

# Novel echocardiographic score to predict duct-dependency after percutaneous relief of critical pulmonary valve stenosis/atresia

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## Abstract

**Objectives:** This study aimed to identify clinical, hemodynamic, or echocardiographic predictive features of persistent duct-dependency of pulmonary circulation (PDDPC) after effective percutaneous relief of pulmonary atresia with the intact ventricular septum (PA-IVS) or critical pulmonary stenosis (CPS).

**Methods:** From 2010 to 2021, 55 neonates with PA-IVS or CPS underwent percutaneous right ventricle (RV) decompression at our Institution. After successfully relief of critical obstruction, 27 patients (group I) showed PDDPC, whereas RV was able to support the pulmonary circulation in the remaining 28 patients (group II). Clinical, hemodynamic, and echocardiographic features of these two groups were compared.

**Results:** No significant difference in clinical and hemodynamic data was found between the groups, although the group I had a lower oxygen saturation at hospital admission. However, tricuspid valve (TV) diameter <8.8 mm, TV z-score  $\leftarrow$ 2.12, tricuspid/mitral valve annular ratio <.78, pulmonary valve diameter <6.7 mm, pulmonary valve z-score  $\leftarrow$ 1.17, end-diastolic RV area <1.35 cm<sup>2</sup>, end-systolic right atrium area >2.45 cm<sup>2</sup>, percentage amount of interatrial right-to-left shunt >69.5%, moderate/severe tricuspid regurgitation, RV systolic pressure >42.5 mmHg, tricuspid E/E' ratio >6.6 showed each significant predictive value of PDDPC. These parameters were used to build a composite echocardiographic score (PDDPC-score), assigning one point each above the respective cut-off value. A score  $\geq$ 4.00 showed high sensitivity (100%) and specificity (86%) in predicting PDDPC.

**Conclusion:** Clinical and hemodynamic features fail to predict the short-term fate of the pulmonary circulation after successful treatment of PA-IVS/CPS. However, a simple, composite echocardiographic score is useful to predict PDDPC and could be crucial in the management of this frail subset of patients.

## KEYWORDS

arterial duct stenting, echocardiography, pulmonary atresia, pulmonary stenosis, shunt

## 1 | INTRODUCTION

Pulmonary atresia with the intact ventricular septum (PA-IVS) and critical pulmonary stenosis (CPS) are congenital heart diseases (CHDs) with duct-dependent pulmonary circulation. Over time, surgical approach was progressively replaced by transcatheter balloon pulmonary valvuloplasty (BPV).<sup>1</sup> However, these patients often remain duct-dependent despite successful right ventricular decompression, requiring additional pulmonary blood flow sources. In this setting, arterial duct (AD) stenting is currently deemed as the best cost-effective strategy to ensure a short-term additional pulmonary blood flow, leaving surgical systemic-to-pulmonary shunt as a valuable alternative only in selected cases.<sup>2–5</sup> Finding predictive markers of persistent duct-dependency of pulmonary circulation (PDDPC) after successful right ventricle (RV) decompression could significantly modify the management of these patients, shortening the length of hospitalization and prostaglandin (PGE) support, with resulting improvement in mid-term outcome and cost savings.

In this study, we analyzed the clinical, hemodynamic, and echocardiographic data of all neonates submitted to PA-IVS or CPS percutaneous treatment at our Institution (Monaldi Hospital, University of Campania “Luigi Vanvitelli”, Naples) from 2010 to 2021 to find predictive features of persistent duct-dependency of the pulmonary circulation (PDDPC) after successful right ventricular decompression.

## 2 | METHODS

This is an observational, prospective blinded, single-center study which analyzed 62 consecutive neonates with PA-IVS or CPS referred to our Institution from January 2010 to September 2021. In seven cases, RV decompression was not performed because of severe right ventricular hypoplasia (four cases) or RV-dependent coronary circulation (three cases). Effective percutaneous right ventricular decompression was achieved in the remaining 55 neonates, whose demographic, clinical, and hemodynamic data are reported in Table 1. Written informed consent was obtained from the parents before any interventional procedure. After successful right ventricular decompression, intravenous PGE infusion (.01–.1 mcg/kg/min) was maintained to ensure ductal patency as temporary support to the pulmonary circulation. Within 48 h from the interventional procedure, transthoracic echocardiographic evaluation (Vivid 7 or E90 echocardiographer, GE Healthcare, Wauwatosa, USA) was performed to record all anatomic and functional data potentially related to PDDPC. As anatomic markers, tricuspid and pulmonary valve annulus diameter and z-score, tricuspid/mitral valve annular ratio, right atrium end-systolic area, and RV end-diastolic area were recorded in apical 4-chamber view. As functional markers, right

ventricular systolic function inferred by tricuspid annular plane systolic excursion (TAPSE), tricuspid S' wave, RV fractional area change (FAC%), and RV diastolic function by estimation of tricuspid E/E' ratio were recorded in apical 4-chamber view. Amount of tricuspid regurgitation (trivial, mild, moderate, or severe), estimated RV systolic pressure, and residual pulmonary maximum gradient were recorded in apical 4-chamber, subcostal long-axis, and parasternal short-axis views. Finally, atrial shunt direction (left-to-right, bidirectional, or right-to-left) and amount of atrial right-to-left shunt (measured as the VTI ratio between right-to-left shunt and overall shunt on pulsed-wave Doppler) were evaluated by the sub-costal bi-caval view. All echocardiographic parameters were recorded following the “recommendations for quantification methods during the performance of a pediatric echocardiogram.”<sup>6</sup> Some days after ventricular decompression ( $6 \pm 4$  days, range 1–20 days), PGE infusion was discontinued, monitoring the arterial saturation as a marker of duct-dependency of the pulmonary circulation. At that time, 27 patients (group I) showed a significant fall of arterial oxygen saturation (<80%) and required a supplemental source of pulmonary blood flow, while the remaining 28 patients (group II) were discharged without further procedure. The clinical, hemodynamic, procedural, and echocardiographic data were compared between the groups to detect any predictive feature of persistent duct-dependency of the pulmonary circulation. In addition, all echocardiographic variables were analyzed to identify predictive cut-off values and were used to build a predictive echocardiographic score (PDDPC-score) of persistent duct-dependent circulation.

### 2.1 | PDDPC-score analysis

Based on the significant echocardiographic data and their cut-off values, the PDDPC-score was built to predict the need for an additional pulmonary blood flow source. The considered variables were tricuspid valve (TV) z-score, tricuspid/mitral valve annular ratio, pulmonary valve z-score, end-diastolic RV area, end-systolic right atrium area, the percentage amount of interatrial right-to-left shunt, tricuspid regurgitation, RV systolic pressure, and E/E' ratio. Among these nine echocardiographic parameters were arbitrary assigned +1 point each when they passed the respective cut-off value. Thus, the PDDPC-score ranged from 0 to 9 points (Table 2).

### 2.2 | Patient and public involvement statement

No patient and public involvement were deemed necessary in this study. Thus, it was not appropriate to involve patients or the public in the design, conduct, reporting, or dissemination plans of our research.

**TABLE 1** Demographic and procedural data

Baseline demographic and clinical data				
	Overall (n = 55)	Group I (n = 27)	Group II (n = 28)	P-value (group I vs. group II)
<b>Demographic and clinical data</b>				
Sex category (male)	27 (49%)	16 (59%)	11 (39%)	.1
Weight (kg)	2.9 ± .5 (1.7–4.2)	3.0 ± .4 (2.2–3.7)	2.9 ± .6 (1.7–4.2)	.35
BSA (m <sup>2</sup> )	.20 ± .02 (.14–.24)	.21 ± .02 (.16–.24)	.19 ± .03 (.14–.24)	.02
Arterial oxygen saturation	89.3 ± 6.3 (72.0–99.0)	85.4 ± 6.8 (72.0–99.0)	92.5 ± 4.4 (80.0–99.0)	<.01
PA-IVS	15 (27%)	13 (48%)	2 (7%)	<.01
CPS	40 (73%)	14 (52%)	26 (93%)	
<b>Haemodynamic and procedural data at interventional cardiac catheterization</b>				
RV systolic pressure pre-RVD (mmHg)	77.7 ± 18.1 (45.0–140.0)	79.6 ± 20.2 (50.0–140.0)	76 ± 16 (45.0–120.0)	.47
RV systolic pressure post-RVD (mmHg)	41.9 ± 8.9 (28.0–60.0)	42 ± 9.1 (30.0–60.0)	41.8 ± 8.8 (28.0–60.0)	.95
RV/Ao systolic peak pressure ratio pre-RVD	1.6 ± .4 (1.0–2.3)	1.7 ± .3 (1.0–2.3)	1.5 ± .4 (1.0–2.3)	.05
RV/Ao systolic peak pressure ratio post-RVD	.8 ± .2 (.3–1.0)	.9 ± .1 (.6–1.0)	.8 ± .2 (.3–1.0)	.03
Balloon diameter (mm)	8.4 ± 1.3 (6.0–12.0)	7.8 ± 1.1 (6.0–10.0)	9.0 ± 1.3 (6.0–12.0)	<.01
Balloon/annulus ratio	1.3 ± .2 (1.0–2.0)	1.3 ± .2 (1.0–2.0)	1.3 ± .1 (1.0–1.6)	.93
Peak-to-peak pulmonary gradient post-RVD (mmHg)	10.6 ± 7.9 (.0–31.0)	10.6 ± 8.5 (.0–30.0)	10.5 ± 7.5 (.0–31.0)	.99
Ventricle partition:				
Bipartite	8 (15%)	8 (30%)	0	–
Tripartite	47 (85%)	19 (70%)	28 (100%)	
Adverse event	1 (2%)	1 (4%)	0	–

Continuous variables are expressed as mean ± standard deviation (range), and dichotomic variables as n (%). Student's *t*-test and chi-square test were used to compare continuous and dichotomic/categorical variables, respectively. Ao, aorta; BSA, body surface area; CPS, critical pulmonary stenosis; PA-IVS, pulmonary atresia with intact ventricular septum; RV, right ventricle; RVD, right ventricle decompression.

### 2.3 | Statistical analysis

All statistical analysis was performed using Statistical Package for Social Sciences, for Windows, version 25 (SPSS Inc., Chicago, USA). Continuous variables were presented as mean ± standard deviation (or median and range), as appropriate. Categorical data were expressed as frequency (percentage). Univariate analysis was performed to compare the two groups. Continuous and categorical variables were analyzed with paired Student's *t*-test and Chi-square test, respectively. Receiver operating curves (ROCs) were used to detect significant predictors for patients needing additional pulmonary blood flow and establish the best cut-off value (Youden's index analysis). A paired Student's *t*-test was adopted to compare the two groups about the PDDPC-score, and the ROCs were used to identify a valuable cut-off of the duct-dependent pulmonary circulation and analyze its predictive value.

The data were analyzed at 95% of confidence. Therefore, statistical significance was set at  $P < .05$ .

## 3 | RESULTS

### 3.1 | Procedural, hemodynamic, and echocardiographic data

#### 3.1.1 | Procedure outcome

Fifteen patients (27%) had PA-IVS and were submitted to radiofrequency (11 cases, 73%) or mechanical (four cases, 27%) perforation of the pulmonary valve. The remaining 40 patients (73%) had CPS that was submitted to balloon valvuloplasty. The balloon diameter and balloon/annulus ratio were  $8.4 \pm 1.3$  mm and  $1.3 \pm .2$  mm, respectively.

**TABLE 2** PDDPC-score

Variable	Cut-off value	Score point
TV annulus diameter (z-score)	<−2.12	+1
TV/MV annular ratio	<.78	+1
PV annulus diameter (z-score)	<−1.17	+1
RV end-diastolic area (cm <sup>2</sup> )	<1.35	+1
RA end-systolic area (cm <sup>2</sup> )	>2.45	+1
Interatrial R-L shunt (%)	>69.5	+1
Tricuspid regurgitation	Moderate/ severe	+1
RVSP (mmHg)	>42.5	+1
E/E' ratio	>6.6	+1

MV, mitral valve; PV, pulmonary valve; RA, right atrium; R-L, right-to-left; RV, right ventricle; RVSP, right ventricle systolic pressure; TV, tricuspid valve.

The interventional procedure was effectively completed in all patients but one (2%), in whom pulmonary valve perforation was complicated by pulmonary trunk perforation that required emergent surgical repair.

### 3.1.2 | Hemodynamic data

Transcatheter approach resulted in effective RV decompression with a significant decrease of both RV systolic pressure ( $77.7 \pm 18.1$  vs.  $41.9 \pm 8.9$  mmHg,  $P < .01$ ) and RV/aorta systolic peak pressure ratio ( $1.6 \pm .4$  vs.  $.8 \pm .2$ ,  $P < .01$ ) (Table 1).

### 3.1.3 | Echocardiographic data

Effective right ventricular decompression was also confirmed by echocardiography that showed a significant decrease of both RV systolic pressure (from  $93.2 \pm 26.3$  to  $48.7 \pm 13.6$  mmHg,  $P < .01$ ) and maximum pulmonary peak pressure gradient ( $78.1 \pm 12.8$  to  $26 \pm 10.5$  mmHg,  $P < .01$ ) (Table 3).

## 3.2 | Comparison between groups

### 3.2.1 | Procedure outcome

Neonates with PA-IVS had a higher risk of PDDPC than CPS ones (87% vs. 35%,  $P < .01$ ). In addition, all patients with a bipartite RV (eight cases) required an additional source of pulmonary blood flow after pulmonary valvuloplasty.

### 3.2.2 | Hemodynamic data

The two groups did not show significant differences both in pre-operative ( $79.6 \pm 20.2$  vs.  $76 \pm 16$  mmHg,  $P = \text{NS}$ ) and post-operative RV systolic pressure ( $42 \pm 9.1$  vs.  $41.8 \pm 8.8$  mmHg,  $P = \text{NS}$ ) (Table 1).

### 3.2.3 | Echocardiographic data

TV diameter ( $9.1 \pm 1.8$  vs.  $10.8 \pm 2$  mm,  $P < .01$ ; z-score  $-1.95 \pm 1.07$  vs.  $-.9 \pm .98$ ,  $P < .01$ ), tricuspid/mitral valve annular ratio ( $.75 \pm .13$  vs.  $.96 \pm .15$ ,  $P < .01$ ), and pulmonary valvular annulus (diameter  $6.1 \pm .7$  vs.  $7.1 \pm 1$  mm,  $P < .01$ ; and z-score  $-1.62 \pm .81$  vs.  $-.51 \pm .87$ ,  $P < .01$ ) were significantly smaller in the group I. In addition, this group showed smaller RV end-diastolic area ( $1.2 \pm .6$  vs.  $2 \pm .7$  cm<sup>2</sup>,  $P < .01$ ) and larger right atrium end-systolic area ( $4 \pm 1.44$  vs.  $2.5 \pm 1.05$  cm<sup>2</sup>,  $P < .01$ ). Preserved and similar RV systolic function, as inferred by the analysis of TAPSE ( $7.3 \pm 1.7$  vs.  $7.3 \pm 1.4$  mm,  $P = \text{NS}$ ), RV lateral S' wave ( $7.8 \pm 2.1$  vs.  $7.2 \pm 1.4$  cm/s,  $P = \text{NS}$ ), and FAC% ( $43 \pm 11.4$  vs.  $41.6 \pm 10$ ,  $P = \text{NS}$ ) was recorded in both groups. However, group I neonates had worse RV diastolic function, as inferred by higher E/E' ratio ( $9.7 \pm 4.2$  vs.  $6.9 \pm 3.2$ ,  $P < .01$ ) and percentage amount of atrial right-to-left shunt ( $75 \pm 15.7$  vs.  $56.4 \pm 27.8\%$ ,  $P < .01$ ). No differences were found in pulmonary residual maximum gradient ( $27.8 \pm 13.5$  vs.  $24.1 \pm 6.2$  mmHg,  $P = \text{NS}$ ), even if group I showed higher RV systolic pressure ( $56.4 \pm 14.5$  vs.  $41.3 \pm 6.9$  mmHg,  $P < .01$ ) estimated by tricuspid regurgitation. Finally, the rate of moderate or severe tricuspid regurgitation was higher in group I (78% vs. 29%,  $P < .01$ ) (Table 3).

### 3.2.4 | Cut-off values and PDDPC-score

The analysis of ROCs allowed determining the cut-off values of all variables predicting the need for additional pulmonary blood-flow sources. The ROCs identified the following cut-off values of persistent duct-dependent pulmonary circulation: TV diameter <8.8 mm, TV z-score  $\leq -2.12$ , tricuspid/mitral valve annular ratio <.78, pulmonary valve diameter <6.7 mm, pulmonary valve z-score  $\leq -1.17$ , RV area <1.35 cm<sup>2</sup>, right atrium area >2.45 cm<sup>2</sup>, percentage amount of atrial right-to-left shunt >69.5%, RV systolic pressure >42.5 mmHg. The E/E' ratio analysis allowed the identification of two different cut-off values with similar statistical significance: >6.6 (sensitivity 85% and specificity 61%) and >7.9 (sensitivity 63% and specificity 82%) (Table 4) (Figure 1).

Group I had a mean PDDPC-score value significantly higher than group II ( $6.3 \pm 1.5$  vs.  $1.9 \pm 1.3$ ,  $P < .01$ ). The analysis of ROCs demonstrated that a value of PDDPC-score  $\geq 4.00$  was able to predict the need for pulmonary blood-flow support with high sensitivity (100%) and specificity (86%). No patient with a score  $\leq 3$  needed an additional pulmonary blood flow source, whereas all patients with a score  $\geq 6$  remained duct-dependent despite effective right ventricular decompression (Figure 2). These cut-off values increase the predictive ability of this score in identifying two different groups (0–3 and 6–9 points) in which it can predict the fate of the patients with reasonable certainty.

## 4 | DISCUSSION

Duct-dependency of the pulmonary circulation in patients with PA-IVS and CPS may persist even after successful percutaneous right ventricular decompression. In these cases, an additional, stable source of

**TABLE 3** Echocardiographic data after right ventricle decompression

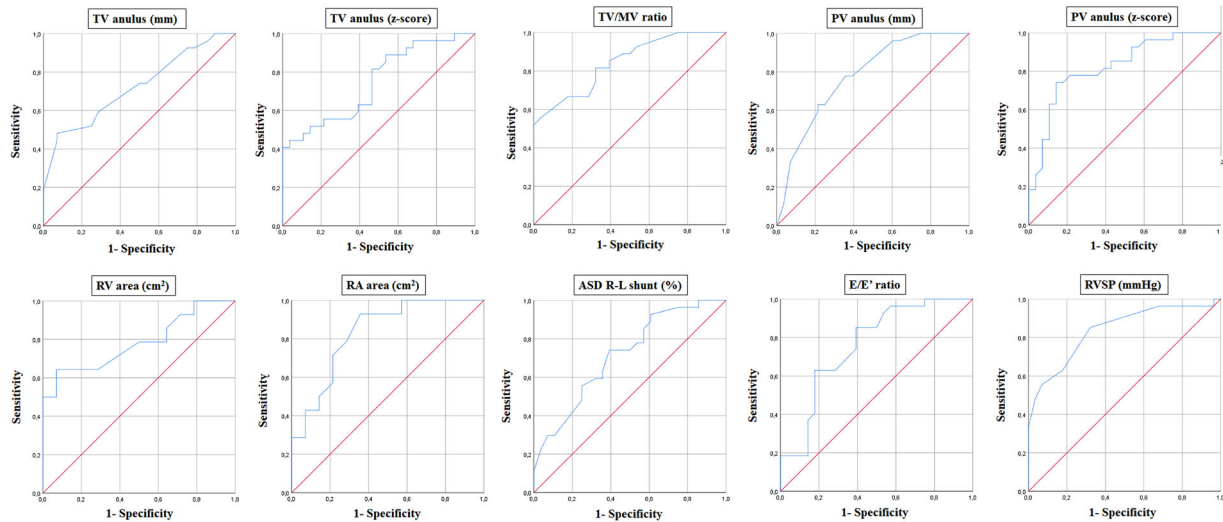
Variable	Overall (n = 55)	Group I (n = 27)	Group II (n = 28)	P-value (group I vs. group II)
TV annulus diameter (mm)	9.9 ± 2.1 (6.0–17.0)	9.1 ± 1.8 (6.0–13.0)	10.8 ± 2.0 (8.0–17.0)	<.01
TV annulus diameter (z-score)	-1.42 ± 1.15 (-4.05–1.53)	-1.95 ± 1.07 (-4.05–.35)	-.90 ± .98 (-2.19–1.53)	<.01
TV/MV annular ratio	.86 ± .17 (.55–1.20)	.75 ± .13 (.55–1.00)	.96 ± .15 (.75–1.20)	<.01
PV annulus diameter (mm)	6.6 ± 1.0 (5.0–9.0)	6.1 ± .7 (5.0–7.5)	7.1 ± 1.0 (5.0–9.0)	<.01
PV annulus diameter (z-score)	-1.06 ± 1.0 (-3.23–1.26)	-1.62 ± .81 (-3.23–.14)	-.51 ± .87 (-2.35–1.26)	<.01
RV end-diastolic area (cm <sup>2</sup> )	1.6 ± .8 (.5–3.6)	1.2 ± .6 (.5–2.4)	2.0 ± .7 (1.2–3.6)	<.01
RA end-systolic area (cm <sup>2</sup> )	3.2 ± 1.5 (1.3–6.7)	4.0 ± 1.4 (2.2–6.7)	2.5 ± 1.1 (1.3–4.9)	<.01
TAPSE (mm)	7.3 ± 1.5 (3.0–10.0)	7.3 ± 1.7 (3.0–10.0)	7.3 ± 1.4 (5.0–10.0)	.95
Tricuspid S wave (cm/s)	7.5 ± 1.8 (4.5–15.0)	7.8 ± 2.1 (4.5–15.0)	7.2 ± 1.4 (5.0–10.0)	.29
RV-FAC (%)	42.3 ± 10.7 (31.0–70.0)	43.0 ± 11.4 (31.0–70.0)	41.6 ± 10.0 (31.0–64.0)	.63
E/E' ratio	8.3 ± 3.9 (1.7–22.0)	9.7 ± 4.2 (4.9 ± 22.0)	6.9 ± 3.2 (1.7–15.0)	<.01
Interatrial R-L shunt (%)	65.6 ± 24.3 (.0–96.0)	75.0 ± 15.7 (25.0–96.0)	56.4 ± 27.8 (.0–90.0)	<.01
RVSP (mmHg)	48.7 ± 13.6 (30.0–100.0)	56.4 ± 14.5 (33.0–100.0)	41.3 ± 6.9 (30.0–60.0)	<.01
PV peak-pressure gradient (mmHg)	26.0 ± 10.5 (5.0–60.0)	27.8 ± 13.5 (5.0–60.0)	24.1 ± 6.2 (10.0–35.0)	.2
Moderate/severe TR	29 (53%)	21 (78%)	8 (29%)	<.01

Continuous variables are expressed as mean ± standard deviation (range), and dichotomic variables as n (%). Student's t-test and chi-square test were used to compare continuous and dichotomic/categorical variables, respectively. MV, mitral valve; PV, pulmonary valve; RA, right atrium; R-L, right-to-left; RV, right ventricle; RV-FAC, right ventricle fractional area change; RVSP, right ventricle systolic pressure; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; TV, tricuspid valve.

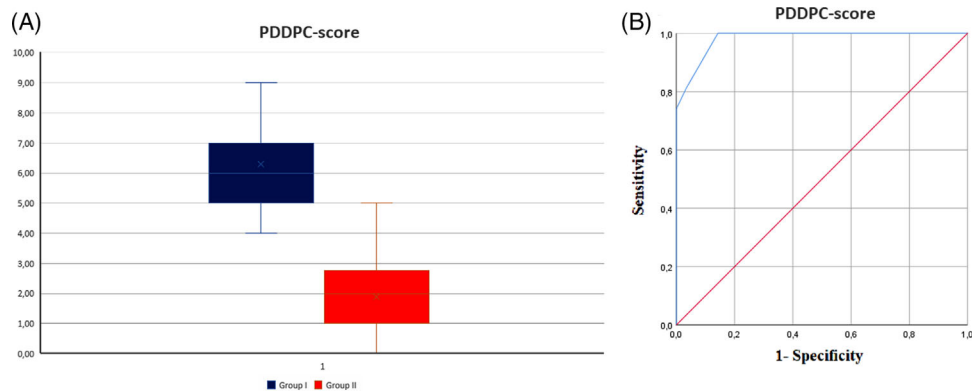
**TABLE 4** Variables cut-off values predicting a duct-dependent pulmonary circulation after right ventricle decompression

Variable	Cut-off value	Sensitivity (%)	Specificity (%)	AUC ± SE	P-value
TV annulus diameter (mm)	<8.8	48	93	.72 ± .07	<.01
TV annulus diameter (z-score)	<-2.12	44	96	.75 ± .07	<.01
TV/MV annular ratio	<.78	56	96	.84 ± .05	<.01
PV annulus diameter (mm)	<6.7	78	64	.78 ± .06	<.01
PV annulus diameter (z-score)	<-1.17	74	86	.82 ± .06	<.01
RV end-diastolic area (cm <sup>2</sup> )	<1.35	64	93	.78 ± .09	.01
RA end-systolic area (cm <sup>2</sup> )	>2.45	93	64	.83 ± .09	<.01
Interatrial R-L shunt (%)	>69.5	74	61	.71 ± .07	<.01
RVSP (mmHg)	>42.5	85	68	.84 ± .05	<.01
E/E' ratio	>6.6 >7.9	85 63	61 82	.76 ± .07	<.01

AUC, area under the curve; MV, mitral valve; PV, pulmonary valve; RA, right atrium; R-L, right-to-left; RV, right ventricle; RVSP, right ventricle systolic pressure; SE, standard error; TV, tricuspid valve.



**FIGURE 1** Receiver operating curves (ROCs) of significant echocardiographic variables



Variable	Cut-off value	Sensitivity (%)	Specificity (%)	AUC±SE	p-value
PDDPC-score	≥ 4.0	100	86	0.98±0.01	<0.01

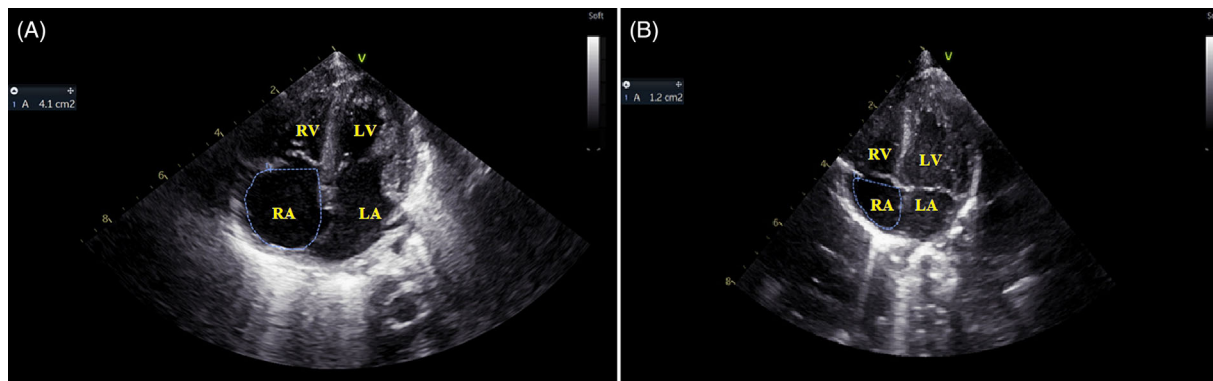
**FIGURE 2** PDDPC score. Distribution of the echocardiographic score values between the groups (A). ROCs of the echocardiographic score: a cut-off  $\geq 4$  show high sensitivity (100%) and specificity (86%) (B). PDDPC, persistent duct-dependency of pulmonary circulation; ROC, received operating curve

pulmonary blood flow is often required after short-term PGE infusion.<sup>7,8</sup> Finding predictive features of persistency of duct-dependent pulmonary circulation could be therefore crucial to optimize the management of these neonates. Several reports highlighted the predictive role of anatomical features such as TV size (diameter, z-score, and tricuspid/mitral valve ratio) and pulmonary valve size (diameter, z-score), RV development, and tricuspid regurgitation.<sup>3,9–12</sup> However, despite technical advances in echocardiography and wide diffusion of new echocardiographic indexes of systolic and diastolic cardiac function, other potential predictive parameters have not so far been evaluated. This paper was the first to analyze the impact of both “old” anatomical and “novel” functional data in predicting the PDDPC after successful percutaneous RV decompression. These parameters were also grouped into a simple and easily reproducible

echocardiographic score to increase the potential of echocardiography to predict the fate of these neonates.

In our study, TV anatomic parameters showed high specificity in selecting neonates with persistent duct-dependent pulmonary circulation being a small, dysplastic, stenotic TV often associated with poor ventricular filling and hence reduced stroke volume and pulmonary blood flow, as a sort of RV “in-flow regulator.”<sup>13</sup> As previously reported in literature,<sup>14</sup> also pulmonary valve size and end-diastolic RV area were significantly associated with high risk of PDDPC after successful RV decompression, possibly due to low pulmonary stroke volume.

From the functional point of view, RV diastolic dysfunction, as inferred by echocardiographic evaluation of tricuspid  $E/E'$  ratio, was another valuable determinant of PDDPC, as already reported in the literature.<sup>15</sup> In this setting, a key predictive value is right atrium size



**FIGURE 3** Echocardiographic 4-chamber apical view of a dilated right atrium (end-systolic area 4.1 cm<sup>2</sup>) of a patient who required arterial duct stenting after right ventricle decompression (A) versus a normal right atrium (end-systolic area 1.2 cm<sup>2</sup>) of a patient who did not require further procedures after successful RV decompression (B). LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle

and function which can depend on TV development and RV diastolic function. Right atrium volume could be an independent variable that “mirrors” the right ventricular compliance different from atrial shunt that depends on atrial septal defect anatomy, left atrial pressure and volume, in turn related to left ventricular compliance.<sup>16–18</sup> Thus, a larger right atrial volume and a higher amount of right-to-left atrial shunt were found in neonates with PDDPC. In our analysis, the right atrium area showed the highest sensitivity in predicting PDDPC (Figure 3).

Overall, several anatomic and functional echocardiographic parameters significantly predicted the fate of the neonates with PA-IVS or CPS after RV decompression, although with different sensitivity and specificity. TV annulus (diameter, z-score, or tricuspid/mitral valve ratio) and end-diastolic RV area showed the highest specificity while end-systolic right atrium area the highest sensitivity. Summarizing all significant echocardiographic parameters into a comprehensive echocardiographic score (PDDPC-score), we obtained a highly effective predictive tool. In fact, a score cut-off  $\geq 4$  was able to predict the fate of these patients with both high sensitivity (100%) and specificity (86%). Furthermore, this score index allowed identifying patients consistently without (score  $\leq 3$ ) or with PDDPC (score  $\geq 6$ ). This simple echocardiographic score could be useful in clinical practice to improve the counseling with parents either in terms of therapeutic strategy or mid-term prognosis. In addition, it could be useful in reducing the time of PGE administration, the overall hospital stays and the number of complications.

## 5 | STUDY LIMITATIONS

Some theoretical limitations might hamper the aim of this study of evaluating the role of anatomic and functional echocardiographic parameters in predicting PDDPC after successful percutaneous RV obstruction relief. First, the design of this study hampered reporting of some other anatomic echocardiographic parameters (such as RV length, RV basal, and mid-cavity diameters), which could have provided further analysis information about the fate of these patients. Second, some of

the echo parameters have shown some good predictive value in the past, while some others (such as quantification of atrial level net right to left shunt, RV FAC, right atrium, and ventricle area) may not be easily reproducible with likely significant inter-observer operator variability. At the same time, the well-known limits of echocardiography in evaluating RV volume and function could be improved by using more accurate imaging tools (such as three-dimensional echocardiographic analysis, myocardial strain rate, or cardiac magnetic resonance) could improve the analyses in these patients. Third, the wide anatomic and functional variability of patients with PA-IVS/CPS partially precludes any generalization of this score index. For all these reasons, our results should be validated in a larger prospective multicenter study.

However, wide diffusion of this diagnostic tool and simplicity of the echocardiographic parameters used to build this score might be a starting point to set any initial therapeutic plan and counseling approach.

## 6 | CONCLUSION

Transcatheter approach is a safe and effective tool for treatment of PA-IVS and CPS in neonatal age. Echocardiographic analysis of combined simple anatomic and functional parameters after successful RV decompression made possible to build a highly sensible and specific novel comprehensive score allowing to predict the fate of these patients. This approach could be useful to potentially improve long-term management of these frail patients. However, these results need to be validated in a larger cohort before their wide diffusion in clinical practice could be advised.

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## CONFLICTS OF INTEREST

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