

Pulmonary-to-Systemic Arterial Shunt to Treat Children With Severe Pulmonary Hypertension



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ABSTRACT

BACKGROUND The placement of a pulmonary-to-systemic arterial shunt in children with severe pulmonary hypertension (PH) has been demonstrated, in relatively small studies, to be an effective palliation for their disease.

OBJECTIVES The aim of this study was to expand upon these earlier findings using an international registry for children with PH who have undergone a shunt procedure.

METHODS Retrospective data were obtained from 110 children with PH who underwent a shunt procedure collected from 13 institutions in Europe and the United States.

RESULTS Seventeen children died in-hospital postprocedure (15%). Of the 93 children successfully discharged home, 18 subsequently died or underwent lung transplantation (20%); the mean follow-up was 3.1 years (range: 25 days to 17 years). The overall 1- and 5-year freedom from death or transplant rates were 77% and 58%, respectively, and 92% and 68% for those discharged home, respectively. Children discharged home had significantly improved World Health Organization functional class ($P < 0.001$), 6-minute walk distances ($P = 0.047$) and lower brain natriuretic peptide levels ($P < 0.001$). Postprocedure, 59% of children were weaned completely from their prostacyclin infusion ($P < 0.001$). Preprocedural risk factors for dying in-hospital postprocedure included intensive care unit admission (hazard ratio [HR]: 3.2; $P = 0.02$), mechanical ventilation (HR: 8.3; $P < 0.001$) and extracorporeal membrane oxygenation (HR: 10.7; $P < 0.001$).

CONCLUSIONS A pulmonary-to-systemic arterial shunt can provide a child with severe PH significant clinical improvement that is both durable and potentially free from continuous prostacyclin infusion. Five-year survival is comparable to children undergoing lung transplantation for PH. Children with severely decompensated disease requiring aggressive intensive care are not good candidates for the shunt procedure. (J Am Coll Cardiol 2021;78:468-77)

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Over the last 20 years, with improved medical therapies, specialized training, and increased awareness, survival of children with pulmonary hypertension (PH) has steadily improved with current 5-year survival rates of 80% or better (1). Nonetheless, children still die from their disease despite the advances over the last 2 decades. Similar to adults with PH, children who are World Health Organization functional class (WHO-FC) IV despite PH-specific therapy, have a median survival of <2 years (2,3). For children with severe PH who fail medical therapy, bilateral lung transplantation has been the ultimate palliative procedure. However, survival in pediatric lung transplantation remains relatively limited with a current 5-year survival rate of 64% for children with idiopathic PH and 43% for nonidiopathic PH (4). Furthermore, lung transplantation involves highly technical and expensive care that is offered at relatively few centers around the world, thus limiting its accessibility.

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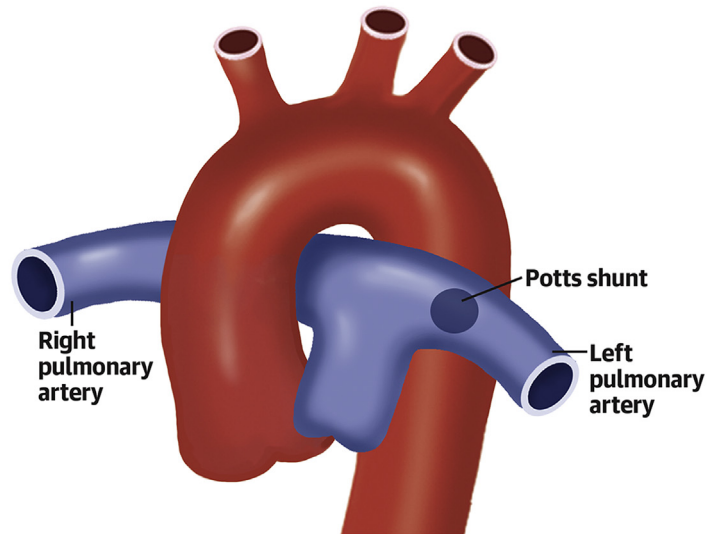
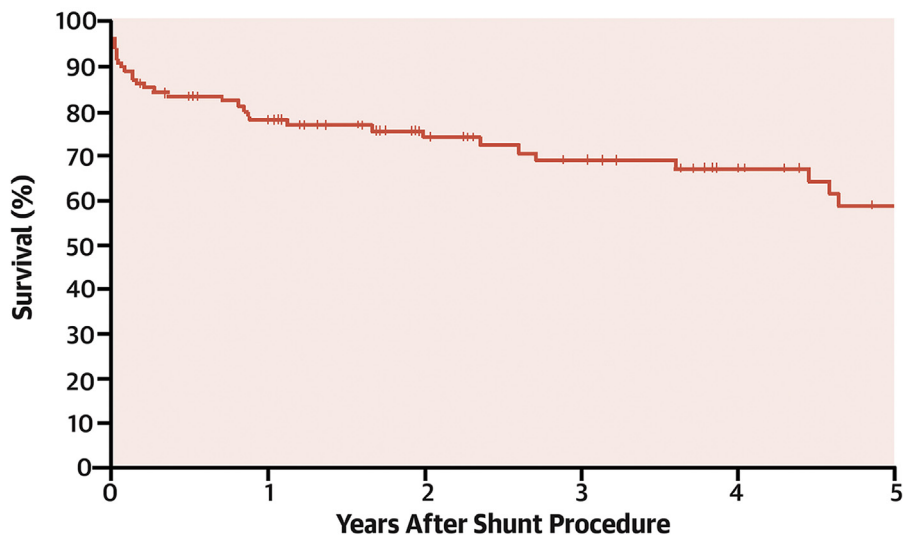
An alternative palliation to transplantation that has been used since the late 1990s to treat severe, progressive PH is an atrial septostomy. In most PH patients, end-stage disease is characterized by right ventricular failure with falling systolic pressures and rising end diastolic and right atrial pressures. Having an atrial communication, therefore, could “decompress” the failing right ventricle by allowing for right-to-left atrial shunting, thereby improving left ventricular preload and in turn augmenting cardiac output (albeit with overall reduced systemic oxygen saturations). A number of small series, almost exclusively in adults, have shown that an atrial septostomy can, in fact, improve symptoms in someone with severe PH (5). However, whether it can improve survival is unclear. Very few studies have looked at the role of atrial septostomy in treating children with PH (6). One retrospective study of 20 children with PH demonstrated clinical improvement after undergoing an atrial septostomy (7). Despite limited data, atrial septostomy is included as part of PH treatment guidelines for children on maximal medical therapy who exhibit symptoms of right ventricular failure, both acute (syncope) and chronic (8,9). It may also serve as a bridge to transplantation.

In 2004, a group from Paris, France, introduced a new interventional option for children with severe PH (10). Their innovative idea described treating severe PH (defined as having pulmonary artery systolic pressures higher than aortic systolic pressures) by

creating a surgical anastomosis between the left pulmonary artery and the descending aorta, reprising a surgical procedure first described by Dr. Willis Potts in 1946 to treat cyanotic congenital heart disease (**Central Illustration**) (11). In theory, by creating an unrestrictive shunt between the pulmonary and systemic arterial systems, the afterload upon the right ventricle would be reduced from suprasystemic to systemic levels. Equalizing right and left ventricular systolic pressures recapitulates the pathophysiology seen in patients with Eisenmenger’s syndrome. In doing so, the clinicians hoped to confer upon the children the superior life expectancy purported for patients with Eisenmenger’s syndrome (12). Furthermore, because the Potts shunt directly reduces the systolic burden upon the right ventricle, it has the potential to intervene early in a child’s disease course. This contrasts with an atrial septostomy which relies upon high diastolic pressures to be of benefit, a typical end-stage disease development. In addition, whereas an atrial septostomy results in global hypoxemia, the Potts shunt would still direct the highest oxygenated blood to the child’s brain. In 2014, the French group detailed their results in using the Potts shunt to treat 24 children with severe pulmonary arterial hypertension (13). Nineteen of the children had a traditional Potts shunt. The other 5 had a remnant patent ductus arteriosus (PDA) opened with a stent as part of a cardiac catheterization procedure. Early mortality in the study was 12.5%. However, for survivors with a 2.1-year median follow-up, results were encouraging with significant clinical improvement observed in the majority of children. Furthermore, this improvement was associated with a significant reduction in PH-specific medications, especially in the use of continuous prostacyclin infusions. Since these initial studies, several small series have been published describing the treatment of severe PH in children with a similar shunt procedure with similar promising results (14,15). As awareness among the pediatric PH community has increased regarding the possible efficacy of a pulmonary-to-systemic arterial shunt to treat children with severe PH, so too have questions such as safety of the procedure, who might best benefit, and what are the longer-term outcomes. To address these and other questions, an international registry was established among 13 institutions to collate data on a total of 110 children who had undergone a shunt procedure for their PH (**Supplemental Appendix**). This report details the registry’s findings.

ABBREVIATIONS AND ACRONYMS

- BNP** = brain natriuretic peptide
- CHD** = congenital heart disease
- ECMO** = extracorporeal membrane oxygenation
- PDA** = patent ductus arteriosus
- PGI₂** = prostacyclin
- PH** = pulmonary hypertension
- WHO-FC** = World Health Organization functional class

CENTRAL ILLUSTRATION Potts Shunt and Pulmonary Hypertension**Potts Shunt and Pulmonary Hypertension****Freedom from Death or Lung Transplant Post-Shunt Procedure**

At Risk:	110	72	48	39	27	19
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Creation of an anastomosis between the left pulmonary artery and the descending aorta (Potts shunt) in a patient with severe pulmonary hypertension and supra-systemic pulmonary artery pressures. Desaturated pulmonary blood can flow into the systemic circulation, decreasing right ventricular afterload.

TABLE 1 Characteristics Before Procedure (N = 110)

Age, y	7.7 (3 weeks to 20 y)
Female	56 (51)
Presence of CHD	27 (25)
WSPH group	
1	97 (88)
2	3 (3)
3	10 (9)
Time from diagnosis to procedure, y	3.6 (0.0-16.7)
WHO-FC	
I	1 (1)
II	10 (9)
III	61 (55)
IV	38 (35)
PH-specific medications	
PDE5i	99 (90)
ERA	85 (77)
Intravenous/subcutaneous PGI ₂	70 (64)
All 3	66 (56)
None	9 (8)
ICU admission	36 (33)
Intravenous inotropes	20 (18)
Mechanical ventilation	14 (13)
ECMO	11 (10)
Procedure	
Surgery	74 (67)
Direct	47
Conduit	27
PDA stent	26 (24)
Transcatheter	10 (9)

Values are mean (range), n (%), or n.

CHD = congenital heart disease; ECMO = extracorporeal membrane oxygenation; ERA = endothelin receptor antagonist; ICU = intensive care unit; PGI₂ = prostacyclin; PDA = patent ductus arteriosus; PDE5i = phosphodiesterase type 5 inhibitor; PH = pulmonary hypertension; WHO-FC = World Health Organization functional class; WSPH = World Symposium on Pulmonary Hypertension.

METHODS

The registry includes 13 institutions and was formed under the auspices of the Association for Pediatric Pulmonary Hypertension ([Supplemental Appendix](#)). All institutions had approval from their respective institutional review/ethics board with appropriate consent to supply data. Study data were collected retrospectively and managed using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at Washington University, St. Louis, Missouri. All patients undergoing a pulmonary-to-systemic arterial shunt procedure who were aged 20 years or less to treat PH were eligible for inclusion. The number of entries per center ranged from 1 to 36. Data reflect shunts placed from 2000 to 2020. Institutions varied in their testing for brain natriuretic peptide (BNP) levels, using either BNP levels, N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, or both. To allow for the aggregation of data,

both tests were standardized as a multiple above the upper limit of normal for that test, 100 pg/ml for BNP and 300 pg/ml for NT-proBNP. Thus, a normal value for either would be 1. Surgically created shunts between the left pulmonary artery and the descending aorta were performed via a left thoracotomy or sternotomy using a direct anastomosis, an interposition tube graft, or a valved conduit. Shunts created in the catheterization laboratory included: 1) dilation (if needed) and intravascular stenting of a PDA; and 2) transcatheter shunts involving the direct puncture between the left pulmonary artery and the descending aorta with subsequent placement of a covered stent. Data on the diameter of the shunts were not collected.

The univariate Cox proportional hazards model was used to assess risk factors for death or lung transplantation with significance considered at $P < 0.05$. The multivariate Cox proportional hazards model was performed using the stepwise variable election method to select for risk factors for early and late events. Because of the relatively small data set and event sizes, probability of entering and remaining in the multivariate model was set at 0.4 and 0.1 with type I error rate set at 0.1 and significance considered at <0.1 . The Firth method was used to adjust for the potential biases in estimating hazard ratios (HRs) due to small event sizes and data sets. HRs were presented with 90% (multivariate) and 95% (univariate) confidence intervals (CIs). For paired, nominal data, McNemar test was used. For normally distributed, independent, continuous data, the 2-sample Student's *t*-test was used. For non-normally distributed, continuous, paired data, the Wilcoxon signed rank test was used. A $P < 0.05$ was considered significant. "Early" or "in-hospital" event was defined as death in a child who never left the hospital postprocedure. "Late" events were defined as death or lung transplantation. Kaplan-Meier curves were generated to show event-free rates. Post-hospitalization data were obtained at the time of last recorded follow-up and included children who subsequently died or underwent lung transplantation.

RESULTS

PREPROCEDURAL ASSESSMENT. A total of 110 children had data entered into the registry. The mean age at the time of the shunt was 7.7 years (range: 3 weeks to 20 years), with equal gender distribution ([Table 1](#)). The majority of children, 97 (88%), had their PH classified as World Symposium on Pulmonary Hypertension (WSPH) group 1 (pulmonary arterial hypertension); 3 (3%) were classified as group 2 (PH

TABLE 2 Univariate Analysis of Risk Factors for Early Mortality			
	HR	95% CI	P Value
Preprocedure			
Age at time of procedure, y	1.0	0.9-1.1	0.70
Sex	1.2	0.5-3.1	0.70
History of CHD	1.4	0.5-3.8	0.60
Time from diagnosis to procedure	1.0	0.9-1.0	0.10
WSPH group			
1	0.4	0.2-1.2	0.10
2	0.04	0-138	0.50
3	5.4	1.9-15	0.002
Use of intravenous/subcutaneous PGI ₂	0.7	0.3-1.7	0.40
ICU admission	3.2	1.2-8.3	0.02
Intravenous inotropes	2.9	1.1-7.9	0.04
Mechanical ventilation	8.3	3.1-22	<0.001
ECMO	10.7	3.9-29	<0.001
Shunt type			
Surgical	0.7	0.3-1.8	0.40
PDA stent	0.7	0.2-2.3	0.50
Transcatheter	3.6	1.2-11	0.03

CI = confidence interval; HR = hazard ratio; PGI₂ = prostacyclin; other abbreviations as in Table 1.

due to left-sided heart disease); and 10 (9%) as group 3 (PH due to lung disease and/or hypoxemia). Twenty-seven children had what each center considered hemodynamically significant congenital heart disease (CHD) and all but 2 (large atrial septal defect and pulmonary vein stenosis) had reparative interventions before their shunt procedure. Of these 27 children, 24 were classified as having group 1 PH and 3 as group 2 PH. CHD lesions included transposition of the great arteries (n = 9), ventricular septal defect (n = 6), PDA (n = 4), atrial septal defect (n = 3), Shone complex (n = 2), and other (n = 3).

Median time from PH diagnosis to time of shunt procedure was 2.0 years, ranging from 0 days (3 children were diagnosed with PH and underwent a shunt procedure on the same day) to 16.7 years. At the time of the shunt, 99 of 110 (90%) children were receiving a phosphodiesterase 5 inhibitor, 85 (77%) were receiving an endothelin receptor antagonist, and 70 (64%) were receiving either intravenous or subcutaneous infusions of prostacyclin (PGI₂) (17 on epoprostenol, 53 on treprostinil). Sixty-one (56%) children were receiving all 3 medications, with 31 (28%) on dual-therapy and 9 (8%) on monotherapy. Nine (8%) children were receiving no PH-specific medications. Usage of these medications, especially of PGI₂ infusions, depended mainly on acuity of presentation and availability. Other considerations included tolerance of side effects and quality-of-life decisions. At the time of their shunt, 99 (90%) of the children were considered WHO-FC III-IV.

Although data were limited, suprasystemic right ventricular pressures were reported in 40 of 47 (87%) patients using catheterization data and in 44 of 57 (77%) patients using echocardiographic data.

At the time of their intervention, 74 (67%) of the children were outpatients whereas 36 (33%) were being treated in the intensive care unit (ICU). Twenty (18%) children were receiving intravenous inotropic medications, 14 (13%) were mechanically ventilated, and 11 (10%) were on extracorporeal mechanical oxygenation (ECMO). The most common (noted in 92% of cases) reason cited for proceeding with a shunt was worsening or insufficient improvement despite the use of PH-specific medications. Other reasons included unavailability of lung transplantation and acute decompensation requiring ICU care.

PROCEDURAL DATA. Seventy-four of 110 (67%) children had a surgical shunt placed (median age: 7.0 years), 26 (24%) had dilation and stenting of a PDA remnant (median age: 3.5 years), whereas the remaining 10 (9%) had a transcatheter created shunt (median age: 10.5 years) (Table 1). Of the 74 children who underwent a surgical shunt, 47 (64%) were direct anastomoses between left pulmonary artery and descending aorta (a Potts shunt), whereas the other 27 (36%) involved the use of a conduit: a simple tube graft (n = 23) or a valved composite graft (n = 4). Diameter and length of the conduits were not consistently specified.

ASSESSMENT OF IN-HOSPITAL OR EARLY MORTALITY. Of 110 children who underwent the shunt procedure, 17 (15%) died during their hospitalization. The median length of time from procedure to death was 10 days, with a range from the same day of the procedure to, in a unique instance, 316 days postprocedure. Reasons for death were both acute and progressive cardiac failure (n = 8), respiratory failure (n = 6), thromboembolic events (n = 2), and bleeding (n = 1). For the 93 children who survived to discharge, the median number of days on mechanical ventilation was 1 (range: 0-224 days) with a median ICU stay of 3 days (range: 0-110 days). The median total hospitalization stay was 9 days (range: 1-223 days). The median upper extremity/lower extremity saturation differential at time of discharge was 10% (range: 0%-25%).

The impact of preprocedural variables upon in-hospital mortality was assessed using univariate Cox proportional hazards analysis. Despite the wide range in ages at the time of the shunt procedure, age did not appear to impact in-hospital mortality (HR: 1.0; P = 0.70) (Table 2). Sex and time from a child's initial diagnosis of PH to their subsequent shunt procedure did not correlate with in-hospital mortality (HR: 1.2,

$P = 0.70$ and HR: 1.0, $P = 0.10$, respectively). The presence of pre-existing CHD also did not significantly increase risk of early mortality (5 of 27 patients [18%] died) (HR: 1.4; $P = 0.60$). The underlying etiology of a child's PH did appear to influence in-hospital mortality, with 5 of the 10 (50%) children diagnosed as group 3 PH dying (HR: 5.4; $P = 0.002$) compared to 12 of 97 (12%) patients diagnosed as group 1 (HR: 0.4; $P = 0.10$), and none of the 3 for group 2 (HR: 0.04; $P = 0.50$). Whether a child was receiving intravenous/subcutaneous PGI₂ before intervention did not correlate with in-hospital mortality (HR: 0.7; $P = 0.40$).

Preprocedural indicators of severe disease progression, including ICU admission (HR: 3.2; $P = 0.02$), use of intravenous inotropes (HR: 2.9; $P = 0.04$), use of mechanical ventilation (HR: 8.3; $P < 0.001$), and use of ECMO (HR: 10.7; $P < 0.001$) proved significant risk factors for in-hospital mortality. Of the 11 children who were placed on ECMO before their procedure, 7 died in-hospital (64% mortality). Furthermore, data indicated that using the transcatheter approach to create a shunt was also associated with an increased early mortality with 4 of 10 (40%) patients dying postprocedure (HR: 3.6; $P = 0.03$). This compares to 3 of 26 (12%) patients with in-hospital mortality for the PDA stented shunts (HR: 0.7; $P = 0.50$) and 10 of 74 (14%) patients with the surgically placed shunts (HR 0.7; $P = 0.40$). Two of the 4 children who died after transcatheter shunt placement were on ECMO at the time of their procedure. Furthermore, all 3 deaths after PDA stenting were in critically ill infants (<3 months of age) with group 3 PH. Finally, given that shunt placement ranged over a 20-year period, the date of surgery was assessed for in-hospital mortality and no correlation was noted ($P = 0.20$).

Multivariate analysis was performed using variables listed in Table 2. Because of small sample sizes, we considered $P < 0.10$ as significant (see Methods section). Results showed that percutaneous shunt placement (HR: 3.2; 90% CI: 1.1-9.5; $P = 0.07$), group 3 PH (HR: 3.3; 90% CI: 1.1-9.8; $P = 0.07$), and use of ECMO (HR: 5.1; 90% CI: 1.9-13.2; $P = 0.006$) continued to be risk-factors for early mortality.

POST-HOSPITALIZATION FOLLOW-UP. Ninety-three of 110 children were discharged home. Average follow-up was 3.1 years with a median of 2.2 years (range: 25 days to 17 years). Of the 93 children discharged from the hospital, 18 (19%) had a late event: 12 died and 6 underwent lung transplantation (median duration to event: 1.8 years; range: 76 days to 12.5 years). Seven (39%) of these late events occurred within 1 year of the procedure. The rate of overall freedom from death or transplant for the entire

TABLE 3 Clinical Parameters Preprocedure Versus Postprocedure in Children Discharged Home (N = 93)

	Preprocedure	Postprocedure, at Time of Last Follow-Up	P Value
WHO-FC (n = 93), %			
I	1	26	<0.001
II	11	52	
III	59	15	
IV	29	7	
Mean BNP/NT-proBNP levels (multiple above the ULN) (n = 57), pg/ml	11.1	4.1	<0.001
Mean 6-minute walk distance (n = 30), m	363	406	0.047
Intravenous/subcutaneous PGI ₂ , n	61	25	<0.001

BNT = brain natriuretic peptide; NT-proBNP = N-terminal brain natriuretic peptide; ULN = upper limit of normal; other abbreviations as in Tables 1 and 2.

cohort of 110 children was 77% at 1 year and 58% at 5 years (Central Illustration). Excluding the 17 in-hospital deaths, the 1- and 5-year rates of freedom from a late event were 92% and 68%, respectively. Reasons for late events were progressive disease with right ventricular failure (n = 8), infection (n = 3), hemoptysis (n = 3), PDA stent occlusion (n = 1), accidental tracheostomy tube dislodgement (n = 1), and refusal to take PH medications (n = 2).

Three measures of disease severity, WHO-FC, 6-minute walk distances, and BNP/NT-proBNP levels, were compared before and after shunt placement (Table 3). Postprocedure values were obtained at the time of last follow-up and included children who experienced a late event. Preprocedure, 90% of the children were classified as WHO-FC III-IV, postprocedure this percentage decreased to 22% ($P < 0.001$). For children where pre- and postprocedure 6-minute walk distances were recorded (n = 30), distances improved from a mean of 363 to 406 (median: 344-404) meters ($P = 0.047$). Likewise, biochemical assessment of cardiac strain using BNP and/or NT-proBNP levels also showed a significant improvement postprocedure. Preprocedure, 50 children had a mean BNP/NT-proBNP level that was on average 11.1 times above the upper limit of normal (median: 3.9 times above the upper limit of normal). Postprocedure, the average level decreased to 4.1 times above normal (median: 1.0 times above normal) ($P < 0.001$). These postprocedural improvements in clinical markers for disease were accompanied by a reduction in the overall use of intravenous/subcutaneous PGI₂. Of the 61 children receiving PGI₂ infusion preprocedure who were discharged home, 36 (59%) were weaned completely off the drug upon subsequent follow-up ($P < 0.001$).

TABLE 4 Univariate Analysis of Risk Factors for Late Event (Death or Lung Transplantation)

	HR	95% CI	P Value
Preprocedure			
Age at time of procedure	1.1	0.9-1.2	0.09
Sex	1.4	0.6-3.7	0.50
History of CHD	1.1	0.4-3.2	0.80
WSPH group			
1	0.6	0.2-1.6	0.30
2	0.8	0.1-3.7	0.70
3	4.2	1.2-14	0.03
ICU admission	4.7	1.7-12	0.002
Intravenous inotropes	6.1	2.3-15	<0.001
Mechanical ventilation	5.9	1.9-18	0.002
ECMO	6.5	1.8-23	0.004
Shunt type			
Surgical	0.8	0.3-2.2	0.70
PDA stent	1.2	0.4-3.5	0.70
Transcatheter	0.9	0.1-6.8	0.90

Abbreviations as in [Tables 1 and 2](#).

Preprocedural variables of age, sex, and history of CHD did not prove significant for late death or transplant (HR: 1.1; $P = 0.09$ and HR: 1.4; $P = 0.50$ and HR: 1.1; $P = 0.80$, respectively) ([Table 4](#)). As it did with early mortality, group 3 PH proved a risk factor for a late event (HR: 4.2; $P = 0.03$). Three of 5 (60%) children with group 3 PH experienced a late event compared to 14 of 85 (16%) with group 1 PH and 1 of 3 (33%) with group 2 PH. The type of shunt and, in particular, transcatheter shunts, no longer proved a significant risk factor for a late event (HR: 0.9; $P = 0.90$). Interestingly, preprocedural factors that impacted early survival, specifically ICU admission, use of intravenous inotropes, use of mechanical ventilation, and use of ECMO, also carried a strong negative association with late survival or transplant (HR: 4.7, $P = 0.002$; HR: 6.1, $P < 0.001$; HR: 5.9, $P = 0.002$; and HR 6.5, $P = 0.004$, respectively). Multivariate analysis of [Table 4](#) variables showed that preprocedural use of intravenous inotropes continued to be a risk factor for a late event (HR: 6.1; 90% CI: 2.7-13.6; $P < 0.001$). These data suggest that children who are severely compromised preprocedure continue to carry a significant risk for a poorer late outcome.

DISCUSSION

This paper represents the most comprehensive assessment to date regarding the use of a pulmonic-to-systemic arterial shunt to treat children with severe PH. The data, compiled from 13 pediatric centers in both the United States and Europe, shows that these interarterial shunts can provide durable, clinical

improvement. The majority of children who were discharged home from the procedure had a significant improvement in their WHO-FC scores, 6-minute walk tests, and BNP/NT-proBNP levels. Of equal significance was that these improvements came with a number of the children weaning off their intravenous PGI₂ infusion. With a mean follow-up of 3.1 years and a range up to 17 years, the shunt procedure provided an overall 5-year freedom from death or lung transplantation rate of 58%. The 5-year freedom from death or transplant rate improved to 68% in those children who were successfully discharged home after their shunt procedure. These outcomes are comparable to the 5-year survival one sees with pediatric lung transplantation: 64% for children with idiopathic PH and 43% for children with nonidiopathic PH (4). The registry outcomes are all the more notable knowing that children who are WHO-FC group IV despite PH-specific therapy, typical of many children in this study, have a median survival of <2 years (2). Thus, data from this registry suggest that in a child with severe PH, the pulmonary-to-systemic arterial shunt is a viable treatment option.

A significant finding of this study is that children who required aggressive ICU care, including intravenous inotropes, mechanical ventilation, and/or ECMO support before their procedure had a significantly higher risk of dying postprocedure. The starkest evidence was observed in children requiring ECMO before their intervention, where 7 of the 11 children died postprocedure. Not only did these markers for severely decompensated disease align with in-hospital mortality, they were also associated with late death or transplantation. Because the traditional Potts shunt is an open communication, it still requires the right ventricle to generate at least systemic systolic pressures to prevent substantial blood flow back into the lungs. Perhaps, therefore, it is not surprising that a child in severe cardiorespiratory failure preprocedure continues to fail postprocedure, suggesting that their heart failure has progressed beyond the ability of the shunt to provide benefit. In clinically stable children, one can use a variety of tests to assess right ventricular function and thus their suitability for a shunt. However, such assessments in critically ill children are less straightforward and may explain in part why these children, particularly ones on preprocedural ECMO, have such high mortality rates postprocedure. Treatment of children who require such aggressive ICU support remains problematic. The instability that makes these children poor shunt candidates also increases their risk for transplantation as well (16). Perhaps further development of mechanical support techniques will

be able to provide this fragile population with better outcomes (17). Overall, assessment of right ventricular function before shunt consideration is critical for a good outcome regardless of a child's clinical status. Current preprocedural registry data from echocardiography, cardiac catheterization, and cardiac magnetic resonance imaging (MRI) were too incomplete to provide specific guidance. Hopefully, however, with time these gaps can be filled.

Children in this study with either group 1 (pulmonary arterial hypertension) or group 2 (left-sided heart disease) PH benefitted from having a shunt. Furthermore, a history of significant CHD did not appear to impact outcomes. However, children whose PH was caused by lung disease and/or hypoxemia (group 3 PH) were at high risk for a poor outcome. Of the 10 children identified as group 3, 8 either died or underwent transplantation. Significantly, 7 of these 8 children were infants (ages ranged from 1 to 7 months) who required intensive care at the time of their intervention. The 2 event-free survivors were the oldest of the group at the time of their procedure at 10 and 17 years of age. Worse outcomes in group 3 children may reflect the fact that their disease often includes a significant component of hypoxia that is independent of pulmonary pressures. Although conclusions are tempered by the relatively few numbers, for severely affected children (and for critically ill infants in particular) with group 3 PH, lung transplantation may be the better intervention.

Dilating and stenting an existing PDA or its remnant would seem the safest way to create a pulmonary-to-systemic arterial shunt, eliminating surgical morbidity and minimizing postprocedural care. Therefore, during preprocedural assessment, looking for a possible PDA remnant would not be an unreasonable consideration, especially in younger children. While offering similar benefits as PDA stenting but potentially to a wider patient population, the transcatheter approach to creating a shunt has obvious appeal. However, the relatively high mortality detailed here and elsewhere argue for improved refinement before this technique gains widespread acceptance (18,19). The most common technique for shunt creation in this study was a traditional Potts shunt with direct anastomosis of the left pulmonary artery and descending aorta via a left thoracotomy. However, in a number of children, a tube graft was used to complete the connection. Although reasons were not always delineated, in some cases the need arose due to the inability to mobilize the 2 vessels in direct apposition, especially in older children. Four children from this study had placement of a valved conduit via a sternotomy. This relatively newer

approach has the obvious advantage of preventing significant systemic-to-pulmonic flow both in systole and diastole. Its use could also widen the number of children who might benefit from a shunt. For instance, a child who at rest has systemic to even subsystemic right-sided pressures but with exertion develops suprasystemic pressures with symptoms might benefit from such a unidirectional shunt. Another advantage includes easier control of the shunt at the time of possible lung transplantation. Nonetheless, potential loss of valve competency and/or stenosis and its efficacy in small children are serious concerns that deserve further investigation (20).

As discussed above, this study has shown that children on ECMO, children with group 3 PH, and children who had a transcatheter shunt procedure were all at increased risk for early mortality. Indeed, 12 of the 17 early mortalities (70%) included at least 1 of these 3 features. If children with these risk factors were excluded from the data, the overall early mortality would decrease from 15% to 6%. Furthermore, this study argues that excluding critically ill children from shunt consideration would not only improve early mortality but long-term outcomes as well.

Registry data argue that better outcomes, both early and late, are achieved in children who undergo shunt placement when they are in a compensated, relatively stable state. Questions then arise at what point in a child's disease course should one consider a shunt? In a child with suprasystemic right heart pressures, does the practitioner trial all available PH-specific medications first before offering an intervention? Although the registry data does not specifically address these questions, current guidelines for treating pediatric PH suggest considering a shunt only after a child fails intravenous/subcutaneous PGI₂ therapy (8,9). Yet almost 40% of the children in the registry did not receive prostacyclin infusions before their procedure with no obvious impact upon early outcomes. Should a shunt be considered in lieu of intravenous/subcutaneous PGI₂ knowing how onerous that therapy is for the child and family and how often children wean from it postprocedure? Certainly, the possibility that a shunt could preclude the need for infusion therapy would be of prime interest to patients and their families. Equally compelling is the observation that many children in this study weaned completely from their PGI₂ infusion post-shunt. Undoubtedly, freedom from infusion therapy would be a major quality of life improvement for any child. However, some caution in this regard is needed. Shunts are obviously not curative and do not guarantee that a child's disease will not progress even after initial benefit. Perhaps

longer-term outcomes would be even better if infusion therapy was maintained? In addition, the registry does not address the role that relatively newer inhaled or oral prostacyclin therapies may play in post-shunt care. More long-term data will be needed to address these questions.

The issue of lung transplantation after a shunt procedure was not specifically addressed with this study. Although the registry data show that treating a child with severe PH with a pulmonic-to-systemic arterial shunt can prove beneficial, it still remains a palliative procedure. Even with initial benefit, a child's underlying disease can eventually progress beyond the ability of the shunt to help. In these situations, lung transplantation could be the only remaining interventional option. Six children in the registry had a successful shunt procedure but then went on to undergo lung transplantation. Limited subsequent data were collected in these children, but 5 of 6 patients survived transplantation. Although more data are needed, risk of transplantation in these children is likely increased in part due to the development of pleural adhesions and aortopulmonary collaterals, especially to the shunted lung. Control of shunt flow at the time of transplantation also must be considered. Given the challenging nature of pediatric lung transplantation itself, some transplantation centers, both pediatric and adult, may consider a shunt a contraindication to future lung transplantation. Until more information is gathered, before proceeding with a shunt procedure, open discussions with families about future limitations and risks regarding transplantation would be important in helping them make informed decisions.

STUDY LIMITATIONS. Registry data were collected in a retrospective manner. Like all registries, data accuracy is dependent upon the multiple sites entering the information. Most assessments discussed are relatively objective, reducing informational bias. Overall, the relatively small number of children within the study and of observed events may limit the generalization of some of the findings. Data reflect shunt procedures performed over a 20-year period. Changes in techniques, therapies, and treatment strategies over that period could affect outcomes that

may not be elucidated in this study. Of note, however, year of intervention did not correlate with early, in-house mortality ($P = 0.20$).

CONCLUSIONS

This study represents the largest assessment of using a pulmonary-to-systemic arterial shunt to treat children with severe PH. Children who survive the procedure have improved clinical measures with less use of PGI₂ infusions. The 5-year freedom from death or lung transplant rate is comparable to 5-year mortality in children undergoing primary lung transplantation for PH. Children who required significant intensive care support before their shunt procedure had a significantly higher risk of death or transplantation postprocedure.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Creation of a pulmonary-to-systemic arterial shunt can provide sustained benefit in selected children with severe PH.

TRANSLATIONAL OUTLOOK: Longer-term follow-up is needed to identify factors associated with better outcomes following the shunt procedure and determine the implications for later lung transplantation.

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KEY WORDS pediatric pulmonary hypertension, Potts shunt

APPENDIX For a listing of the centers and researchers who are members of the International Registry Potts Shunt, please see the online version of this paper.