Outcome predictors in catheter interventions for severe right ventricular outflow tract obstructions
Outcome Predictors in Catheter Interventions for Severe Right Ventricular Outflow Tract Obstructions

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Abstract

Introduction & aim of work: Transcatheter treatment for critical pulmonary stenosis and membranous pulmonary atresia has become the gold standard of care in many centers. We aimed at evaluating the predictors of outcome in interventions for treatment of duct-dependent right ventricular outflow tract obstruction with intact interventricular septum.

Subjects & methods: 68 cases with pulmonary atresia with intact interventricular septum (PA/IVS) and 50 cases with critical pulmonary stenosis (CPS), all younger than 3 months of age, were operated during the period of 10 years; excluding patients with tricuspid valve annulus Z-score smaller than -4, evidence of right ventricular-dependent coronary circulation or additional malformations.

Results: Age, weight, body surface area as well as tricuspid & pulmonary valve Z-scores were significantly less in PA/IVS; right ventricular pressure was similar in both groups however procedural success and survival to hospital discharge was higher in the CPS group. Lower age, weight and body surface area were associated with procedural failure. Weight was the only predictor of procedural success; while weight and lower post-procedural right ventricular pressure were independent predictors for survival to hospital discharge. Post-procedural right ventricular pressure and length of stay were less in the CPS group. tricuspid and pulmonary valve annulus Z-scores were the only independent predictors of the post-procedural milrinone duration in PA/IVS.

Conclusion: We advocate for the use of larger balloon/pulmonary annulus ratio, to achieve a lower right ventricular pressure not fearing excessive pulmonary regurgitation that might be beneficial for right ventricular growth; and for the combination with ductal stenting in borderline or bipartite right ventricles.

Keywords: Critical pulmonary stenosis, Pulmonary atresia, Transcatheter intervention, Outcome

1. Introduction

Neonates with critical pulmonary stenosis (CPS) or complete pulmonary atresia (PA) with intact interventricular septum (IVS) display a wide range of hypoplasia affecting the different right ventricular (RV) components [1]. These are rare cyanotic congenital heart defects (CHD) constituting about 3% of all CHD [2,3].

Currently, percutaneous balloon pulmonary valvuloplasty (PBPV) with or without perforation of the atretic valve has proven effective and could be applied as the principal treatment with few complications [4]. However, selective and stratified methods have become more sophisticated in the last 2 decades greatly contributing to improvement in the clinical outcome [5–7]. Strictly following the management algorithms is proposed to achieve best outcomes [7].

The pediatric cardiac intensivist is faced with a challenging spectrum of post-interventional pathophysiological statuses [1]. However, given the rarity of this CHD, there is paucity of data regarding clinical outcomes [8]. This study aimed at evaluating the predictors of procedural success, survival and length of ICU stay following primary catheter intervention in neonates with PA/IVS and CPS/IVS.
2. Patients and methods

This is a retrospective study that included all patients with right ventricular outflow tract obstruction (RVOTO), IVS and no major sinusoidal communications that received transcatheter treatment at Cairo University Children’s Hospital during the period from October 2009 to August 2019. A total of 118 patients were included in the study: of these 68 patients had PA/IVS (group 1); and 50 patients had CPS/IVS (group 2). All procedures were performed by the same team of operators. Patients with additional malformations were excluded. Tricuspid valve variables such as Ebstein’s anomaly or various hypoplasia/dysplasia were included, however, a tricuspid valve (TV) annulus Z-score smaller than −3 were referred from the start for patent ductus arteriosus (PDA) stenting or a modified Blalock-Taussig (MBT) shunt.

This study was approved by the Cairo University ethical committee.

2.1. Patient preparation

Clinical data obtained included age, weight and length at intervention; and baseline oxygen saturation. Electrocardiograms and chest radiograms were performed for all cases. Anatomical details by echocardiography were obtained using a Vivid 5 machine and a 5 MHz phased array probe (GE, Vingmed Ultrasound AS, Horten, Norway). Echocardiographic assessment protocol included the TV and mitral valve (MV) annuli from the apical 4 chamber view; the pulmonary valve (PV) annulus and main pulmonary artery (MPA) from the parasternal short axis view; PDA morphology and size in the parasternal ductal view; and the size of the interatrial communication from the subcostal view. Z-scores were calculated from the algorithms published by the Daubeney group [9]. Informed consents for the required intervention and for utilizing data in research were obtained from the parents prior to interventions, whether radiofrequency perforation of the PV and valvuloplasty for PA/IVS, or PBPV for CPS/IVS.

Neonates with CPS were patients presenting with cyanosis related to right-left shunting across the patent foramen oval (PFO) and duct-dependent pulmonary circulation; PA was considered when there was complete membranous atresia of the PV with an adequate-sized MPA. Neonates were nominated suitable for transcatheter approach if the RV was tripartite or bipartite; with a TV annulus Z score −3 or larger; and showing no right ventricular-dependent coronary circulation (RVDCC). All our included patients were diagnosed in the neonatal period, however, some of the cases (14) were operated later on in life being referred from remote areas and presenting to our center later than the neonatal period.

2.2. Catheterization procedure

Procedures were performed under general anesthesia; patients were monitored throughout the procedure by an anesthesiologist. After obtaining vascular accesses, a 4 or 5-F multipurpose (MPA 1) catheter (Cordis, Miami, FL, USA) was used to measure RV pressure (RVP) and perform a diagnostic right ventriculogram in the lateral and frontal projections to assess the RV morphology, rule-out coronary sinusoids and measure the PV annulus. In cases of PA/IVS, a 4-F pigtail catheter (Cordis, Miami, FL, USA) was used to measure aortic pressure (AoP). An aortogram was performed to define PDA morphology, size, and coronary anatomy. The MPA was then approached retrogradely via the PDA using a cut pigtail catheter and a snare was placed.

In both conditions, a 4- or 5-F Judkins right catheter with 1.5, 2 or 3.5 curve (Cordis, Miami, FL, USA) was maneuvered into the infundibulum with a Y-connector (Cook, Bloomington, IN), allowing intermittent contrast injections to define the valve plane. In cases with PA/IVS the PV was perforated after good positioning by a radiofrequency wire (Nykänen RF wire, Baylis Medical, Montréal, Canada) or the stiff end of a coronary wire (Boston scientific, this was used in a few cases at the start of our
experience), followed by snaring of the wire and forming an arterio-venous loop. Alternatively, a coronary wire was passed adjacent to the Nykanen wire to track it to a pulmonary artery branch or the descending Aorta. Hybrid procedure was attempted in only 2 cases were peripheral vascular access failed in the first, and proper positioning of the radio frequency (RF) wire was difficult in the latter. The tiny opening of the PV was subsequently crossed by a coronary or Terumo wire, balloon dilatation was then performed using a Tyshak II or Tyshak MINI balloon, of size around 120% of the PV annulus. Pre-dilatation using a coronary balloon was attempted in most cases. In a few (3) cases, PDA stenting was performed following pulmonary valvuloplasty based on small RV volume and the expectation of a restrictive RV physiology.

Following successful interventions, post-intervention care of patients with PA/IVS at the pediatric cardiac intensive care unit (PCICU) included continuation of prostaglandin E1 (PGE1) and milrinone infusions until the RV was rehabilitated, evidenced by stabilization of oxygen saturation above 70% and left-to-right shunting across the PFO. Furosemide doses were frequently administered upon evidence of pulmonary and/or systemic congestion. Propranolol was given whenever hyperdynamic RVOTO was seen on echocardiography. Post- intervention care for babies with CPS seldom required PGE1 infusion for a short period to support pulmonary circulation until saturations stabilized. The patients were maintained also on both propranolol and angiotensin converting enzyme inhibitor (captopril) [10].

A successful procedure was defined as procedures where the RVP was reduced to less than half the pre-procedural pressure, and the patients were discharged to the PCICU in a stable condition. Otherwise, the procedure was defined as a failure.

### 2.3. Statistical methods

Data were analyzed using IBM® SPSS® Statistics version 23 (IBM® Corp., Armonk, NY). Continuous numerical variables were presented as mean and SD and inter-group differences were compared using the unpaired t-test. Categorical variables were presented as number and percentage or ratio, and differences were compared using the Pearson chi-squared test. Correlations between numerical variables were tested using the Pearson correlation. Multivariable binary logistic regression analysis (after adjustment for the effect of included variables) was used to examine the predictors of success of the procedure. To examine the predictors of post-procedure RVP, multivariable linear regression was used; while Cox proportional hazard regression was used to identify predictors of survival to hospital discharge (after adjustment of other cofounders in both methods). Two-tailed p-values <0.05 were considered statistically significant.

### 3. Results

A total of 118 patients were performed during the study period. This included 68 PA/IVS and 50 CPS patients. All patients included were below three months of age. Table 1 shows the anthropometric and pre-procedural data. The age, weight, height and BSA of PA/IVS cases were significantly less than those with CPS [p < 0.001, 0.001, 0.002, and <0.001 respectively].

By comparing pre-procedural echocardiographic parameters (Table 2): TV annulus, TV z-scores and PV z-scores were significantly lower in the PA/IVS cases (p = 0.018, <0.001, and <0.001 respectively).

On comparing procedural and post-procedural data, radiation time was significantly lower in the CPS group (p < 0.001). Pre-intervention RVP was similar in both groups (Table 3).

Procedural success was higher in the CPS than the PA/IVS group (86% compared to 73.5%): were 8 out of 50 cases with CPS failed versus 18 out of 68 in the PA/IVS group, mainly due to failure to achieve a suitable subpulmonic RVOT position. Similarly, survival to hospital discharge was higher in cases with CPS (97%) compared to 54% in the PA/IVS group (Table 4). Mortality in the CPS group was mostly due to postprocedural sepsis; also in the PA/IVS...
IVS causes were mainly related to sepsis in addition to cardiac tamponade and metabolic disturbances in a minority (Fig. 1).

On comparing the patients receiving a successful procedure with those who failed (Table 5), we found that lower age, weight and body surface area (BSA)
were associated with procedural failure (p-values of 0.044, 0.038 and 0.034, respectively) (Fig. 2). No association was found with pre-procedural echocardiographic parameters, duration of PGE1 duration, pre-intervention RVP or AoP, or operative technique.

Predictors of procedural success were observed by multivariable binary logistic regression analysis (Suppl. Table 1): no statistically significant relation with the interventional technique, i.e., initial diagnosis (p = 0.272), age (p = 0.697), weight (p = 0.154), pre-procedure RVP (p = 0.435), TV annulus Z-score (p = 0.634) or PV annulus Z-score (p = 0.354). Using multivariable backward binary logistic regression, weight was the only variable retained in the model with a statistically significant relation to success of the procedure (OR = 1.824, 95% CI = 1.022 to 3.254, p = 0.042). Each 1 kg increase in the baby’s weight was associated with an increase of 0.824 in the odds of success (Suppl. Table 2). Although weight is linked with diagnosis, as patients with PA/IVS tend to present earlier, however, age did not have a similar impact on outcome.

On studying predictors of survival to hospital discharge using Cox- proportional hazard regression (Suppl. Table 3): weight (Cox proportional hazard = 0.545, 95% CI = 0.302 to 0.983, p = 0.044) and post-procedure RVP (Cox proportional hazard = 1.023, 95% CI = 1.010 to 1.037, p = 0.001) were independent predictors of survival to hospital discharge. There was no statistically significant relation between survival and the interventional technique (p = 0.312) or age (p = 0.865) (Fig. 3).

The secondary outcome measures that were studied in both groups included post-procedure RVP and ICU length of stay (LOS), and both were significantly lower in CPS group [p < 0.001 for both] (Table 6, Fig. 4).

The interventional procedure was the only independent predictor of post-procedure RVP (B = −15.224, SE = 4.911, p = 0.002) where CPS was associated with a lower RVP of about 15 mmHg compared with PA/IVS (Suppl. Table 4). On correlating the post-procedure RVP with all variables (Suppl. Table 5), a weak positive correlation was found with the pre-intervention AoP (p = 0.037) and post-procedure PGE1 (p = 0.044) (Fig. 5).

### Table 5. Comparison of patients with failed or successful procedure.

| Variable                     | Failed procedure (n = 25) | Successful procedure (n = 93) | Mean Difference | 95% CI | P-value* |
|------------------------------|---------------------------|-------------------------------|----------------|-------|----------|
| Age (days)                   | 23.6 ± 22.6               | 34.7 ± 27.9                   | −11.1          | −22.0 | 0.044    |
| Weight (kg)                  | 3.0 ± 0.7                 | 3.5 ± 1.0                     | −0.5           | −0.9  | 0.038    |
| Height (cm)                  | 51.5 ± 3.4                | 51.7 ± 4.6                    | −0.2           | −2.2  | 0.808    |
| BSA (m²)                     | 0.203 ± 0.027             | 0.218 ± 0.041                 | −0.015         | −0.029| 0.034    |
| Duration of pre-procedure    | 9.3 ± 7.8                 | 7.6 ± 8.2                     | 1.7            | −2.8  | 0.450    |
| PDA diameter (mm)            | 2.9 ± 0.7                 | 3.3 ± 0.9                     | −0.4           | −0.9  | 0.047    |
| PFO diameter (mm)            | 4.9 ± 1.7                 | 4.9 ± 1.7                     | 0.0            | −1.0  | 0.973    |
| MV annulus (mm)              | 13.8 ± 2.5                | 12.7 ± 1.9                    | 1.0            | −0.1  | 0.227    |
| MV annulus Z-score           | 2.08 ± 1.38               | 1.58 ± 1.08                   | 0.50           | −0.14 | 0.124    |
| TV annulus (mm)              | 13.9 ± 3.9                | 13.0 ± 2.8                    | 0.8            | −0.5  | 0.230    |
| TV annulus Z-score           | 0.89 ± 1.51               | 0.52 ± 1.21                   | 0.37           | −0.2  | 0.200    |
| PV annulus (mm)              | 7.3 ± 1.5                 | 7.6 ± 1.2                     | −0.4           | −0.9  | 0.218    |
| PV annulus Z-score           | −0.64 ± 1.33              | −0.68 ± 1.17                  | 0.05           | −0.49 | 0.865    |
| Pre-procedure RVP (mmHg)     | 118.6 ± 28.2              | 113.5 ± 29.8                  | 5.1            | −8.1  | 0.445    |
| AoP (mmHg)                   | 66.7 ± 7.9                | 68.8 ± 12.5                   | −2.1           | −8.4  | 0.502    |
| Operative technique (RF/CSP) | 18/7                      | 50/43                         | −              | −     | 0.101    |

Data are mean ± standard deviation (SD) or ratio. 95% CI, 95% confidence interval.

*Independent samples t-test unless otherwise indicated.

†Pearson chi-squared test.
Studying correlations between different parameters and need to post-intervention drugs in patients with PA/IVS (Suppl. Table 6) showed that RVP was directly proportionate with the need for PGE1 infusion; while the period on milrinone was inversely proportionate to the MV and TV valve annuli, but was directly proportionate to the PV annulus (Fig. 6).

The TV annulus Z-score ($B = -0.695, SE = 0.302, p = 0.025$) and PV annulus Z-score ($B = 0.908, SE = 0.330, p = 0.008$) were the only independent predictors of the post-procedural milrinone duration in patients with PA/IVS (Suppl. Table 7), while lower TV Z-score and higher PV Z-scores were associated with longer duration of post-procedure milrinone. However, no independent predictor of the post-procedural PGE1 duration was found (all $p$-values $>0.05$).

4. Discussion

Percutaneous balloon valvuloplasty of the pulmonary valve was first described by Kan et al., in 1982 [11]. A decade later another remarkable advance in transcatheter intervention was RF perforation for PA/IVS introduced by Qureshi et al., in 1991 [12], this led to significant improvement of outcomes in these lesions, and it has been adopted by the majority of cardiac centers as a gold standard procedure in appropriately-selected patients [4,5]. Intervventional therapy for PA/IVS during the neonatal period was reported to have a high success rate, with a mid-and long-term survival rate ranging from 81.0 to 92.5% [6,7,13].

We aim whenever possible for biventricular repair due to better long-term outcome than univentricular repair; however, proper selection of borderline cases is extremely important to avoid intervening in

### Table 6. Secondary outcome measures in patients with PA/IVS and CPS.

| Variable             | PA/IVS group (n = 68) | CPS group (n = 50) | Mean Difference | 95% CI   | P-value* |
|----------------------|-----------------------|--------------------|-----------------|----------|----------|
| Post-procedure RVP (mmHg) | 56.8 ± 25.5          | 42.5 ± 8.7         | 14.3            | 7.7–20.9 | <0.001   |
| ICU LOS (days)       | 8.1 ± 4.8             | 3.4 ± 1.8          | 4.7             | 3.4–5.9  | <0.001   |

Data are mean and standard deviation (SD).
95% CI, 95% confidence interval.
*Independent samples t-test.

![Fig. 3. Cox proportional hazard survival curves for patients with PA/IVS and CPS.](image1)

![Fig. 4. a) Mean post-procedure RVP in patients PA/IVS and CPS; and b) mean ICU LOS in patients with PA/IVS and CPS. Error bars represent the standard error (SE).](image2)
cases that will fail biventricular repair [14,15]. Restoration of RV to pulmonary artery continuity (RACHS-1 category 2) [16] is an absolute requirement for growth of the hypoplastic RV. In its absence, the dimensions of the RV and the TV actually decrease as the patient grows [17,18]. Even the systemic-to-pulmonary arterial shunt does not influence RV growth [19].

To the best of our knowledge, this study is reporting the largest number of patients who underwent interventional cardiac catheterization for CPS or PA/IVS mostly in the neonatal period. The study included patients considered suitable to achieve biventricular repair with either tripartite or bipartite RV with no RVDCC. In some cases ductal stenting was done in patients where a complementary source of pulmonary flow was expected like bipartite RV with small PV and TV.

In our study, procedural success was related to age, weight and BSA rather than the interventional technique (i.e., initial diagnosis). These parameters were lower in the PA/IVS group which explains the discrepancy in procedural outcomes between the two groups. Weight was the only predictor for success of the procedure. Similarly, multiple reports are available on the association of weight and gestational age with procedural outcome [20].

Survival was similarly associated with weight, and also to post-intervention RVP. Given that pre-intervention RVP was similar in both groups unlike the post-intervention RVP that was significantly less by around 15 mmHg in the CPS group, the need for achieving a lower post-RVP by repeat dilatations or balloon over-sizing is reasoned: it was documented that the rate of reintervention is associated with higher post-RVP and residual pulmonary valve pressure gradient rather than the PV annulus or balloon/annulus ratio [21].

Whether the pulmonary annulus is underestimated in the setting of complete atresia versus the need to use a larger balloon/annulus ratio than traditionally selected was always checked by the fear of development of significant PR, however, it might be argued that such a volume load to the RV might be advantageous on the long-term by promoting RV growth, analogous to what was described in a large multicenter cohort for the strong association of tricuspid regurge severity with tricuspid valve

Fig. 5. Scatter plots illustrating a) the correlation between pre-procedure AoP and post-procedure RVP: there is weak negative correlation between both variables ($r = -0.254$, $p = 0.037$, $R^2 = 0.064$); and b) the correlation between the duration of post-procedure PGE1 and post-procedure RVP: there is weak positive correlation between both variables ($r = 0.245$, $p = 0.044$, $R^2 = 0.060$).

Fig. 6. Scatter plot illustrating a) the correlation between the duration of post-procedure milrinone and MV annulus Z-score: there is weak negative correlation between both variables ($r = -0.242$, $p = 0.047$, $R^2 = 0.058$); b) the correlation between the duration of post-procedure milrinone and TV annulus Z-score: there is weak negative correlation between both variables ($r = -0.262$, $p = 0.031$, $R^2 = 0.069$); and c) the correlation between the duration of post-procedure milrinone and PV annulus Z-score: there is weak positive correlation between both variables ($r = -0.245$, $p = 0.044$, $R^2 = 0.060$).
annular dimension and tricuspid inflow duration, suggesting that the regurgitant physiology affects right ventricular development [22].

It is known that critical stenosis and complete atresia of the pulmonary valve represent a spectrum of the same disease that share similar physiology and outcome. Our study supports that understanding as we show that the type of procedure was not associated with procedural success or outcome, but rather the post-operative RVP. Hence we can postulate that conclusions could be applied to both groups [23].

All our patients with PA/IVS and selected cases with CPS were infused with milrinone post-intervention to overcome RV stiffness until rehabilitation of the RV stiffness occurs evidenced by the shift of shunting across the PFO from RT-LT to LT-RT and the rise of arterial saturations. As expected, smaller TV z-score - that reflects RV hypoplasia [24] predicted a longer duration on milrinone infusion post-intervention. Nevertheless, whilst this adaptation takes time especially with the smaller, more restrictive RVs [25], it exposes the patients to higher risk of ICU-related complications. We came to accept a bidirectional shunt and lower discharge saturations to minimize hospital stay.

Post-procedure RVP had some correlation with a longer post-procedural need for PGE1 infusion which also reflects the RV stiffness and inadequacy of forward pulmonary flow. This advocates for the need to combine RV decompression with ductal stenting in borderline or bipartite RVs, to provide adequate pulmonary flow and maintain oxygen saturations until rehabilitation of RV takes place over time. A report by Chubb et al. on the long-term outcome for patients with PA/IVS over a 19 year period involving 39 cases reports a less hospital stay for patients receiving PDA stenting in addition to pulmonary valvotomy [26]. Another report by Shwartz et al. including 23 cases over 11 years concluded that a smaller TV z-score predicted the need for supplementary blood flow [27].

We have adopted the practice of combining RV decompression with ductal stenting in the latter years of our experience, whenever the team predicted a longer time for RV rehabilitation. Although we seldomly intervened on cases with a TV z-score smaller than −4, where patients were routed to the univentricular pathway from the beginning by ductal stenting or MBTS: based on the theory that such RVs will not tolerate biventricular circulation [26,28].

Conversely, higher PV z-scores predicted longer duration on milrinone. Thus, it is postulated that the PV annulus is not related to the RV stiffness and hence, RV volume. Literature have described the correlation between a smaller PA annulus with the rates of re-stenosis [29], and reintervention [30]. Yet, little is known on the relationship between the PA annulus and the RV size or physiology. Nonetheless, dilating the pulmonary valve is known to promote catch-up growth of the pulmonary annulus [31,32], another advocate for the use of a larger balloon/annulus ratio.

5. Conclusion

In interventions for severe RVOTO, weight is the predictor for procedural success, while survival to hospital discharge is predicted by weight and lower post-procedural RVP: which explains the fewer rates in PA/IVS in both outcomes. The use of large balloon/annulus ratio, and the combination with ductal stenting in PA/IVS with borderline or bipartite RVs might prove benefit in procedural success and outcome. Further studies are needed to confirm these findings by including trans-valvular gradients for the complete assessment of RVp, and the comparison for the effect of combining PDA stenting on outcomes.

Author contribution

Conception and design of Study: SAES, WAA. Literature review: WAA, BMH. Acquisition of data: SAES. Analysis and interpretation of data: WAA, BMH. Research investigation and analysis: SAES, WAA, AAER, BMH. Data collection: AAER, BMH. Drafting of manuscript: SAES, BMH. Revising and editing the manuscript critically for important intellectual contents: WAA, AAER, BMH. Data preparation and presentation: BMH. Supervision of the research: SAES. Research coordination and management: SAES. Funding for the research: SAES, AAER.

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Conflict of interests

All authors declare no conflict of interest.
Appendix A

Supplementary Table 1. Multivariable binary logistic regression analysis for predictors of success of the procedure.

| Variable                        | B     | SE    | Wald  | p-value | Odds ratio | 95% CI       |
|---------------------------------|-------|-------|-------|---------|------------|--------------|
| CPS (–1)*                       | 0.659 | 0.600 | 1.208 | 0.272   | 1.933      | 0.597 to 6.259 |
| Age (days)                      | 0.005 | 0.012 | 0.152 | 0.697   | 1.005      | 0.981 to 1.030 |
| Weight (kg)                     | 0.533 | 0.374 | 2.030 | 0.154   | 1.703      | 0.819 to 3.544 |
| Pre-procedure RVP (mmHg)        | –0.006| 0.008 | 0.610 | 0.435   | 0.994      | 0.978 to 1.010 |
| TV annulus Z-score              | –0.094| 0.197 | 0.226 | 0.634   | 0.911      | 0.619 to 1.339 |
| PV annulus Z-score              | 0.208 | 0.224 | 0.861 | 0.354   | 1.231      | 0.793 to 1.911 |
| Constant                        | 0.170 | 1.357 | 0.016 | 0.900   |            |              |

B = regression coefficient, SE = standard error, Wald = Wald chi-squared statistic, 95% CI = 95% confidence interval.

*Referenced to RF (=0).

Supplementary Table 2. Multivariable backward binary logistic regression analysis for predictors of success of the procedure.

| Variable                        | B     | SE    | Wald  | P-value | Odds ratio | 95% CI       |
|---------------------------------|-------|-------|-------|---------|------------|--------------|
| Weight (kg)                     | 0.601 | 0.295 | 4.137 | 0.042   | 1.824      | 1.022 to 3.254 |
| Constant                        | –0.636| 0.947 | 0.451 | 0.502   |            |              |

B = regression coefficient, SE = standard error, Wald = Wald chi-squared statistic, 95% CI = 95% confidence interval.

*Referenced to RF (=0).

B = statistically-significant outcomes.

Supplementary Table 3. Cox proportional hazard regression for predictors of survival to hospital discharge.

| Covariate                       | B     | SE    | Wald  | P-value | Exp(b) | 95% CI of Exp(b) |
|---------------------------------|-------|-------|-------|---------|--------|------------------|
| CPS (–1)*                       | –0.789| 0.780 | 1.023 | 0.312   | 0.455  | 0.099 to 2.096   |
| Age (days)                      | –0.002| 0.010 | 0.029 | 0.865   | 0.998  | 0.978 to 1.019   |
| Weight (kg)                     | –0.607| 0.301 | 4.064 | 0.044   | 0.545  | 0.302 to 0.983   |
| Post-procedure RVP (mmHg)       | 0.023 | 0.007 | 11.291| 0.001   | 1.023  | 1.010 to 1.037   |

b = regression coefficient, SE = standard error, Exp(b) = Cox proportional hazard, 95% CI of Exp(b) = 95% confidence interval of Cox proportional hazard.

*Referenced to PA/IVS (=0).

B = statistically-significant outcomes.

Supplementary Table 4. Multivariable regression analysis for predictors of post-procedure RVP.

| Independent variables | B     | SE    | T     | P-value |
|-----------------------|-------|-------|-------|---------|
| (Constant)            | 62.732|       |       |         |
| CPS (–1)*             | –15.224| 4.911 | –3.100| 0.002   |
| Age (days)            | 0.003 | 0.095 | 0.029 | 0.977   |
| Weight (kg)           | –1.627| 2.513 | –0.648| 0.519   |
| TV annulus Z-score    | –1.053| 1.659 | –0.635| 0.527   |
| PV annulus Z-score    | –0.792| 1.860 | –0.426| 0.671   |

B = regression coefficient, SE = standard error, t = t-statistic.

*Referenced to RF (=0).

B = statistically-significant outcomes.

Supplementary Table 5. Correlation between post-procedure RVP and other quantitative variables.

| Variable                        | Post-procedure RVP | Pearson r | p-value |
|---------------------------------|--------------------|-----------|---------|
| Age                             | –0.181             | 0.050     |
| Weight                          | –0.163             | 0.078     |
| Height                          | –0.021             | 0.823     |
| BSA                             | –0.151             | 0.102     |
| Duration of pre-procedure PGE1  | –0.062             | 0.618     |
| PDA diameter                    | 0.047              | 0.705     |
| PFO diameter                    | 0.012              | 0.919     |
| MV annulus                      | 0.161              | 0.191     |
| MV annulus Z-score              | –0.029             | 0.811     |
| TV annulus                      | 0.137              | 0.138     |
| TV annulus Z-score              | 0.070              | 0.449     |
| PV annulus                      | –0.085             | 0.359     |
| PV annulus Z-score              | 0.121              | 0.191     |

(continued on next page)
### Supplementary Table 5. (continued)

| Variable | Post-procedure RVP | Pearson r | P-value |
|----------|--------------------|-----------|---------|
| TV annulus/MV annulus | 0.001 | 0.995 |
| Pre-procedure RVP | 0.058 | 0.532 |
| Pre-procedure AoP | 0.254* | 0.037 |
| Irradiation time | 0.181 | 0.050 |
| Irradiation dose | 0.024 | 0.796 |
| Duration of post-procedure PGE1 | 0.245* | 0.044 |
| Duration of post-procedure milrinone | 0.096 | 0.437 |
| ICU LOS | 0.156 | 0.095 |

*Correlation is significant at the 0.05 level (2-tailed).
Bold + statistically-significant outcomes.

### Supplementary Table 6. Correlation of the duration of post-procedure PGE1 or milrinone with other numerical variables in patients with PA/IVS.

| Variable | Duration of post-procedure PGE1 | Pearson r | P-value |
|----------|----------------------------------|-----------|---------|
| Age | 0.010 | 0.935 |
| Weight | 0.042 | 0.732 |
| Height | 0.008 | 0.949 |
| BSA | 0.032 | 0.797 |
| Duration of pre-procedure PGE1 | 0.067 | 0.590 |
| PDA diameter | 0.080 | 0.517 |
| PFO diameter | 0.204 | 0.995 |
| MV annulus | 0.010 | 0.095 |
| MV annulus Z-score | 0.161 | 0.095 |
| TV annulus | 0.276* | 0.023 |
| TV annulus Z-score | 0.165 | 0.180 |
| PV annulus | 0.144 | 0.240 |
| PV annulus Z-score | 0.144 | 0.240 |
| TV annulus/MV annulus ratio | 0.187 | 0.012 |
| Pre-procedure RVP | 0.002 | 0.949 |
| Pre-procedure AoP | 0.063 | 0.610 |
| Irradiation time | 0.111 | 0.369 |
| Irradiation dose | 0.013 | 0.919 |
| Post-procedure RVP | 0.245* | 0.096 |

*Correlation is significant at the 0.05 level (2-tailed).
Bold + statistically-significant outcomes.

### Supplementary Table 7. Multivariable regression analysis for predictors of the duration post-procedure milrinone in patients with PA/IVS.

| Independent variables | B | SE | t | P-value |
|-----------------------|---|----|---|---------|
| (Constant)            | 5.860 |    |    |         |
| Age (days)            | -0.027 | 0.022 | -1.226 | 0.225 |
| Weight (kg)           | -0.196 | 0.758 | -0.258 | 0.797 |
| MV annulus Z-score    | -0.592 | 0.370 | -1.599 | 0.115 |
| TV annulus Z-score    | -0.695 | 0.302 | -2.299 | 0.025 |
| PV annulus Z-score    | 0.908 | 0.330 | 2.751 | 0.008 |
| Post-procedure RVP (mmHg) | 0.011 | 0.016 | 0.670 | 0.505 |

B = regression coefficient, SE = standard error, t = t- statistic.
Bold + statistically-significant outcomes.

### Supplementary Table 8. Multivariable regression analysis for predictors of the duration post-procedure PGE1 in patients with PA/IVS.

| Independent variables | B | SE | t | P-value |
|-----------------------|---|----|---|---------|
| (Constant)            | 4.358 |    |    |         |
| Age (days)            | -0.011 | 0.028 | -0.391 | 0.697 |
| Weight (kg)           | 0.208 | 0.949 | 0.219 | 0.828 |
| MV annulus Z-score    | -0.405 | 0.464 | -0.874 | 0.386 |
| TV annulus Z-score    | -0.464 | 0.379 | -1.225 | 0.225 |
| PV annulus Z-score    | 0.653 | 0.413 | 1.580 | 0.119 |
| Post-procedure RVP (mmHg) | 0.039 | 0.020 | 1.958 | 0.055 |

B = regression coefficient, SE = standard error, t = t- statistic.
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