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ORIGINAL ARTICLE

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Outcomes of Blalock-Taussig shunts in current era: A single center experience

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Abstract

Objectives: Mortality associated with the modified Blalock–Taussig shunt (MBTS) remains high despite advanced perioperative management. This study was formulated to provide data on (1) current indications, (2) outcomes, and (3) factors affecting mortality and morbidity.

Design: A retrospective single center chart review identified 95 children (excluding hypoplastic left heart lesions) requiring a MBTS. Mortality and major morbidity were analyzed using the Kaplan Meier method and risk factor analysis using Cox's proportional hazard regression.

Results: Median age was 8 (0–126) days, weight 3.1(1.7–5.4) kg. Seventy-three percent were neonates, 58% duct dependent and 73% had single ventricle physiology. Ninety-seven percent had a sternotomy approach for shunt placement with 70% receiving a 3.5 mm graft. Mean graft index (shunt cross sectional area [mm^2]/BSA [m^2]) was 44.39 ± 8.04 and shunt size (mm) to body weight (kg) ratio 1.1 ± 0.2. Hospital mortality was 12%, with an interval mortality of 6%. Shunt thrombosis/stenosis occurred in 23% and pulmonary over circulation in 30%, while shunt reoperation was required in 12% and catheter intervention in 8% of the cohort. At 1-year, survival was 82.0% (95% CI [72.7%, 88.4%]), and survival free of major morbidity 61.4% (95% CI [50.7%, 70.5%]). Duct dependency predisposed to mortality ($P = .01$, HR 6.74 [1.54, 29.53]) and composite outcome (mortality and major morbidity) ($P = .04$, HR 2.15, CI [1.036, 4.466]) and higher graft index to mortality ($P = .005$, HR 1.07 [1.02, 1.12]).

Conclusions: The commonest indication for a MBTS in the current era was single ventricle palliation. Morbidity and mortality was considerable, partly explained by the higher at risk population. Alternative methods to maintain pulmonary blood flow in place of a MBTS requires further investigation.

KEYWORDS

Blalock–Taussig shunt, congenital heart surgery, outcomes

1 | INTRODUCTION

In 1945, the description and application of the aortopulmonary Blalock–Taussig shunt (BTS) marked the beginning of surgical palliation for cyanotic congenital heart disease.[1] In the current era, early primary repair is generally preferred to palliative strategies. When palliation is warranted, depending on the anatomical circumstances, alternative options such as patent arterial duct or right ventricular outflow tract dilation and/or stenting have become increasingly utilized. However the BTS, in particular its modified form (MBTS), remains the primary procedure to secure pulmonary blood flow. Despite over 7 decades of experience, mortality and morbidity associated with a MBTS is high in spite of progress in perioperative management.[2] Indeed, recent studies from national databases from both The Netherlands and United Kingdom have noted a trend of increasing mortality for systemic to pulmonary shunts compared to earlier eras[3,4] making the BTS the only pediatric cardiac surgery which is associated with increase in mortality in the modern era, often attributed to the changing patient clinical profile. With this background we formulated this retrospective single center study to provide data on (1) the current use of the MBTS in the background of early surgical palliation and recent advances in interventional palliation; (2) examination of short- and long-term outcomes after a MBTS; and (3) attempt to identify factors affecting mortality and morbidity.

2 | METHODS

2.1 | Patients

This was a retrospective chart review of children undergoing a MBTS at our center over a 10-year period, from January 2004 to December 2014 and approved by the institutional research ethics board. Children who underwent an isolated MBTS as the first intervention and had confluent branch pulmonary arteries (PA), whether or not they had a concurrent pulmonary arterioplasty, and those who underwent prior catheter interventions were included. Children with nonconfluent PAs, shunts to unifocalized aortopulmonary collaterals, or as a rescue procedure after a previous surgery (eg, bidirectional cavopulmonary connection), a shunt after takedown of another operation (eg, a Fontan) and those undergoing other concomitant procedures were excluded. Attempts to uncouple the influence of the complexity of the imperfect post Norwood physiology on postoperative morbidity and mortality from that attributed to that of the MBTS was deemed a challenging proposition, hence these children were also excluded. The MBTS was performed in the standard fashion as previously described.[5] Demographic, diagnostic and surgical variables were collected from the electronic patient record as listed in Tables 1 and 2. Additionally, perioperative data, duration of intensive care unit (ICU) and hospital stays, mortality, major and minor morbidity data, time to subsequent surgery (next stage in surgical correction or palliation) and status of repair (complete or incomplete) at last follow up were gathered.

2.2 | Definitions

Major morbidity was defined as any one or more of the following: postoperative ECMO, cardiac arrest or need for reoperation (any cause) prior to subsequent planned correction or staged palliative surgery and catheter intervention for shunt obstruction (thrombosis or stenosis). Pulmonary over circulation (POC) was defined as an oxygen saturation of $>$85% in a FiO_2 $\leq$25%, and two or more of the following during the immediate postoperative ICU stay: (a) need to modify systemic and pulmonary vascular resistance, (b) evidence of decreased cardiac output (decreasing MVO_2, widening SaO_2 to MVO_2, increasing lactate $>$2 mmol/L), and (c) the added need for diuretics. Postoperative low cardiac output syndrome (LCOS) was defined by a combination of clinical, hemodynamic and biochemical parameters (decreasing MVO_2, widening SaO_2 to MVO_2, and increasing lactate $>$2 mmol/L). In addition to the absolute shunt size (mm), two other variables were considered to assess the effect of shunt size on outcomes: shunt size (mm) to weight (kg) ratio and a graft index: the ratio of graft cross sectional area (mm^2) to body surface area (m^2). Planned surgery was the treatment pathway, ie, a bidirectional cavopulmonary connection for those with univentricular physiology or a biventricular repair. The observation period for shunt thrombosis or stenosis was from insertion to takedown at the planned surgery. Diagnosis of shunt thrombosis required confirmation angiographically, at surgery or autopsy. Stenosis was diagnosed in children presenting with arterial desaturation, by angiography or cross sectional imaging. Death after hospital discharge, prior to planned surgery was defined as interval mortality. Any lesion with decreased pulmonary blood flow, requiring patency of the arterial duct to maintain systemic

TABLE 1 Demographic and diagnostic variables

	n = 95
Age (days)	20.7 ± 25.8
median (range)	8 (0–126)
Neonates	69 (72.6%)
Sex (male:female)	63:33
Weight (kg)	3.2 ± 0.7
median (range)	3.1 (1.7–5.4)
Weight <2.5kg	14 (14.7%)
BSA (m^2)	0.2 ± 0.04
median (range)	0.2 (0.1–0.3)
Prematurity (<37 weeks gestation)	18 (19%)
Diagnostic categories (n)	
Univentricular connection	49
Pulmonary atresia, intact ventricular septum	11
Critical pulmonary stenosis	2
Ebstein's anomaly	3
d-TGA	8
l-TGA	5
DORV	9
TOF, pulmonary atresia with ventricular septal defect	8
Duct dependent pulmonary circulation	55 (58%)
Clinical conditions prior to surgery	
Mechanical circulatory support	5 (5%)
Mechanical ventilator support	22 (23%)
Acidosis or shock	5 (5%)
Prior BTS procedures (n)	
RVOT interventions	10
Attempted ductal stenting	11
Atrial septal interventions	13

Abbreviations: BTS, Blalock–Taussig shunt; DORV, double outlet right ventricle; d-TGA, d-transposition of the great arteries; l-TGA, l-transposition of the great arteries; RVOT, right ventricle outflow tract; TOF, tetralogy of Fallot.

TABLE 2 Surgical details

	n = 95
Approach	
Sternotomy	92 (97%)
Thoracotomy	3 (3%)
BT shunt size	
3.0 mm	24 (25%)
3.5 mm	66 (70%)
4.0 mm	5 (5%)
Arterial connection	
Innominate artery	84 (88%)
Subclavian artery	11 (12%)
Shunt size (mm) to weight (kg)	1.1 ± 0.2
Graft index (shunt CSA/BSA)	44.39 ± 8.04
Concomitant pulmonary arterioplasty	17 (18%)
ECMO support for surgery	4 (4%)
CPB	11 (12%)
Duration of ICU stay (days):	
Median (range)	8 (1–268)
Duration of hospital stay (days):	
Median (range)	15 (1–294)

Abbreviations: BSA, body surface area (m^2); CPB, cardiopulmonary bypass; CSA, cross-sectional area (mm^2); ECMO, extracorporeal membrane oxygenation.

oxygen saturation (anatomic/functional pulmonary atresia or critical pulmonary stenosis) was considered duct dependent.

2.3 | Statistical analysis

2.3.1 | Descriptive analysis

Clinical characteristics were summarized using mean (standard deviation) or median (range) for continuous variables as appropriate and frequencies (proportions) for dichotomous and polytomous variables. Pair-wise correlations were calculated using Spearman's correlation. A composite outcome: mortality and major morbidity, was assessed as the earliest date of occurrence; this time-to-event outcome was right censored at the planned surgery (as defined above). Both composite outcomes and mortalities were analyzed using the Kaplan-Meier method for survival with 95% confidence intervals (CI). In addition, the duration of ICU and hospital stay was separately analyzed using competing risk models. The cumulative proportions of children discharged were estimated over time.

2.3.2 | Risk factor analysis

Risk factor analysis was performed for mortality, composite outcomes of mortality and morbidity and duration of ICU and hospital stays using Cox's proportional hazard regression. Risk factors were identified using the analytic strategy recommended by Collett.[6] To assess the performance of this variable selection strategy, bootstrap was applied to assess performance and reliability. Specifically, 500 bootstrap samples were constructed, and the same variable selection strategy was applied for each bootstrap sample. Risk factor reliability was calculated as the proportion of the bootstrap models containing the risk factor. The risk factors in the final multivariate models with reliability of >50% and $P < .05$ were considered to be significant.

3 | RESULTS

3.1 | Patients and diagnosis

Ninety-five children met the inclusion criteria. Demographic variables are listed in Table 1, with 69 children (73%) following a univentricular palliation pathway. The proportion of children undergoing a MBTS with single ventricle physiology was not different when comparing the first and second halves of the study ($P = .7$).

3.2 | Index operation and postoperative complications

The surgical variables are noted in Table 2. The 3 shunts performed by thoracotomy were early in the series making a sternotomy the current default approach. Three of 4 children who were on ECMO preoperatively had attempted ductal stenting that was unsuccessful due to technical reasons, PA stenosis, a tortuous duct, or ductal spam. These were early in the series, at the time of the learning curve of the team for ductal stenting. Mortality, major morbidity and other postoperative complications are listed in Table 3. The numbers of children who had a thoracotomy as well as those in whom the subclavian artery was the proximal anastomotic site were too small for valid statistical subanalysis for differences in postoperative complications. POC was identified in 30% of children with shunt size-to-weight ratio and the graft index not significantly different between those who did and did not develop POC ($P = .16$ and .98, respectively). Similarly, duct dependency ($P = .43$; 95% CI [−0.30, 0.11]) neonatal age ($P = .93$; 95% CI [−0.19, 0.26]), or the presence of antegrade pulmonary blood flow or shunt thrombosis appeared to have no influence on the development of POC ($P = .26$, and .76, respectively).

After shunt placement, 11 children required reoperation at a median 8 (IQ range 36) days, but not all reoperations were related to cyanosis (Table 3). Another 7 children underwent 8 catheter interventions at a median 20 (IQ range 74) days for arterial desaturation (Table 3). In these 7 children, shunt stenosis (n = 6) or thrombosis (n = 2) was treated by balloon dilation/stenting, with immediate improvement in all. In 3 of these 7 children, the improvement was short lived and surgery was required at 6, 18, and 32 days after the catheter intervention (shunt revision or early planned surgery). There were 12 confirmed (angiography, surgery or autopsy) instances of shunt thrombosis at median 10 (IQ range 50) days from shunt placement. Five of these were identified in the operating room or within the first 24 h. Medical management of such thrombosis with thrombolysis was not attempted due to the relationship to surgery, and no child responded to a heparin infusion. In addition, 2 interval deaths were suspected to be due to the same, but unconfirmed as there was no autopsy performed. Out of those presenting with arterial desaturation, shunt stenosis was noted in 10 children at a median 29.5 (IQ range 143) days after surgery.

TABLE 3 Postoperative complications n = 95

In hospital mortality	
Cause of death	11 (12%)
Coronary ischemia	2
Intracranial bleed	2
Pulmonary over circulation	1
Lung disease	1
Pulmonary vascular obstructive disease	1
Recurrent lactic acidosis of unknown cause	1
Unknown	3
Cardiac arrest	16 (17%)
Post MBTS ECMO	14 (15%)
Reoperation	11 (12%)
Shunt revision	7
Shunt banding	3
PAplasty	3
PA sling repair	1
Aortopexy and PApexy for suspected coronary compression	1
Catheter interventions	8 (8%)
Stent insertion to MBTS	5
Balloon dilation of MBTS	3
Postoperative low cardiac output syndrome	20 (21%)
Pulmonary over circulation	28 (30%)
Pericardial effusion requiring drainage	8 (8%)
Prolonged chest tube drainage (>1 week)	10 (11%)
Chylothorax	10 (11%)
Arrhythmias requiring intravenous medications, cardioversion or permanent pacing	7 (7%)
Cerebrovascular accident	12 (13%)
Ischemic	4
Hemorrhagic	4
Combined	4
Thrombosis	
Arterial	4 (4%)
Venous	16 (17%)
Necrotizing gastroenteritis	19 (20%)
Infection (septicemia, pneumonia, UTI)	12 (13%)
Wound infection	15 (16%)
Seroma	4 (4%)
Diaphragmatic palsy	4 (4%)
Vocal cord palsy	10 (11%)
Interval mortality	6 (6%)
Cause of death	
Unknown	3
Shunt thrombosis	2
Noncardiac surgery	1
Shunt thrombosis	9 (10%)
Shunt stenosis	7 (7%)
Stenosis and thrombosis	3 (3%)

Abbreviations: ECMO, extracorporeal membrane oxygenation; MBTS, modified Blalock–Taussig shunt, UTI, urinary tract Infection.

3.3 | Anticoagulation

The majority of children (94.05%, 79/84) were discharged on enoxaparin while 5 children discharged on acetylsalicylic acid alone.

3.4 | ICU and hospital stays

The median ICU stay was 6 (IQ range 11) days and hospital stay 15 (IQ range 27) days. Although 48% (95% CI [38%, 58%]) of children were discharged from the ICU at 7 days after the shunt, only 6% (95% CI [3%, 12%]) could be discharged home in this time frame. By 30 days, this rose to 78% (95% CI [68%, 85%]) and 57% (95% CI [46%, 66%]), respectively. Figure 1 shows the cumulative proportion of children discharged alive from the ICU and hospital.

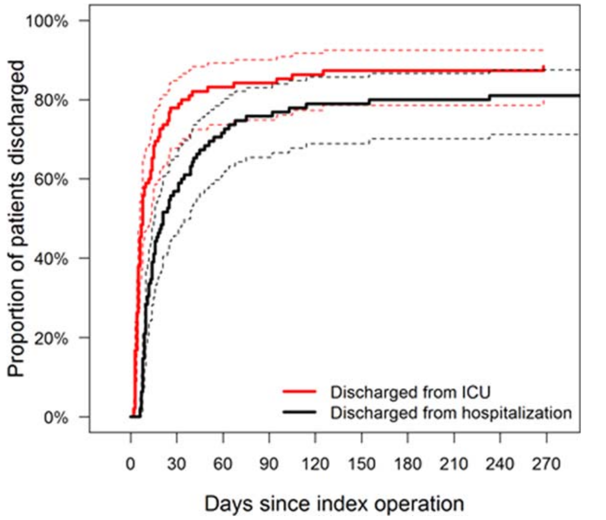

FIGURE 1 Cumulative proportion of patients discharged from ICU and hospital

3.5 | Long-term outcomes after MBTS

Median follow-up duration for the cohort was 1375 (IQ range 2008) days from the MBTS. Seventy-three children (77%) underwent planned surgery at median 171 (IQ range 65) days after shunt placement. Ninety-six percent (70/73) survived the planned surgery, with 53 (73%) requiring a concomitant pulmonary arterioplasty noting that it is our standard to perform a patch-plasty from hilum to hilum in its inferior aspect in the majority of the single ventricles at stage II palliation unless the pulmonary artery size is very large. Figure 2 summarizes the overall outcomes of the cohort.

3.6 | Survival analysis

One week after the MBTS, cumulative survival was 97.9% (95% CI [91.8%, 99.5%]). This fell to 87.4% (95% CI [78.8%, 92.6%]) at 1-month and 82.0% (95% CI [72.7%, 88.4%]) at 1-year (Figure 3). The estimated complication-free survival free of major morbidity at 1-week, 1-month and 1-year was 83.2%; (95% CI [74.0%, 89.3%]), 70.5%; (95% CI [60.2%, 78.6%]), and 61.4%; (95% CI [50.7%, 70.5%]), respectively (Figure 4).

3.7 | Risk factors for mortality and composite outcomes

Supporting Information Table S1 depicts the pairwise correlation matrix between the potential risk factors. As expected, weight correlated highly with shunt size-to-weight ratio ($r = -0.94$) and shunt size

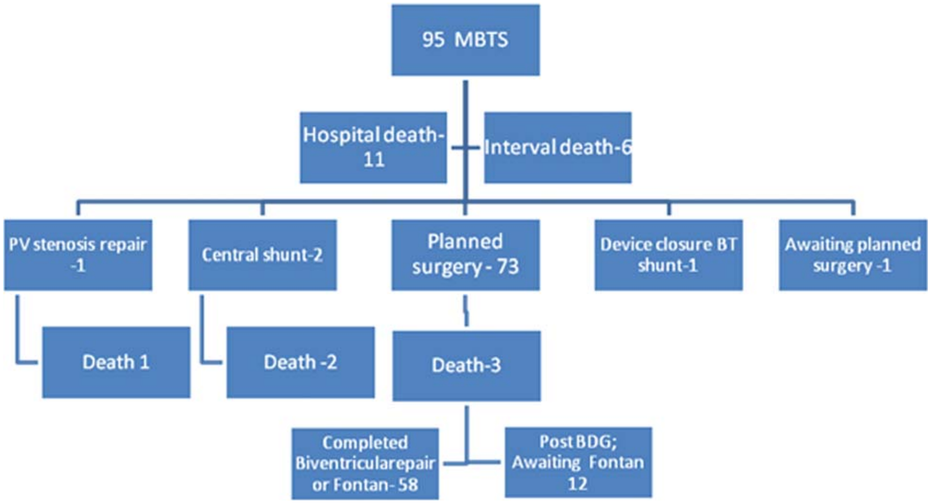

FIGURE 2 Outcomes of the cohort undergoing a modified Blalock–Taussig shuntAbbreviations: BDG, bidirectional Glenn; MBTS, modified BT shunt; PV, pulmonary vein

($r = 0.64$) and was only considered in the univariate analysis. Children who were duct dependent were at higher risk of the composite outcomes (Supporting Information Table S2). Children with higher graft index and duct dependency were at a higher risk of mortality by both univariate and multivariate analysis (Supporting Information Table S3). No other demographic factor influenced composite outcomes.

3.8 | Risk factors for longer ICU and hospital stay after MBTS

Postoperative infections trended toward a prolonged ICU stay, but were not statistically significant (Supporting Information Table S4), while hospital stays were significantly prolonged by an acquired infection (Supporting Information Table S5). A lower body weight, higher shunt-to-weight ratio, larger shunt size and noncardiac complications (necrotizing enterocolitis (NEC) or cerebral vascular accident (CVA)) were associated with a lower likelihood of ICU discharge in the univariate analysis, while higher shunt-to-weight ratio, NEC and CVA were significant on multivariate analysis (Supporting Information Table S4). Age, prematurity, CPB time and concomitant PAplasty did not influence ICU (Supporting Information Table S4) or hospital stays (Supporting Information Table S5).

4 | DISCUSSION

This studies' aim was to identify risk factors for morbidity and mortality after a MBTS in the current era. Duct dependency prior to the shunt predisposed the child to mortality and the composite outcomes of mortality and major morbidity. A higher graft index was identified as an additional risk factor for mortality, while a higher shunt-to-weight ratio and noncardiac complications contributed significantly to postoperative morbidity, prolonging ICU and hospital stays.

In hospital mortality after a MBTS was 12%, with an additional 6% interval mortality. In this regard, Dorobatu and colleagues reported a 9.8% mortality between 2007 and 2012 vs 5.1% between 2000 and 2006; while Bove et al documented an 11% mortality between 2002 and 2013 vs 7% between 1995 and 2002.[3,7] Additionally, mortality

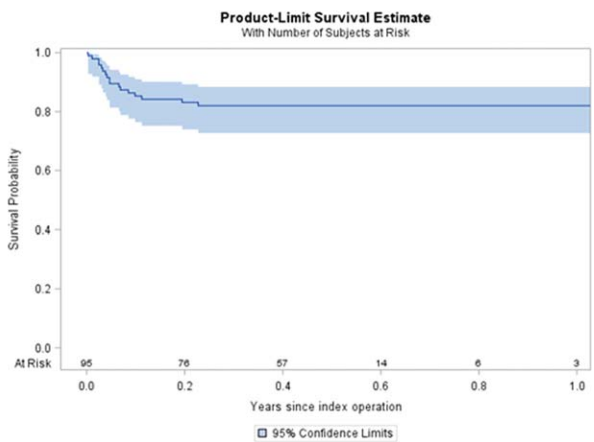

FIGURE 3 Freedom from mortality after index operation

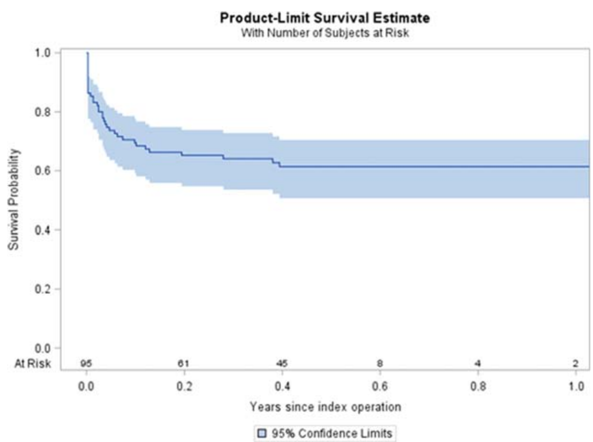

FIGURE 4 Freedom from major complications and mortality after index operation

was higher than the discharge mortality of 7.2% documented from the Society of Thoracic Surgeons (STS) database from 2002 through 2009.[2] This paradoxical increase in mortality for children undergoing a MBTS in an era marked by Advances in operating room and ICU care is intriguing.[3,7] Earlier, the MBTS was done primarily for securing pulmonary blood flow for children with tetralogy of Fallot until they reached an age and weight at which complete repair could be safely performed. Acceptance of an earlier complete repair as the norm for biventricular hearts as well as the utilization of catheter based right ventricular outflow tract interventions for augmenting pulmonary blood flow for such children decreased the number of MBTS performed today for this classical indication.[8] Mohammadi et al. studied 226 BTS performed between 1988 and 2005, noting that univentricular connections constituted only 5.5% of the cohort.[9] In sharp contrast, neonates with univentricular physiology were the largest group (73%) having a MBTS in this cohort. The current findings also differ from the STS database cohort, where 62% of children had a biventricular repair. They did however; identify univentricular physiology as predictive of mortality and morbidity. As such, the higher proportion of univentricular hearts in this current cohort could explain the higher risk (13/17 deaths, 75% were in patients with single ventricles). The volume overload imposed on a univentricular heart by an arterial shunt may be an important factor predisposing these children to adverse outcomes. POC and shunt thrombosis/stenosis were the two principal shunt related complications, contributing to adverse outcomes[10–12] with a rate in the current study comparable to that as noted by others.[7] However, the incidence of POC in this cohort was 30% (despite ligation of alternative sources of pulmonary blood flow and the use of a 3.5 mm shunt), which was much greater ($P < .0001$) then the 5% incidence reported by Bove et al,[7] despite their cohort having a higher shunt-to-weight (1.4 vs 1.1) ratio. While the definition of POC was slightly different, it is compelling to ask whether the 84% of shunts in the Bove series were thoracotomies and hence the subclavian artery was the proximal anastomotic site and contributed to this difference. As flow is proportional to the 4th power of radius of the vascular conduit (Poiseuille's law), the more proximal (on the innominate artery) the anastomosis, the greater the flow would be compared to a distal anastomosis (subclavian artery), the subclavian artery becoming the "flow regulator" in a MBTS.[13] Hence, loss of the flow regulating boundaries using a sternotomy to place the shunt could contribute to the increased incidence of POC. We also observed that the shunt-to-weight ratio and graft index were not significantly higher in children who developed POC. This suggests that not only an anatomically larger shunt, but also other confounding physiologic variables not accounted for in the present review could influence pulmonary and systemic vascular resistances and increase shunt flow. As three-quarters of the children were neonates, their labile pulmonary vascular bed could play a role in promoting POC as the vascular resistance falls. Nevertheless, it is reassuring to note that POC as defined in this study was not associated with an increased risk for mortality or the composite outcomes.

Although not specifically addressed in this study, placement of the shunt on the innominate rather than the subclavian artery and more proximal placement onto the PA could contribute to the increase in composite outcomes as described above. Unfortunately, the small number of children operated through a thoracotomy precluded a meaningful statistical analysis. Additionally, while the low PA distortion rates have been reported with a sternotomy approach,[10] the requirement of a pulmonary arterioplasty at subsequent surgery was high in this cohort.

From risk factor analysis, duct dependency increased the likelihood of morbidity and mortality. As such, this may only be a marker for the tenuous nature and marginal stability of such children. Early deterioration preoperatively, apnea, the need of ventilation while on prostaglandins and the devastating effect of shunt thrombosis and stenosis all contribute to poor outcomes in these children.

We did note a higher graft index was associated with increased mortality risk and this could predispose the child to POC, low cardiac output, cardiac arrest and death. Indeed, POC was identified as the cause of death in previously reported sternotomy cohorts, although not in this study.[7] It is sobering to note that the morbidity associated with a MBTS was considerable in spite of advances in critical care. Just over half of the children were discharged from the hospital 30 days after the procedure, underscoring that the procedure and postoperative care is resource intense. In this regard, larger absolute shunt size (univariate analysis) and a higher shunt-to-weight ratio (multivariate analysis) were significant for prolonging ICU and hospital stays, presumably by predisposing to POC from anatomical factors that would be difficult to manage.

5 | LIMITATIONS

This is a retrospective cohort study and suffers from the bias and known limitations of nonprotocolized procedures. Outcomes described here must be considered in the background pattern of practice in each institution. Statistically, variable selection is often subject to random noise, and the results can be affected by a small number of subjects influencing observations. Using bootstrap methods to assess the reliability of variable selection can mitigate, but not eliminate the uncertainty associated with the variable selection strategy. The influence of PA size on affecting the outcomes was not analyzed in this study. The small numbers assigned to each diagnostic and risk factor subset—influenced by center specific management strategies posed challenges in risk factor analysis.

6 | CONCLUSIONS

The largest diagnostic subset of children undergoing a MBTS in the current era at our center, were those with univentricular physiology. This is different from other published large databases and the result of early complete repair for children with biventricular hearts or interventional palliation as appropriate. The morbidity and mortality associated with a MBTS remains high, partly explained by this higher at risk population. The incidence of POC was high compared to earlier published series, but did not directly influence morbidity or mortality. An anatomically larger shunt predisposed to mortality and morbidity, while duct dependency predisposed the child to the composite outcomes of major morbidity and mortality. Noncardiac complications also contributed significantly to postoperative morbidity. Choosing the appropriate sized shunt and balancing the risk of POC and shunt thrombosis remains far from an exact science. Prospective studies comparing different approaches to securing a reliable pulmonary blood flow and shunt sizes could address some of these unresolved issues. Whether wider adaption of an interventional palliation (ductal stent or right ventricular outflow tract dilation or stenting) would help decrease mortality and morbidity compared to a MBTS in suitable children needs to be established with prospective studies.[8,14]

CONFLICT OF INTEREST

None

AUTHOR CONTRIBUTIONS

Manuscript preparation: Sasikumar, Hermuzi, Fan, Lee, Chaturvedi, Hickey, Honjoi, Van Arsdell, Caldarone, Agarwal, Benson
Study design: Sasikumar, Hermuzi, Fan, Lee, Chaturvedi, Hickey, Honjoi, Van Arsdell, Caldarone, Agarwal, Benson
Data analysis: Sasikumar, Hermuzi, Fan, Lee, Chaturvedi, Hickey, Honjoi, Van Arsdell, Caldarone, Agarwal, Benson
Data interpretation: Sasikumar, Hermuzi, Fan, Lee, Chaturvedi, Hickey, Honjoi, Van Arsdell, Caldarone, Agarwal, Benson
Critical revision: Sasikumar, Hermuzi, Fan, Lee, Chaturvedi, Hickey, Honjoi, Van Arsdell, Caldarone, Agarwal, Benson
Final approval: Sasikumar, Hermuzi, Fan, Lee, Chaturvedi, Hickey, Honjoi, Van Arsdell, Caldarone, Agarwal, Benson

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

TABLE S1 Pairwise correlation matrix between all potential risk factors using Spearman's correlation
TABLE S2 Univariate and multivariate risk factor analyses for composite outcome
TABLE S3 Univariate and multivariate risk factor analyses for mortality
TABLE S4 Univariate and multivariate risk factor analyses for the length of ICU stay
TABLE S5 Univariate and multivariate risk factor analyses for the length of hospital stay

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