Reasons for Failure of Systemic-to-Pulmonary Artery Shunts in Neonates

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Abstract

Background Systemic-to-pulmonary artery shunt placement is an established palliative procedure for congenital heart disease. Although it is thought to be a simple operation, it is associated with significant morbidity and mortality.

Methods Data for all neonates who underwent surgery for a systemic-to-pulmonary artery shunt between 2000 and 2016 were reviewed. The study endpoints were shunt failure and shunt-related mortality. Shunt failure was defined as a shunt dysfunction because of thrombosis or stenosis requiring intervention or reoperation; shunt mortality was defined as death because of a shunt dysfunction.

Results A total of 305 shunts (central shunt, n = 135; Blalock–Taussig shunt, n = 170) were implanted in 280 patients. The median patients’ age at the time of surgery was 9 days (1–31 days). The median shunt size was 3.5 mm (3–4 mm). Twenty-four patients (8%) were diagnosed with a shunt failure, with a median time of 7 days (0–438 days). Freedom from shunt failure at 1 year was 91.6% ± 2%. A shunt-related mortality was ascertained for 12 patients (4%). Freedom from shunt-related mortality at 1 year was 96% ± 1%. Perioperative platelet transfusion (p = 0.01), central shunt (p = 0.02), 3-mm shunt size (p = 0.02), and postoperative extracorporeal membrane oxygenation (ECMO) (p < 0.01) were identified as risk factors for shunt failure. Platelet transfusion (p = 0.04) and postoperative ECMO (p < 0.01) were further identified as risk factors for shunt mortality.

Conclusion Based on these data, we recommend implanting a modified Blalock–Taussig shunt of at least 3.5 mm in neonates. Perioperative platelet transfusion and postoperative ECMO increase the risk of shunt failure.

Keywords
► congenital heart disease
► shunts
► cardiac

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Introduction

Systemic-to-pulmonary artery shunt surgery is a palliative procedure for congenital heart disease associated with diminished or absent pulmonary blood flow. Systemic-to-pulmonary artery shunts were first described by Blalock and Taussig in 1945 (subclavian-to-pulmonary artery shunt),1 Potts in 1946 (descending aorta-to-left pulmonary artery [PA] shunt),2 and Waterston and Cooley in 1962 and 1966 (ascending aorta-to-right PA shunt).3 In 1975, de Leval modified the technique, using a polytetrafluoroethylene (PTFE) interposition graft known as a modified Blalock–Taussig shunt (mBTS).4

Despite numerous improvements in diagnosis, intensive care medicine, and intraoperative management in recent decades, overall outcomes remain unsatisfactory with an mBTS. Morbidity is considered relatively high with an average of 10%×6–8 Complications including shunt stenosis or thrombosis are reported in 8% to 13%.9 Several single institution studies or case series investigated risk factors for morbidity and mortality after mBTS and identified age, weight,10–13 and single ventricle circulation9,14 as risk factors for death.

However, outcomes of shunt surgery are often reported in generalizing terms, regardless of patients’ ages. Therefore, we sought to study the neonatal population specifically to identify potential risk factors for adverse outcomes after lifesaving shunt surgery.

Materials and Methods

All neonates who underwent implantation of a systemic-to-pulmonary artery shunt between 2000 and 2016 at the German Heart Centre Munich were included in the study. Patients were identified from our clinical database, and medical records and operative notes were reviewed. All patients were examined regularly after surgery in our outpatient clinic or by the referring pediatric cardiologist.

We defined two study endpoints:

- Shunt failure defined as shunt thrombosis or stenosis, and
- Shunt-related mortality defined as a subsequent death after shunt failure.

After surgery, the patients were examined daily using echocardiography during their intensive care unit (ICU) stay and once before discharge. After hospital discharge, all patients were seen every 4 to 6 weeks in our outpatient clinic and were examined using echocardiography. Angiography was routinely planned for all patients 3 to 6 months after shunt implantation prior to further surgery. If there were any signs of reduced shunt flow on echocardiography, an angiography was performed at an earlier time. In patients with a remarkably reduced shunt flow or acute hypoxemia, an operative revision was performed immediately, without prior angiography.

Surgical Technique

For nearly all patients, surgery was performed using a median sternotomy on cardiopulmonary bypass. The brachiocephalic trunk and right PA were dissected free. A bolus of 100 IU/kg of heparin was administered if surgery was performed without bypass. The brachiocephalic trunk was clamped with a side-biting clamp, and a longitudinal arteriotomy was performed. An obliquely fashioned thin-walled Gore-Tex stretch vascular graft (W. L. Gore & Associates, Inc., Arizona, United States) was sutured end-to-side to the brachiocephalic trunk. The clamp was released, and good shunt flow was ascertained. After trimming the shunt to the right length, it was Anastomosed to the right PA. If the aortic arch descended to the right, the shunt was anastomosed to the left PA. A central shunt was placed for anatomical reasons or at the discretion of the attending surgeon. The anatomy was considered unsuitable for mBTS if the PAs were hypoplastic. Central shunt placement was performed by interposing a thin-walled Gore-Tex stretch vascular graft between the ascending aorta and PA in a similar fashion using the pulmonary trunk or bifurcation in cases of hypoplastic peripheral PAs.

RV-PA (Sano) shunts used in patients with single ventricle circulation were excluded from the study.

Postoperative anticoagulation was performed according to the internal clinic standards as follows:

- Shunts < 4 mm: intravenous heparin (5,000 IE/m²/d) beginning 6 hours after surgery until removal of the central venous catheter. Oral aspirin (3–5 mg/kg) was administered thereafter.
- Shunts > 4 mm: intravenous heparin (5,000 IE/m²/d) beginning 6 hours after surgery until removal of the central venous catheter; no postoperative aspirin was administered.

Statistical Analysis

Statistical analysis was performed using SPSS 22.0 software (SPSS Inc., Chicago, Illinois, United States). Frequencies are presented as absolute numbers and percentages. Continuous data are presented as medians with ranges or means with standard deviation. A comparison of categorical variables was calculated using a two-tailed χ² test or Fisher exact test, as appropriate. A comparison of continuous variables was calculated using a t-test for independent samples. The Kaplan–Meier method was used to estimate the probability of freedom from events. The Cox regression analysis was used to identify the risk factors for events. For all tests, a p-value of <0.05 was considered significant.

Results

Patients

A total of 305 shunts were implanted in 280 patients. The median patient age at the time of surgery was 9 days (1–31 days). Sixty-one percent (n = 172) of the patients had single ventricle circulation. Preoperative patients’ characteristics are summarized in Table 1.

The shunts were implanted with an mBTS in 170 cases (56%) and a central shunt in 135 cases (44%). All mBTS were positioned between the brachiocephalic trunk and right PA. There were no left mBTS implanted. The shunt sizes were 3, 3.5, and 4 mm, respectively. Heparin-coated shunts were used in almost one-half of the patients (48%, n = 148). The indexed shunt size (mm/kg) was 1.2 ± 0.2. The indexed...
to ensure adequate circulatory blood flow on ECMO.

At the time of the ECMO implantation, the shunt was partially clamped in six patients to ensure adequate circulatory blood flow on ECMO.

### Table 1 Preoperative characteristics of 280 neonates

| Total, n | 280 |
| Age (days) | 9 (1–31) |
| Weight (kg) | 3.8 [1.8–4.6] |
| Male, n (%) | 173 (62) |
| Diagnosis, n (%) | |
| HLHS | 144 (51) |
| TGA, VSD, LVOTO/ccTGA, PS | 42 (15) |
| PA, VSD ± MAPCA | 37 (13) |
| TOF | 36 (13) |
| PA IVS | 21 (8) |
| Type circulation, n (%) | |
| Single ventricle | 172 (61) |
| Biventricular | 108 (39) |

### Table 2 Characteristics of 305 implanted shunts

| Total, n (%) | 305 |
| mBTS with ECC | 161 (53) |
| mBTS without ECC | 9 (3) |
| Central shunt with ECC | 124 (41) |
| Central shunt without ECC | 11 (3) |
| ECC | 285 (94) |
| 3 mm | 42 (14) |
| 3.5 mm | 108 (35) |
| 4 mm | 155 (51) |
| Heparin coated | 148 (48) |
| Indexed shunt size, mm/kg | 1.2 ± 0.2 |

Abbreviations: ccTGA, congenitally corrected transposition of the great arteries; HLHS, hypoplastic left heart syndrome; LVOTO, left ventricular outflow tract obstruction; MAPCA, multiple aortopulmonary collateral arteries; PA, pulmonary atresia; PA IVS, pulmonary atresia with intact ventricular septum; PS, pulmonary stenosis; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

shunt size was >1 for 225 patients and >1.5 for 20 patients. All shunt characteristics are summarized in Table 2.

A competitive antegrade flow was present after shunt placement in 16 patients (16/280, 6%) who had pulmonary atresia, a ventricular septal defect, and major aortopulmonary collateral arteries (PA, ventricular septal defect [VSD], and multiple aortopulmonary collateral arteries [MAPCAs]).

Postoperative extra corporeal membrane oxygenation (ECMO) was urgently required for 17 patients (5.5%) in the ICU during the postoperative period and was implanted under cardiopulmonary resuscitation (CPR). Reasons for ECMO were an acute cardiac failure for 13 patients and acute hypoxemia for four patients. At the time of the ECMO implantation, the shunt was partially clamped in six patients to ensure adequate circulatory blood flow on ECMO.

### Table 2 Characteristics of 305 implanted shunts

One-third of the patients with thrombocytopenia (34%, n = 104) required a platelet transfusion. All patients on ECMO needed platelet substitution. Seven patients had to undergo a reoperation for postoperative bleeding. Five of them were on ECMO.

A total of 243 angiographies were performed after surgery; 231 were regularly scheduled prior to an additional operation, and 12 were scheduled earlier if on echocardiography was detected a reduced or not clear shunt flow. Another 12 patients underwent surgery on an emergency basis without prior angiography after a remarkably reduced shunt flow had been detected on echocardiography.

### Mortality

Thirty-day mortality was 11% (n = 35). A shunt-related mortality was confirmed for 12 patients (4%; shunt stenosis n = 4; shunt thrombosis n = 8). The other 23 patients (23/35) died because of myocardial failure (n = 19) or septicemia (n = 4). For all 23 patients, an autopsy confirmed a patent shunt. After discharge from the hospital, nine patients died, all of whom experienced acute cardiac failure. Two-thirds (n = 234, 78%) of the patients underwent corrective surgery or obtained further palliation. The course for all implanted shunts is depicted in Fig. 1.

### Shunt Failure and Shunt-Related Mortality

A total of 24 patients (8%) had a shunt failure at a median of 7 days (0–438 days). Angiography revealed a stent stenosis in six patients. They were treated with balloon angioplasty (n = 2), stent implantation (n = 1), or shunt exchange (n = 3). After intervention (balloon angioplasty and stent implantation), all patients required reoperation for shunt exchange after a mean time of 6 ± 2 days.

A shunt thrombosis was diagnosed in six patients using angiography. They all required a reoperation for shunt exchange. Additionally, upon autopsy, four patients had a shunt thrombosis. All four patients died after unsuccessful CPR.

Shunt-related mortality was 4% (n = 12) at a median of 9 days (0–433 days). Eight patients died after unsuccessful CPR because of sudden hypoxemia with subsequent brady-cardia and acute myocardial failure. Four patients died from shunt thrombosis. The course for the patients who had a shunt failure is depicted in Fig. 2. The freedom from shunt failure was 91.6% ± 2% at 1 year (Fig. 3). The freedom from shunt-related mortality was 96% ± 1% at 1 year (Fig. 4).

### Risk Factors for Shunt Failure and Shunt-Related Mortality

A perioperative platelet transfusion, central shunt placement, and shunt size of 3 mm, as well as the use of postoperative ECMO, were identified as risk factors for shunt failure. A platelet transfusion and postoperative ECMO were also risk factors for shunt-related mortality (Table 3).

### Discussion

Systemic-to-pulmonary artery shunt surgery is an effective palliative procedure for cyanotic congenital heart disease.
Although it is thought to be technically easy to perform, shunt surgery is still associated with a poor postoperative outcome. Our study reports on 15 years’ experience involving a large single center cohort including 305 shunt procedures in neonates. We found that early postoperative mortality was not always related to shunt pathology. Only 4% ($n = 12$) died because of shunt-related reasons. A total of 24 patients (8%) developed a shunt failure that was affected by the type and size of the shunt. The implementation of postoperative ECMO and a platelet transfusion increased the risk of shunt failure and shunt-related mortality.

Several single center reports evaluated the outcomes of shunt surgery, but the majority was published in an earlier era. These studies reported mortality ranging from 3.7% to 14%. Among these, Gold et al reported the lowest mortality rate, but the patients in their series had a mean age of 3 months. Lamberti et al had a mortality rate of 2.3%, with 1 death of a 1.7-kg neonate who had pulmonary atresia. This series consisted of patients with a mean age of 6 months. Williams et al reported on the largest series of mBTS. They analyzed 2,000 patients over a period of six decades in a multicenter study with an overall mortality of 14%. However, patients who were older than a neonatal age were included in this report. More recent publications analyzed the outcomes after shunt surgery and reported on only neonates. Petrucci et al included 1,273 patients.

![Fig. 1](image1.png)  
**Fig. 1** Course of 305 shunts in 280 neonates.

![Fig. 2](image2.png)  
**Fig. 2** Course of 24 patients with shunt failure.

![Fig. 3](image3.png)  
**Fig. 3** Freedom from shunt failure.

![Fig. 4](image4.png)  
**Fig. 4** Freedom from shunt-related mortality.
using the multi-institutional STS Congenital Database. Remarkably, their data demonstrated that mBTS continues to be a high-risk procedure, with an overall mortality of 7.2%. In 2014, Bove et al reported on 150 neonates who had an overall hospital mortality of 8.7% after shunt surgery. In our study, the 30-day mortality after shunt surgery was 11% (n = 35), but shunt-related mortality was only 4%. There is a lack of publications analyzing the reasons for shunt-related mortality. The autopsy results in our study showed that acute heart failure or sepsis was the predominant cause of death in 23 of the 35 patients who died with a shunt in situ. In these patients, no pathology was found on the shunt. We identified two risk factors for shunt-related mortality in neonates that have not been previously reported: a platelet transfusion and the implementation of postoperative ECMO. A relationship between both factors is evident, as all patients on ECMO (n = 17, 5.5%) in our study underwent a postoperative platelet transfusion. Patients on ECMO have an increased risk of postoperative bleeding because of heparinization and platelet consumption and may require the replacement of platelets. However, not just patients on ECMO needed a platelet transfusion. One-third of our patients (34%, n = 104) underwent a postoperative platelet transfusion to stabilize their postoperative thrombocytopenia. Transfusion of other blood products such as fresh frozen plasma or packed red blood cells had no influence on shunt-related mortality. Another point concerning postoperative ECMO as a risk factor for mortality is the altered blood flow caused by ECMO. Therefore, in six patients, shunt clipping was performed to ensure adequate circulatory blood flow on ECMO to prevent a pulmonary steal effect. We think that shunt clipping could ensure adequate circulatory blood flow on ECMO, but the clipping could lead to shunt thrombosis, a condition more fatal for a neonate. Four out of 17 patients who required ECMO developed a shunt failure. Two of these patients did not survive this condition. These two patients required initially shunt clipping, which underwent with complication; both became shunt thrombosis. Therefore, the shunt was changed. Postoperatively, both patients developed multiple organ failure on ECMO and the ECMO could not be weaned successfully.

A multivariate risk factor analysis for mortality in an older report from 1995 identified that a left mBTS and male sex were associated with increased mortality. Other authors determined that pulmonary atresia with an intact ventricular septum, weight of <3 kg, weight of <2 kg, and univentricular circulation were significant risk factors for mortality after shunt surgery. In our study, low weight, sex, and single ventricle physiology had no influence on postoperative mortality. Considering that the prevalent cause of death in our cohort was acute heart failure (n = 19), we assumed that the underlying diagnosis had a major influence on the outcome. However, we could not identify a correlation between the nature of a patient’s heart defect and mortality after shunt placement.

Bove et al reported that excessive pulmonary blood flow through shunts could contribute to mortality. Dirks et al found that there was a trend toward increased mortality in patients in whom a shunt had to be decreased in size to reduce excessive blood flow. In contrast, in the present study, we did not find that an oversized shunt increased the risk of mortality. Sixteen patients in our study had additional antegrade flow through MAPCAs, and 20 had an indexed shunt size of ≥1.5. However, neither the extra blood flow nor a larger indexed shunt size could be identified as a risk factor.

Another concern after shunt surgery is shunt failure because of thrombosis or a stenosis. We found that a periprostatic platelet transfusion increased the risk of shunt failure. ECMO implantation was proven to have an adverse outcome after shunt surgery in our study. ECMO implantation was identified as the unique independent risk factor for shunt failure in the multivariate analysis. ECMO implantation increases the risk of bleeding, as well as the risk of coagulopathy and thrombosis regardless of the type of surgery. It is well known that a younger age and smaller-sized shunt are significantly related to shunt thrombosis. Other reports have also linked patients’ weight to shunt thrombosis. It is conceivable that a low weight is directly related to the size of the vessels, leading to the more frequent use of smaller shunts in neonates. Weight had no influence on shunt failure in our cohort. However, a shunt size of 3 mm increased the risk of shunt failure. In addition, a central shunt was identified as a risk factor for shunt failure. Central shunts were implanted in patients with hypoplastic pulmonary arteries in whom the postshunt runoff may be compromised.

### Table 3 Risk factors for shunt failure and shunt-related mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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<tbody>
<tr>
<td></td>
<td>HR 95% CI p</td>
<td>HR 95% CI p</td>
</tr>
<tr>
<td><strong>Shunt failure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative ECMO</td>
<td>5.9 2.4–14.5 &lt;0.01</td>
<td>5.8 2–17.1 0.001</td>
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<tr>
<td>Central shunt</td>
<td>2.6 1.1–6.1 0.02</td>
<td></td>
</tr>
<tr>
<td>Shunt size of 3 mm</td>
<td>2.7 1.1–6.5 0.02</td>
<td></td>
</tr>
<tr>
<td>Transfusion of platelets</td>
<td>2.7 1.2–6 0.01</td>
<td></td>
</tr>
<tr>
<td><strong>Shunt-related mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative ECMO</td>
<td>20 5.8–71 &lt;0.01</td>
<td>4.5 1.2–15.9 0.02</td>
</tr>
<tr>
<td>Transfusion of platelets</td>
<td>3.2 1–10.4 0.04</td>
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</table>
We could not find an association between anticoagulation regimens and shunt failure. All our patients were on continuous intravenous heparin after shunt surgery. In addition, patients with a shunt size of less than 4 mm were administered aspirin postoperatively. Further, a smaller shunt size remained a risk factor for shunt failure. The early postoperative period with fresh surgical anastomoses, coupled with periods of low systemic pressures, pulmonary hypertension, and consecutive blood stasis, may initiate thrombus formation. Li et al demonstrated a reduced incidence of shunt thrombosis (p = 0.008) and death (p = 0.057) in patients administered aspirin, as compared with those not administered aspirin. Another prospective study showed significantly higher shunt patency rates with hemodilution while maintaining a hematocrit of 45%.

Heparin-coated PTFE shunts have been available since 2011, and 48% of the shunts in our cohort were heparin coated. Their potential advantage of reducing acute shunt occlusion by lowering thrombus formation and accelerating endothelialization could not be proven in our study. In a previous histopathological workup of PTFE shunts, partial endothelialization and discrete pseudointima proliferation were shown to be equal in both heparin-coated and non-heparin-coated shunts.

Conclusion

In neonates, implantation of an mBTS of at least 3.5 mm may be recommended, as opposed to a central shunt. Platelet transfusion should be avoided after shunt surgery. Postoperative ECMO has a poor prognosis regarding morbidity and mortality after shunt surgery.

Note

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