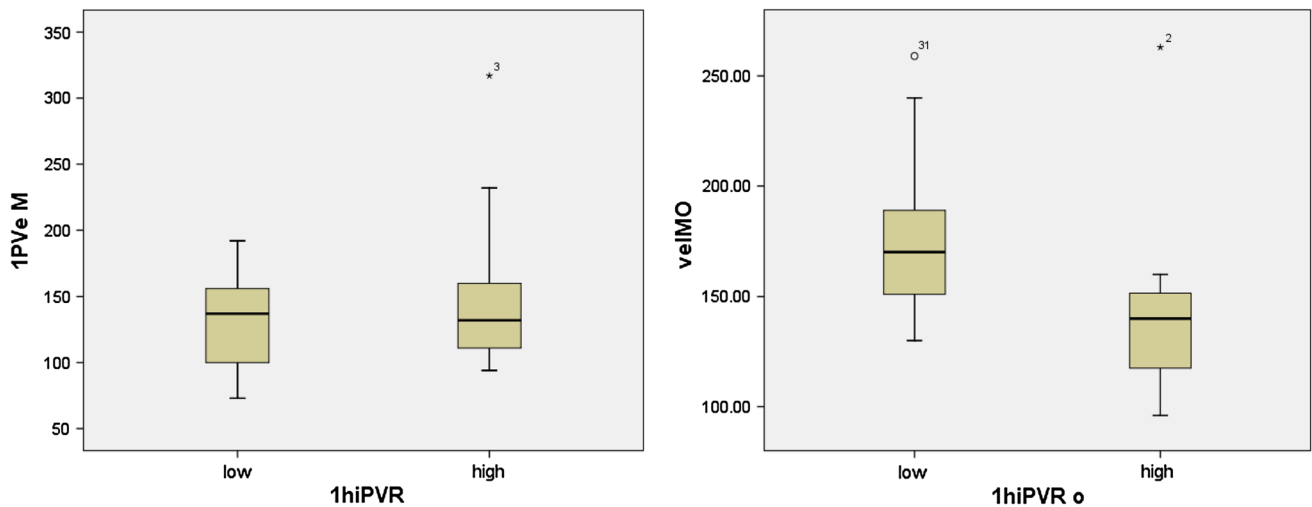
Table 1 Comparison of cardiac catheterization-acquired variables between low and high pulmonary vascular resistance (PVR) groups

	Before oxygen administration			After oxygen administration		
	Low PVR	High PVR	P value	Low PVR	High PVR	P value
mPAP (mmHg)	28.15 ± 7.77	61.40 ± 18.2	<0.001	24 ± 7.2	52 ± 20.8	<0.001
Q_p/Q_s	1.94 ± 0.86	1.81 ± 0.58	0.591	2.82 ± 1.68	2.91 ± 1.57	0.881

mPAP mean pulmonary artery pressure, Q_p/Q_s ratio of total pulmonary blood flow to total systemic blood flow
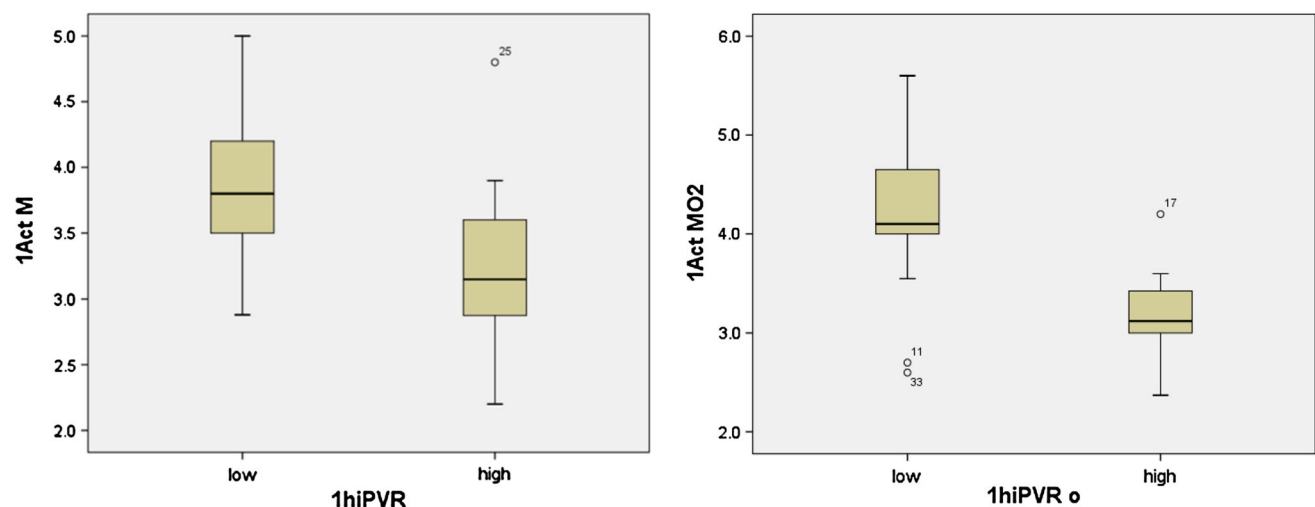
Fig. 3 Comparison of acceleration time corrected in the main pulmonary artery (MPA) before and after oxygen (O$_2$) administration in the low and high pulmonary vascular resistance (PVR) groups

Fig. 4 Comparison of pulmonary velocity in the main pulmonary artery (MPA) before and after oxygen (O₂) administration in the low and high pulmonary vascular resistance (PVR) groups

branches between the low and high PVR groups before and after oxygen administration are demonstrated in Tables 2 and 3, respectively.

The patients also were classified into the two subgroups (responders and nonresponders to oxygen administration) according to changes in the catheter-derived PVR. Changes in the Doppler-derived indices also were evaluated and compared in the high PVR group between the responders and nonresponders to oxygen administration. Based on the results, the mean value of the AcTc changes in the main PA among the responders was 0.55 ± 0.23 versus 0.23 ± 0.21 among the nonresponders ($P = 0.006$). The mean value of the InTc changes in the main PA among the responders was 1.45 ± 1 versus 0.37 ± 0.20 among the nonresponders ($P = 0.021$). The mean value of the PV changes in the main PA among the responders was 44.11 ± 9 versus 16.27 ± 16.2 among the nonresponders ($P < 0.001$), and the mean value of the Acc changes in the main PA among the responders was 6.6 ± 3.7 versus -4.48 ± 10 among the nonresponders ($P = 0.006$).

Table 4 compares the changes in the other Doppler-derived indices between the responders and nonresponders. Of the six Doppler-derived indices, an AcTc value of 3.44 in the main PA before oxygen administration identified high PVR reasonably well with a sensitivity of 81 % and a specificity of 91 % (Fig. 5). After oxygen administration, an AcTc value of 3.7 in the main PA was the cutoff point to identify the high PVR group with 82 % sensitivity and 91 % specificity (Fig. 6).

An AcTc value of 2.98 in the left PA before oxygen administration identified high PVR reasonably well with a sensitivity of 92 % and a specificity of 70 %. After oxygen administration, an AcTc value of 3.18 in the left PA was the cutoff point to identify the high PVR group with 81 % sensitivity and 91 % specificity.

In the right PA, an AcTc value of 3.30 identified high PVR reasonably well before oxygen administration with a sensitivity of 84 % and a specificity of 50 %. After oxygen administration, an AcTc value of 3.37 in the right PA was the cutoff point to identify the high PVR group with 90 % sensitivity and 91 % specificity.

After oxygen administration, a PV value of 126.5 in the main PA was the cutoff point to identify the high PVR group with 100 % sensitivity and 91 % specificity (Fig. 7). Also, a PV value of 100.5 in the left PA before oxygen administration identified high PVR reasonably well with a sensitivity of 89 % and a specificity of 82 %. After oxygen administration, a PV value of 116 in the left PA was the cutoff point to identify the high PVR group with 100 % sensitivity and 91 % specificity.

In the right PA, a PV value of 102.5 identified high PVR reasonably well before oxygen administration with a sensitivity of 89 % and a specificity of 55 %. After oxygen administration, a PV value of 120.5 in the right PA was the cutoff point to identify the high PVR group with 100 % sensitivity and 91 % specificity.

Discussion

The decision to perform surgery for congenital heart disease patients with left-to-right shunting who have PA hypertension requires that a number of factors be considered. One of the most important factors is PVR. The current gold standard for the prediction of PVR and PA reactivity is cardiac catheterization. However, this technique, due to its invasive nature, is not feasible for all patients under treatment of PA hypertension who are facing several follow-up assessments. Therefore, Doppler echocardiography, a noninvasive

Table 2 Comparison of Doppler quantitative results between low and high pulmonary vascular resistance (PVR) groups before oxygen administration

	Low PVR ($n = 13$)	High PVR ($n = 20$)	P value
AcTc			
MPA	3.90 ± 0.63	3.18 ± 0.63	0.032
RPA	3.8 ± 0.62	2.9 ± 0.69	0.011
LPA	3.57 ± 0.59	2.69 ± 0.65	<0.001
DcTc			
MPA	8.2 ± 0.92	8.24 ± 0.84	0.931
RPA	8 ± 0.5	8 ± 0.9	0.28
LPA	7.82 ± 0.59	7.81 ± 0.84	0.881
InTc			
MPA	7.9 ± 0.0[a]	5.61 ± 0.75	0.016
RPA	7.6 ± 0.0[a]	5.7 ± 1.39	0.223
LPA	7.3 ± 0.0[a]	4.98 ± 1.25	0.011
DI			
MPA	0.47 ± 0.0[a]	0.61 ± 0.09	0.611
RPA	0.62 ± 0.0[a]	0.58 ± 0.08	0.701
LPA	0.58 ± 0.0[a]	0.59 ± 0.07	0.852
PV (cm/s)			
MPA	143 ± 29	110 ± 30	0.005
RPA	133 ± 27	106 ± 29	0.035
LPA	125 ± 30	102 ± 29	0.016
Acc			
MPA	37.5 ± 9.5	37.2 ± 10	0.841
RPA	35.9 ± 9.2	37.9 ± 11	0.600
LPA	36 ± 10	39 ± 11	0.441

Values are presented as mean ± standard deviation (SD)

AcTc heart-rate-corrected acceleration time, *MPA* main pulmonary artery, *RPA* right pulmonary artery, *LPA* left pulmonary artery, *DcTc* heart-rate-corrected deceleration time, *InTc* heart-rate-corrected inflection time, *DI* deceleration index, *PV* peak velocity, *Acc* acceleration

[a] The values of InTc and DI without SD are due to the existence of one patient in low PVR group with an inflection point before oxygen administration

Table 3 Comparison of Doppler quantitative results between low and high pulmonary vascular resistance (PVR) groups after oxygen administration

	Low PVR ($n = 22$)	High PVR ($n = 11$)	P value
AcTc			
MPA	4.26 ± 0.62	3.2 ± 0.46	<0.001
RPA	3.97 ± 0.81	2.87 ± 0.55	<0.001
LPA	3.75 ± 0.81	2.7 ± 0.48	<0.001
DcTc			
MPA	9 ± 1.35	8.75 ± 0.96	0.550
RPA	8.75 ± 1.14	8.40 ± 0.9	0.381
LPA	8.37 ± 0.90	8.3 ± 0.83	0.331
InTc			
MPA	7.48 ± 1.85	5.8 ± 0.68	0.046
RPA	7.26 ± 2.3	5.6 ± 1.55	0.112
LPA	6.8 ± 2.3	4.9 ± 0.72	0.641
DI			
MPA	0.59 ± 0.11	0.62 ± 0.07	0.541
RPA	0.66 ± 0.08	0.56 ± 0.05	0.040
LPA	0.58 ± 0.06	0.53 ± 0.07	0.371
PV (cm/s)			
MPA	172 ± 31	107 ± 22	<0.001
RPA	163 ± 33	102 ± 20	<0.001
LPA	153 ± 32	99 ± 21	<0.001
Acc			
MPA	42.2 ± 12	33 ± 7.3	0.044
RPA	43 ± 13	36 ± 8	0.120
LPA	42 ± 12	37 ± 9	0.251

Values are presented as mean ± standard deviation

AcTc heart-rate-corrected acceleration time, *MPA* main pulmonary artery, *RPA* right pulmonary artery, *LPA*, left pulmonary artery, *DcTc* heart-rate-corrected deceleration time, *InTc* heart-rate-corrected inflection time, *DI* deceleration index, *PV* peak velocity, *Acc* acceleration

method, would be a clinical advance in the evaluation of PVR and PA reactivity for this group of patients.

This study evaluated the accuracy of six Doppler echocardiography-derived indices for 33 children with PA hypertension secondary to congenital heart disease with left-to-right shunting. The purpose was to determine a noninvasive method using echocardiography to evaluate the Doppler-derived systolic PA flow velocity curve for predicting high and low PVR groups and for differentiating between responders and nonresponders to the vasoreactivity test among high PVR patients. Nakahata et al. [9] conducted a quantitative assessment of PVR using the four Doppler-derived indices (AcTc, InTc, DI, and PV) in the main PA and its branches.

We evaluated the mentioned indices in addition to DcTc and Acc and found significant differences regarding the mean value of AcTc in the main PA and its branches not only between the low and high PVR groups, but also between the responders and nonresponders before and after oxygen administration in the high PVR group. The mean value of AcTc among our patients was higher than in the Nakahata et al. [9] study. The lower value of PVR among our patients may explain this difference. Given the significant changes of AcTc in the main PA and its branches between our low and high PVR groups, this index may act as a significant factor for predicting low and high PVR groups as well as the rate of the AcT changes to differentiate responders and nonresponders to oxygen.
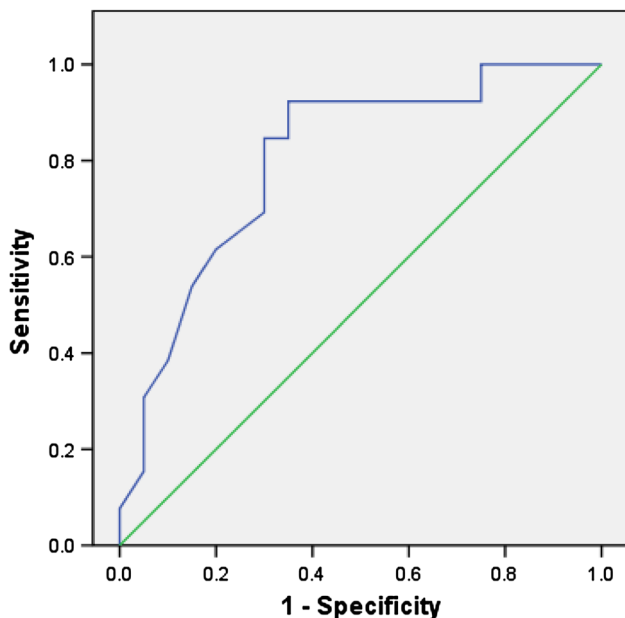
Based on our results, the mean values of DcTc in the main PA and its branches were significantly different in

Table 4 Comparison of changes in Doppler-derived indices between responders and nonresponders
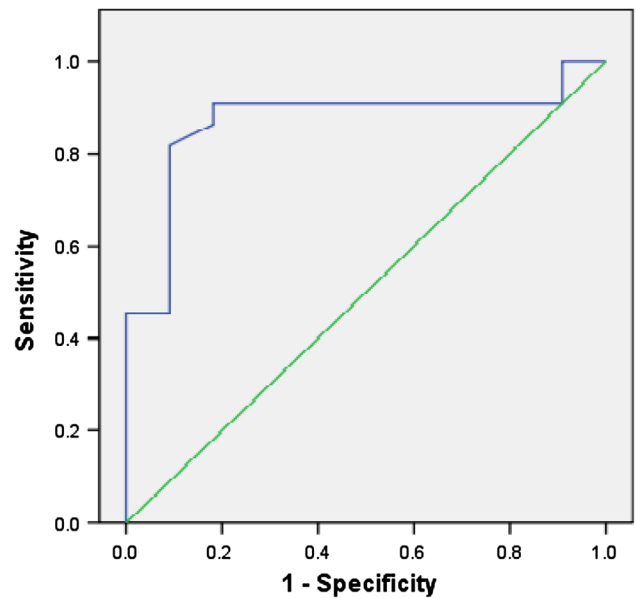
|	Responders	Nonresponders	P value
AcTc			
MPA	0.55 ± 0.23	0.23 ± 0.21	0.006
RPA	0.36 ± 0.12	0.17 ± 0.10	0.014
LPA	0.42 ± 0.19	0.21 ± 0.12	0.008
DcTc			
MPA	0.98 ± 0.66	0.53 ± 0.45	0.091
RPA	0.58 ± 0.33	0.50 ± 0.40	0.602
LPA	0.54 ± 0.22	0.44 ± 0.40	0.500
InTc			
MPA	1.45 ± 1	0.37 ± 0.20	0.021
RPA	0.30 ± 0.25	0.36 ± 0.20	0.241
LPA	0.82 ± 0.70	0.57 ± 0.30	0.120
PV (cm/s)			
MPA	44.11 ± 9	9.3 ± 9.2	<0.001
RPA	40.5 ± 0.6	9.7 ± 8.5	<0.001
LPA	37 ± 9.8	8 ± 6.9	<0.001
Acc			
MPA	6.6 ± 3.7	−4.48 ± 10	0.006
RPA	7.5 ± 3.1	0.63 ± 1.9	<0.001
LPA	7 ± 6.5	0.81 ± 2.6	0.009

Values are presented as mean ± standard deviation

AcTc heart-rate-corrected acceleration time, *MPA* main pulmonary artery, *RPA* right pulmonary artery, *LPA* left pulmonary artery, *DcTc* heart-rate-corrected deceleration time, *InTc* heart-rate-corrected inflection time, *PV* peak velocity, *Acc* acceleration

Fig. 6 Receiver operating *curve* (ROC) of acceleration time corrected (AcTc) in the main pulmonary artery (MPA) after O_2 administration
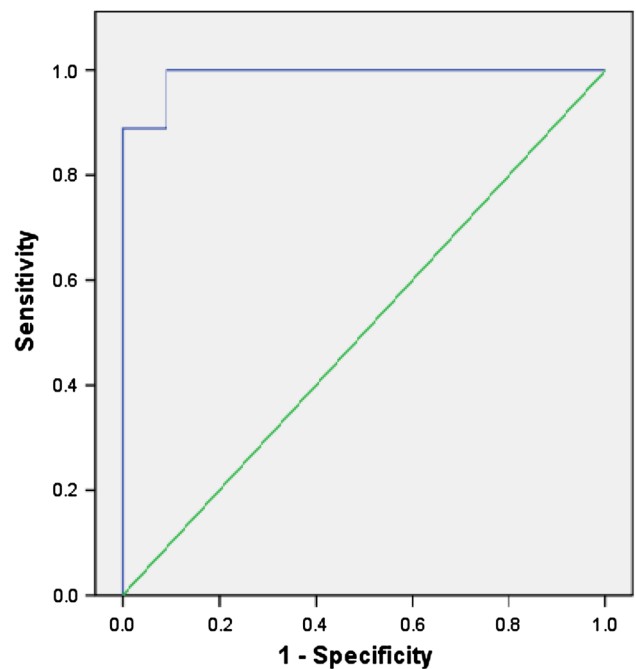
Fig. 7 Receiver operating *curve* (ROC) curve of pulmonary flow velocity in the main pulmonary artery (MPA) after O_2 administration

Fig. 5 Receiver operating *curve* (ROC) of acceleration time corrected (AcTc) in the main pulmonary artery (MPA) before oxygen administration

each patient before and after oxygen administration. Nevertheless, this criterion did not differ significantly between the low and high PVR groups or between the responders and nonresponders. Nakahata et al. [9] demonstrated that the measurement of InTc in the left PA was valuable for differentiation between low and high PVR groups and between responders and nonresponders to the vasoreactivity test.

In contrast, our study demonstrated that changes in the InTc in the left PA did not differ significantly between the responders and nonresponders to oxygen. In our study, the InTc in the main PA was a valuable index for differentiating between the low and high PVR groups and between the responders and nonresponders to oxygen administration.

The Roushdy et al. [10] study concluded that a poor relationship existed between the InTc and PVR in the left PA. In our study, DI did not differ significantly between the low and high PVR groups or between the responders and nonresponders. Among our 33 cases, 12 had an inflection point on the systolic PA flow velocity curve. This small sample size may therefore explain the achieved results regarding the DI. Based on our results, the DI may not be an appropriate indicator for the prediction of PVR and oxygen reactivity evaluation.

Another important index previously studied is the PV [5]. There were significant differences apropos the PV in the main, left, and right PAs between the low and high PVR groups and between the responders and nonresponders to oxygen.

In this study, we evaluated a new Doppler-derived index, the Acc. The Acc is the ratio of the PV in the PA to the heart-rate-corrected AcT (m/s^2), and thus may be more valuable than the other indices for the assessment of PVR. Our results showed a significant difference regarding the mean value of Acc in the main PA and its branches before and after oxygen administration among the patients. Our low and high PVR groups did not differ significantly before oxygen administration, but the mean values of Acc in the main PA and its branches differed significantly between the mentioned groups after oxygen administration. The same differences were observed between the responders and nonresponders to oxygen administration in terms of the changes in Acc in the high PVR group. Nonetheless, further studies are required to verify the accuracy of this index.

Based on our results, AcTc, InTc, PV, and Acc in the main PA had good correlations with the PVR status of the patients. The evaluation and measurement of these indices via Doppler echocardiography are more feasible in the main PA than in its branches. Compared with the other indices, AcTc and PV in the main PA and its branches conferred better discrimination between the low and high PVR groups before and after oxygen administration, with acceptable cutoff points.

Study Limitations

The probability that the hemodynamic conditions were not similar among the patients during echocardiography and cardiac catheterization was one of our study's limitations. Also, oxygen administration for 5 min may not fully represent the status of the pulmonary vascular response to oxygen in patients with PA hypertension. Another limitation of this study was the sample size, which was not sufficient for the appropriate assessment of InTc.

Conclusion

In light of our findings, we conclude that echocardiographic examination alongside PA reactivity testing is a promising technique for the assessment of PVR in children with congenital heart disease. Among the Doppler-derived indices of the main PA, AcTc, InTc, and PV seem to be the most precise ones for diagnosing the severity of PVR and PA reactivity.

References

1. Ajami GH, Cheriki S, Amoozgar H, Borzouee M, Soltani M (2011) Accuracy of Doppler-derived estimation of pulmonary vascular resistance in congenital heart disease: an index of operability. Pediatr Cardiol 32:1168–1174

2. Allen HD, Drocoll DJ, Shaddy RE, Felts TF (2008) Muss and Adam's heart disease in infants, children, and adolescents. In: Clinical management of patients with pulmonary hypertension, 7th edn. Wolters Kluwer, Philadelphia

3. Arkles JS, Opotowsky AR, Ojeda J, Rogers F, Liu T, Prassana V et al (2011) Shape of the right ventricular Doppler envelope predicts hemodynamics and right heart function in pulmonary hypertension. Am J Respir Crit Care Med 183:268–276

4. Castelain V, Hervé P, Lecarpentier Y, Duroux P, Simonneau G, Chemla D (2001) Pulmonary artery pulse pressure and wave reflection in chronic pulmonary thromboembolism and primary pulmonary hypertension. J Am Coll Cardiol 37:1085–1092

5. Chemla D, Castelain V, Humbert M, Hébert JL, Simonneau G, Lecarpentier Y et al (2004) New formula for predicting mean pulmonary artery pressure using systolic pulmonary artery pressure. Chest 126:1313–1317

6. Cooper MJ, Tyndall M, Silverman NH (1988) Evaluation of the responsiveness of elevated pulmonary vascular resistance in children by Doppler echocardiography. J Am Coll Cardiol 12:470–475

7. Kitabatake A, Inoue M, Asao M, Masuyama T, Tanouchi J, Morita T et al (1983) Noninvasive evaluation of pulmonary hypertension by a pulsed Doppler technique. Circulation 68:302–309

8. Naeije R, Huez S (2007) Reflections on wave reflections in chronic thromboembolic pulmonary hypertension. Eur Heart J 28:785–787

9. Nakahata Y, Hiraishi S, Oowada N, Ando H, Kimura S, Furukawa S et al (2009) Quantitative assessment of pulmonary vascular resistance and reactivity in children with pulmonary hypertension due to congenital heart disease using a noninvasive method: new Doppler-derived indexes. Pediatr Cardiol 30:232–239

10. Roushdy AM, Ragab I, Raouf WA (2012) 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. J Saudi Heart Assoc 24:233–241

11. Rubin LJ (2004) Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. American College of Chest Physicians. Chest 126(1 Suppl):4S–6S

12. Shandas R, Weinberg C, Ivy DD, Nicol E, DeGroff CG, Hertzberg J et al (2001) 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 104:908–913

13. Vlahos AP, Feinstein JA, Schiller NB, Silverman NH (2008) Extension of Doppler-derived echocardiographic measures of pulmonary vascular resistance to patients with moderate or severe pulmonary vascular disease. J Am Soc Echocardiogr 21:711–714

14. Yock PG, Popp RL (1984) Noninvasive estimation of right ventricular systolic pressure by Doppler ultrasound in patients with tricuspid regurgitation. Circulation 70:657–662