Early View

Original research article

Management of Systemic to Pulmonary Shunts and Elevated Pulmonary Vascular Resistance

Alexandra N. Linder, Jill Hsia, Sheila V. Krishnan, Emile A. Bacha, Sarah Crook, Erika B. Rosenzweig, Usha S. Krishnan


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Title: Management of Systemic to Pulmonary Shunts and Elevated Pulmonary Vascular Resistance

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Take Home Message: In selected CHD patients with moderately elevated PVR, partial or complete shunt closure and use of targeted PAH therapy was associated with improved haemodynamics and WHO functional class.
Abstract

**Background:** Timing of repair of systemic to pulmonary shunts is aimed at preventing development of irreversible pulmonary vascular disease, including in patients with other factors contributing to pulmonary hypertension. This study assessed outcomes of an individualized strategy for managing patients with mild-moderately elevated PVR deemed borderline eligible for repair.

**Methods:** A retrospective chart review of patients with systemic to pulmonary shunts and baseline PVRi ≥ 3 WU•m⁻² treated at a single centre from 1/1/2005-9/30/2019 was conducted. Data included demographics, WHO Functional Class, medications, and haemodynamic data at baseline and serial follow up.

**Results:** Thirty patients (18 females) met criteria for inclusion. Median age at diagnosis of PAH was 1.3 years (0.03–54) and at surgery was 4.1 years (0.73–56). Median follow up time was 5.8 years (0.2-14.6) after repair. Most patients received at least one targeted PAH therapy prior to repair and the majority (80%) underwent fenestrated shunt closure. There was a significant decrease in mPAP (p<0.01), PVRi (p=0.0001), and PVR/SVR (p<0.01) between baseline and pre-operative catheterization and a decrease in PVRi (p < 0.005), mPAP (p =0.0001), and Qp:Qs (p<0.03) from baseline to most recent catheterization. WHO functional class improved from baseline FC II-III to FC I post repair in most patients (p < 0.003).

**Conclusions:** In carefully selected patients with systemic to pulmonary shunts and elevated PVR considered borderline for operability, the use of preoperative targeted therapy in conjunction with fenestrated or partial closure of intracardiac shunts is associated with improvement in functional class and clinical outcomes.
Introduction

Group 1 pulmonary arterial hypertension (PAH) is a progressive disease with a generally poor prognosis, culminating in right ventricular (RV) failure if left untreated. PAH associated with congenital heart disease (APAH-CHD) can be subclassified into four categories: patients with bidirectional shunts and Eisenmenger physiology, patients with large left-to-right shunts (typically operable), inappropriate PAH with small defects (coincidental congenital heart disease), and post-operative PAH (1). The prognosis for patients with APAH-CHD is variable depending on the subtype and underlying physiology, wherein patients with post-operative PAH and inappropriate PAH with small defects have outcomes comparable to idiopathic pulmonary arterial hypertension (IPAH) (2,3). The prognosis of patients who ultimately develop Eisenmenger physiology in comparison with other subgroups of APAH-CHD is not clear, with some studies demonstrating similar survival rates - possibly due to inclusion of complex shunts - and others demonstrating improved survival compared to IPAH (4,5). However, the approach to patients with shunts and moderately elevated pulmonary vascular resistance (PVR) remains an ongoing dilemma. In the era of novel drug therapy for PAH, the ability to “pre-treat” and optimize PVR is an area of great interest and controversy.

In patients with PAH and systemic to pulmonary shunts, timing of surgical repair is aimed at preventing irreversible damage to the pulmonary vascular bed and subsequent development of worsening of pulmonary arterial hypertension. Unfortunately, patients may not be repaired in an appropriate timeline due to late diagnosis of congenital heart disease (CHD), poor follow up, or lack of access to medical care. Identifying a window of operability before irreversible pulmonary vascular changes occur is crucial. Patients with CHD who present with pulmonary vascular disease need a timely and comprehensive evaluation to determine their candidacy for surgery or transcatheter intervention (6).
In these patients, a “treat and repair” strategy has been adopted in some institutions for the management of patients with PAH and CHD with mixed support (7-13). These patients may have other factors contributing to the development of pulmonary hypertension as well, including genetic syndromes, prematurity, and lung disease (7). In the current therapeutic era, patients with elevated PVR are sometimes treated with PAH targeted therapy in an attempt to improve haemodynamics prior to undergoing repair of their cardiac defect, and therapy is continued with close monitoring following intervention.

While haemodynamic data cannot be utilized in isolation to determine operability, there have been various consensus guidelines for adults and children suggesting indexed PVR (PVRi) cut-offs ranging from 3–8 WU•m$^2$ depending on the lesion, with significant variability in the recommendations for operability in the “grey zone” for patients with elevated pulmonary vascular resistance (1,6,7,14,15). In some consensus guidelines, acute vasoreactivity testing (AVT) is mentioned as a tool used by some practitioners in trying to determine operability, particularly for patients with borderline PVR. However, haemodynamic parameters for AVT in these patients have not been established and criteria do not exist for determining reversibility of PAH in this population using AVT (16).

To date, recommendations to determine operability are largely based on expert consensus opinion, as there are limited studies in adults and children that have looked at long term outcomes in patients with elevated PVR who have been medically treated and subsequently undergo partial or complete repair of a congenital systemic to pulmonary shunt (8-11,17-20). Given the limited evidence describing outcomes in this subset of patients, we aimed to examine the outcomes after surgical and transcatheter shunt closure in patients with pulmonary vascular disease and congenital heart disease who were treated at a large single centre. We hypothesized that partial or total closure of shunts and use of targeted therapy in
carefully selected patients with mild-moderately elevated PVRi halts progression of PAH and improves short and medium-term clinical outcomes.

Methods

Study Subjects

The study cohort included patients with large intracardiac left to right shunts and elevated PVRi treated at Columbia University Irving Medical Center between 1 January 2005 and 30 September 2019 with follow up through 1 September 2022. Inclusion criteria included: PVRi ≥ 3 WU•m² at baseline or a PVR ≥ 2.3 WU on cardiac catheterization prior to surgical and/or transcatheter correction of CHD (1). Patients with univentricular hearts and complex congenital heart disease were excluded. Patients were also excluded if they had desaturations in room air suggesting established Eisenmenger physiology. As an institutional management protocol, patients who continued to have baseline desaturations at rest or exercise and evidence of right to left shunt despite targeted therapy, and/or a PVR/SVR ratio of > 0.4 on repeat haemodynamics following treatment were considered to have more advanced pulmonary vascular disease and Eisenmenger physiology and were not offered shunt closure. The study was approved by the Institutional Review Board of Columbia University Irving Medical Center (IRB-AAAK2059).

Study Design and Methods

A retrospective chart review was conducted of patients treated at Columbia University Irving Medical Center/New York Presbyterian Hospital from January 2005–September 2019 with follow up through September 2022. The objective of this study was to examine the outcomes after surgical and transcatheter shunt closure in patients with congenital heart disease related pulmonary vascular disease treated at a large single centre. Data included
baseline demographics, type of CHD, comorbid conditions, age at diagnosis of PAH, age at repair, postoperative follow up time, biomarkers, echocardiography data, haemodynamic data, PAH medications, and World Health Organization Functional Class (WHO-FC) at baseline, prior to surgery, and at most recent follow up. These data are summarized in Supplemental Table 1 including detailed listing of the medications used before and after surgery. Patients were typically started on a single targeted PAH therapy, with the decision to start additional medications based on clinical expertise after assessing their response to monotherapy. Intravenous prostaglandins were utilized if insufficient response to oral therapy was noted based on repeat catheterizations or echocardiographic assessment at follow up visits.

Haemodynamic measurements included right atrial pressure, pulmonary artery pressure (PAP), PCWP, systemic arterial pressure, and oxygen saturations in superior vena cava, pulmonary artery and aorta. Acute vasodilator testing was performed for the majority of patients using inhaled nitric oxide (iNO) 80 parts per million at the time of diagnosis or prior to repair. The decision to perform AVT was at the discretion of the treating physician and interventional cardiologist performing the catheterization. Balloon occlusion of the PDA was performed in four out of eight patients prior to transcatheter closure based on provider preference for accurate estimation of PVR.

**Analysis**

Descriptive statistics were performed, including mean and standard deviation (SD) or median and interquartile range (IQR) depending on the distribution of the data. Chi square tests for independence were used to compare categorical variables at the different time points and Fischer’s exact tests were used for variables with low incidence. P values for continuous variables were obtained utilizing Wilcoxon signed-rank analysis for paired data. The main
outcome measures were World Health Organization functional class and number of pulmonary hypertension medications at each follow up time point. Statistical analysis was performed utilizing Excel 2016 with Data Analysis Toolpak add-in and STATA version 16.1.

Results

A total of thirty patients (60% female) met inclusion criteria (Table 1). Nine patients were diagnosed with ASD, two with VSD, five with PDA, and fourteen with multiple shunts. The median age at diagnosis of PAH was 1.3 years (0.03-54 years, IQR 5.1). The median age at intervention was 4.1 years (0.73–56 years, IQR 7.9). Five patients (17%) had Trisomy 21. Nineteen patients (67%) were born preterm, of whom sixteen (84%) had a prior history of bronchopulmonary dysplasia. Of the premature patients, nine (47%) were born at less than 30 weeks gestation. Patients less than four years of age with ASDs were more likely to have comorbidities including prematurity, chronic lung disease, and/or Trisomy 21 (Supplemental Table 1). Seven patients (23%) underwent successful PDA closure via cardiac catheterization (Supplemental table 2). Seven patients (23%) underwent complete (non-fenestrated) repair – three ASD repairs, three PDA closures, and one VSD and PDA closure.

At baseline prior to any treatment, the majority of patients had WHO FC II or III symptoms, which improved prior to surgery to FC I or II. Most patients had WHO FC I symptoms at the time of most recent follow up. As shown in Figure 1, there was a significant change in distribution between the baseline period and time of most recent follow up (p =0.003). Median baseline oxygen saturation was 93% (range 77-100%) pre-treatment and improved to a median of 97% (range 84-100%) pre-operatively and 98% (range 95-100%) at most recent follow up. Ten patients (33%) were on supplemental oxygen at the time of PAH diagnosis, of whom two were on oxygen only overnight. This includes nine patients who were premature infants with lung disease and an adult patient with bronchiectasis. The
majority of patients were treated with PAH targeted medications pre-operatively (Figure 2). Twenty out of twenty-three (87%) patients who underwent surgery and six out of seven (86%) patients who underwent transcatheter PDA closure were on medications pre-operatively. The patients who were not on medications prior to repair had closure of the shunt shortly after catheterization, with one patient undergoing transcatheter PDA closure and three who had surgical closure, and one additional patient who was not on medications due to intolerance. Fifteen patients (50%) were no longer on PAH medications at the time of most recent follow up. There was a significant reduction in number of medications from pre-operative to time of most recent follow up (p=0.04). The details of medical treatment including the medications used for each patient pre and post shunt closure are listed in Supplemental Table 1.

There were seven patients (23%) receiving intravenous prostanoids as part of their therapy pre-operatively, compared to only one on parenteral prostanoids, and three on oral prostacyclin agonists at most recent follow up (p=0.05). The patients treated with prostaglandins pre-operatively had a significantly higher median PVRi before medications of 10 WU•m² (7.4-14) compared to 6.2 WU•m² (4.1-8.6) in those who were on oral or no therapy (p=0.03). PVRi improved to 3.2 WU•m² (2.9-6.2) in the patients on IV medications compared to 4.6 WU•m² (2.9-6.4) in those on all oral therapies, with no significant difference in PVRi between these patients at pre-op (p=0.97) or at most recent follow up (p=0.71). Those who were treated with IV prostaglandins pre-operatively were more likely to be on triple therapy at most recent follow up (p=0.03). The patients receiving IV prostaglandins were not more likely to be premature or have Trisomy 21 compared to those who did not.

Cardiac catheterization data when available at baseline, prior to surgery, following surgery, and at time of most recent catheterization are listed in Table 2. There was an improvement in the mean pulmonary arterial pressure (mPAP), PVR, Qp/Qs and PVR/SVR
ratio between the baseline and pre-operative period. There was also a significant improvement in the mPAP, PVRi, and Qp/Qs, from the baseline period and time of most recent catheterization. The PVRi trends over time for each patient are depicted in Figure 3. Twenty three out of the thirty patients (77%) included in the study had AVT performed at the time of diagnosis and fifteen of twenty patients (75%) who had follow up catheterizations pre-operatively had AVT performed at that time. Three patients (15%) met vasoreactivity criteria on cardiac catheterization prior to surgery. One patient met Barst criteria, one patient met Sitbon criteria, and one patient met both Barst and Sitbon criteria for vasoreactivity (Supplemental Table 3).

There were six patients who did not have fenestrations at the time of repair. These patients had a median PVRi of 3.8 WU•m$^2$ (3.6-3.9) at diagnosis. Half of these patients were on one targeted PAH medication pre-operatively and the remainder were not started on medications but underwent shunt closure soon after catheterization. None of these patients were on medications at most recent follow up. The patients who had fenestrations at the time of closure had a significantly higher median PVRi of 7.8 WU•m$^2$ (6.4-10.5) at diagnosis (p=0.00056) compared to those without fenestrations.

**Discussion**

This single institution retrospective study aimed to examine outcomes and management of patients with systemic to pulmonary shunts and elevated PVRi at time of presentation who had a combined medical-interventional/surgical approach to treatment. Patients were treated with PAH targeted therapy prior to and/or following correction of systemic to pulmonary shunt. In this cohort of patients, the mean baseline PVRi at first cardiac catheterization was 7.1 WU•m$^2$ with ten of the 30 patients (33%) with a baseline PVRi greater than 8 WU•m$^2$. With PAH targeted therapy, there was an improvement in
haemodynamics on cardiac catheterization prior to surgery: no patients who underwent repeat catheterization had a PVRi greater than 8 WU\,*m$^2$. This improvement was sustained in the majority of patients until the time of most recent follow up. Of note, prostanoids were used when initial PVRi was very high but dropped significantly on therapy to enable fenestrated repair, and then continued to show improvement.

Given that outcomes for patients who remain unrepaired and develop Eisenmenger physiology are generally more favourable than outcomes in those who develop post-operative PAH, the decision to undergo shunt closure should not be taken lightly. However, the superior survival of patients with Eisenmenger physiology has been less clear in paediatrics, with some studies showing improved survival in children with Eisenmenger syndrome and others showing no difference (3,21). Although there have been PVR cut off ranges suggested between 4-6 WU to proceed with repair, no general consensus has been established (1,6,7).

The 2015 American Heart Association (AHA) and American Thoracic Society (ATS) as well as the European Pediatric Pulmonary Vascular Disease Network guidelines suggest a PVRi of 6–8 WU\,*m$^2$ as an area of individualized consideration for operability (6,7). The AHA/ATS guidelines also include cutoffs of PVR to SVR ratio <1/3 in consideration for operability (7). The 6th World Symposium on Pulmonary Hypertension suggests a PVRi of 4 WU\,*m$^2$ (PVR 2.3 WU) as a cutoff for operability, with individualized consideration for patients with a PVRi between 4-8 WU\,*m$^2$ (PVR 2.3 - 4.6) (1). Patients with a PVRi greater than 8 WU\,*m$^2$ (PVR > 4.6) are considered inoperable (1). The 2022 ESC/ERS Guidelines now recommend consideration of shunt closure with a PVR of 3-5 WU, with a lower class of recommendation for closure (Ib) if PVR is greater than 5 WU. They emphasize individualized decision making for all borderline patients. The level of evidence for all these recommendations is C (based on expert opinion and/or small studies, retrospective studies, or registries) (14).
There have been multiple case series and studies in the adult literature examining the feasibility of delayed closure of ASDs with elevated PVRi with most patients doing well following surgery (8,9,12,22-24). The paediatric literature includes a broad spectrum of congenital heart disease in addition to ASDs which are often the focus in adult studies (10,11,17-20). Given this limited data, there is remains debate about management in terms of interventions due to the risk of closure in the setting of elevated PVR potentially leading to worsening right heart failure, and there are a lack of studies exploring this in paediatric patients.

Our study suggests that selected patients with PAH and CHD with an elevated PVRi at time of presentation could be treated with targeted PAH therapy and re-evaluated for surgical candidacy. Some patients may require multiple medications to sufficiently decrease PVRi to allow for consideration of shunt closure. Such patients clinically and haemodynamically may improve with fenestrated or partial shunt closure, possibly because of reduced shear stress from shunt flow in the pulmonary arteries; however, they may require continued targeted therapy on follow up. Our cohort had a high rate of shunt closure with creation of a fenestration to allow a small pop-off in the post operative period in case of pulmonary hypertensive crises. Given the haemodynamic profiles of our patients pre-operatively, we had a very low threshold to leave or create a fenestration. If patients had a PVRi less than 5 WU•m² at the time of diagnosis and no other concerning features, we did not typically did not leave a fenestration. There were 2 patients with PVRi <5 WU•m² at diagnosis who did have residual fenestrations- one with a residual tiny defect that was not closed and the other with multiple shunts and lung disease who was felt to be at high risk of ongoing PAH at the time. The residual defects were small as seen by the Qp:Qs on post-operative and most recent catheterizations and likely not substantial contributors to any ongoing pulmonary hypertension. In addition, if a larger atrial septal fenestration was created,
it is possible to later close these defects via transcatheter methods if needed. Our institutional practice considerations for leaving a fenestration are listed in table 3.

Of importance, a subgroup of patients in our study were born preterm and may have some degree of pulmonary vascular resistance attributed to a degree of chronic lung disease which is known to improve over time. There may be some component of the improvement of pulmonary hypertension in these patients that is due to the natural history of their co-morbidities in addition to the effects of pulmonary vasodilator therapy and repair of CHD, and the contribution of each of these is sometimes not clear (25). For example, when we looked at patients less than four years old with ASDs only, they all had associated comorbidities that could affect the development of PAH such as prematurity, chronic lung disease, or Trisomy 21. We observed that this was less likely in older patients or those with other lesions. However, the same overall approach to treatment was taken in these patients in terms of medications used and careful consideration of time of closure regardless of age or shunt type.

Overall, this cohort of patients did well following surgery and there was only one death noted at most recent follow up, which was due to a non-cardiac cause. Although PVRi remained elevated in our cohort, it was improved from baseline and patients were on less medication compared to pre-operatively. In addition, patients demonstrated improvement in WHO Functional Class when comparing their most recent follow up to baseline. This is in concordance with Liu et al.’s findings of improved effort tolerance following surgery in patients with a mean pulmonary arterial pressure of greater than 50 mmHg with a VSD (11). Liu et al also found improvements in 6-minute walking test (6MWT) distances. The majority of our patients were too young to perform a 6-minute walking test prior to surgery and during the perioperative period. However, it is important to note that for patients who can complete a 6-minute walking test, it is an objective and validated measure of cardiopulmonary function
in adult patients with pulmonary hypertension and may be utilized to monitor patients over time (6,26). WHO functional class is also not as accurate in younger patients in assessing functional status and there is ongoing study to create better tools for assessing children with PAH (27).

Only three of our patients who underwent cardiac catheterization had documented robust acute vasoreactivity by the Barst or Sitbon criteria prior to undergoing surgery. This is not surprising, as patients with PAH and CHD tend to be less vasoreactive in comparison to patients with IPAH (4,28). Thomaz et al. also found that non-responders still demonstrated improvement on haemodynamics following surgery and targeted therapy (20). Thus, acute vasoreactivity may not be a prognostic indicator of a patient’s candidacy for surgery, but rather potentially an indicator of long-term response to therapy. Further study is warranted to determine the role of AVT in this population.

Very careful patient selection incorporating clinical, echocardiographic and haemodynamic parameters is important in patients who have elevated PVR considered borderline operable by current PAH treatment guidelines. Patients with evidence of baseline right to left shunts and desaturation at rest or on exercise should continue targeted therapy and treated as Eisenmenger syndrome. Only those patients who improve clinically as well as on haemodynamic studies after at least 6-12 months of targeted therapy should be considered for complete or fenestrated shunt closure and as seen in the current study, improve their WHO-FC as well as demonstrate decrease in the number of medications required to treat their PAH. We propose several criteria that should be considered in determining the need for fenestration at the time of shunt closure (Table 3).

Our study had several limitations including its retrospective nature, small sample size, limited follow up period for some patients, and lack of CPET and 6MWT data due to patient ages. One patient had died at the time of last follow up due to a non-cardiac cause, and no
patients required heart or lung transplant listing. While this is a reassuring initial finding, the follow up period varied greatly between patients. In addition, more than half of the patients included in this study had a history of prematurity, some with chronic lung disease, which may have contributed to their pulmonary hypertension presentation. However, due to overall small sample size, we were unable to examine these patients separately in this study. Larger multicentric studies with longer periods of follow up are needed to evaluate the long-term risks closing systemic to pulmonary shunts may confer in patient with elevated PVRi.

In conclusion, in carefully selected patients with congenital heart disease and moderately elevated PVRi, the use of targeted PAH therapy in combination with partial or complete closure of shunts was associated with improvement in haemodynamics and WHO Functional Class. Prospective studies with a larger number of patients followed long term are needed to identify exactly which patients for whom a treat and repair strategy is best suited and determine appropriate haemodynamic values as optimal for operability. Longer-term follow up will help further the understanding of shunt closure in borderline PVR on later-term cardiopulmonary health. Given the relative paucity of patients seen at individual centres who develop PAH secondary to unrepaired CHD and the heterogeneity of the clinical features, multi-centre collaboration will be crucial in order to adequately study outcomes and to establish evidence-based treatment guidelines.

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Table 1. Patient Characteristics (n=30)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Male</th>
<th>12 (40%)</th>
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<tbody>
<tr>
<td></td>
<td>Female</td>
<td>18 (60%)</td>
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<tr>
<td>Ethnicity</td>
<td>African American</td>
<td>9 (30%)</td>
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<tr>
<td></td>
<td>Asian</td>
<td>3 (10%)</td>
</tr>
<tr>
<td></td>
<td>Hispanic</td>
<td>3 (10%)</td>
</tr>
<tr>
<td></td>
<td>Middle Eastern</td>
<td>1 (3%)</td>
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<tr>
<td></td>
<td>South Asian</td>
<td>7 (23%)</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>7 (23%)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>ASD</td>
<td>9 (30%)</td>
</tr>
<tr>
<td></td>
<td>VSD</td>
<td>2 (7%)</td>
</tr>
<tr>
<td></td>
<td>PDA</td>
<td>5 (19%)</td>
</tr>
<tr>
<td></td>
<td>Multiple shunts</td>
<td>14 (47%)</td>
</tr>
<tr>
<td>Comorbid Conditions</td>
<td>Prematurity</td>
<td>19 (63%)</td>
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<tr>
<td></td>
<td>Bronchopulmonary dysplasia</td>
<td>16 (53%)</td>
</tr>
<tr>
<td></td>
<td>Trisomy 21</td>
<td>6 (20%)</td>
</tr>
<tr>
<td>Repair type</td>
<td>Complete closure</td>
<td>6 (20%)</td>
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<tr>
<td></td>
<td>Partial (fenestrated) closure</td>
<td>24 (80%)</td>
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<tr>
<td>Method of Repair</td>
<td>Percutaneous closure</td>
<td>8 (30%)</td>
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<td></td>
<td>Surgical closure</td>
<td>22 (70%)</td>
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<td>Median age at diagnosis of PAH</td>
<td>1.3 years (IQR = 5.1, range 0.03 – 54 years)</td>
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<tr>
<td>Median age at surgery</td>
<td>4.1 years (IQR = 7.7, range 0.73 – 56 years)</td>
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<tr>
<td>Median follow up time</td>
<td>5.8 years (0.2 – 14.6 years)</td>
<td></td>
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<tr>
<td></td>
<td>Baseline (n = 30)</td>
<td>Pre-Op (n = 20)</td>
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<tr>
<td>RA pressure (mmHg)</td>
<td>6 (5-7) N=29</td>
<td>7 (4-9) N=19 P=0.84</td>
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<tr>
<td>mPAP (mmHg)</td>
<td>48 (38-59) N=19 P=0.11</td>
<td>35 (27-51)</td>
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<tr>
<td>mPAP (mmHg)</td>
<td>9 (7-10) N=29 P=0.91</td>
<td>9 (6-11) N=19</td>
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<td>PCWP (mmHg)</td>
<td>7.1 (4.8-10) P=0.001</td>
<td>3.8 (2.9-6.7) P=0.012</td>
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<td>PVRI (WU•m²)</td>
<td>0.45 (0.3-0.92) N=25</td>
<td>0.3 (0.16-0.44) N=16 P=0.0016</td>
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<td>Qp/Qs</td>
<td>1.4 (1-2) N=29 P=0.028</td>
<td>1.9 (1.5-2.2) P=0.019</td>
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<td>Cardiac Index (L/min/m²)</td>
<td>3.6 (2.8-4.6) N=28</td>
<td>3.3 (2.9-3.9) N=18 P=0.59</td>
</tr>
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Values listed are medians with interquartile ranges. *P values listed indicate comparison of paired data (when available) to baseline. The following are significant P values comparing haemodynamics to pre-op: * = p<0.05, †=p<0.01. RA = right atrial. mPAP = mean pulmonary arterial pressure. PCWP = pulmonary capillary wedge pressure. PVRI = indexed pulmonary vascular resistance. SVR = systemic vascular resistance. Qp = pulmonary blood flow. Qs = systemic blood flow.
Table 3. Institutional Practice Considerations for Fenestration at Time of Shunt Closure

<table>
<thead>
<tr>
<th>Consideration</th>
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<tr>
<td>Need for dual or triple PAH therapy pre-operatively</td>
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<tr>
<td>IV prostanoids pre-operatively</td>
</tr>
<tr>
<td>Right ventricular dysfunction</td>
</tr>
<tr>
<td>PVRi &gt; 5 WU•m² at time of diagnosis</td>
</tr>
</tbody>
</table>
References


8. Bradley EA, Chakinala M, Billadello JJ. Usefulness of medical therapy for


Bar chart demonstrating prevalence of each WHO FC at baseline (at time of diagnosis, prior to initiation of targeted PAH medications), pre-op, and most recent follow up. At baseline, 19 of 30 patients had WHO FC II or III symptoms (63%), which improved prior to surgery with 21 out of 30 patients (70%) having FC I or II symptoms. Most patients (18/30, or 60%) had WHO FC I symptoms at most recent follow up. There was a significant change in distribution between baseline period and time of most recent follow up (p =0.003).
Bar chart demonstrating percentage of the 30 patients receiving targeted PAH medications pre-op (prior to surgical or transcatheter closure of systemic to pulmonary shunts) and at most recent follow up. There was a significant change in number of medications from pre-operatively to most recent follow up (p=0.04). Half of patients (15 patients) were no longer on PAH targeted medications at most recent follow up.
Indexed Pulmonary Vascular Resistance Over Time. Spaghetti plot demonstrating the indexed pulmonary vascular resistance (PVRi) calculated for each patient who underwent cardiac catheterization at time of diagnosis, pre-operatively, post-operatively, and at the most recent catheterization. There was a significant decrease in median PVRi from 7.1 WU*m² at diagnosis to 3.8 WU*m² pre-operatively (p=0.0001) and 4.2 WU*m² at most recent follow up (p=0.004).