ORIGINAL ARTICLE

Factors Related to Early Postoperative Modified Blalock-Taussig Shunt Thrombosis and In-Hospital Mortality in Infants

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Objective: The modified Blalock-Taussig shunt (mBTs) is used palliatively in cyanotic congenital heart diseases when definitive surgery is not possible. However, factors contributing to shunt thrombosis and in-hospital mortality in infancy remain unclear. The present study aimed to identify those risk factors.

Materials and Methods: The authors conducted a retrospective review of medical records from the infants diagnosed with cyanotic congenital heart disease who underwent isolated mBTs procedures at Chiang Mai University Hospital between March 1, 2011 and April 30, 2015. Patient characteristics, operative data, and treatment outcomes were extracted. The primary outcome assessed was shunt thrombosis, with in-hospital mortality within 30 days as the secondary outcome. Risk regression analysis was used to identify factors associated with both outcomes.

Results: Forty-nine infants were included in the present study, with a mean weight of 3.81 kilograms (range of 2.05 to 7.70 kg) and an average age of 66 days (range of 3 to 349 days). Early shunt thrombosis occurred in eight patients (16.33%), and five patients (10.2%) died. Multivariable analysis revealed only sepsis as a significant predictor (RR 7.93, 95% CI 1.86 to 33.69). Neither weight at surgery nor shunt size showed a significant association with shunt thrombosis. Prognostic factors for in-hospital mortality in the univariable analysis included prematurity (p=0.01), size of pulmonary artery (p=0.033), preoperative intubation (p=0.043) shunt thrombosis (p=0.002), and body weight at surgery of less than 3 kg (p=0.002). However, multivariable analysis could not demonstrate any difference.

Conclusion: Postoperative sepsis emerged as the sole statistically significant predictor for early shunt thrombosis following isolated mBTs. However, larger studies are needed to ascertain prognostic factors for in-hospital mortality in infants with cyanotic congenital heart disease.

Keywords: Blalock Taussig shunt; Cyanotic congenital heart disease; Thrombosis; Mortality

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A modified Blalock-Taussig shunt (mBTs) is a systemic-to-pulmonary surgical procedure that places a synthetic vascular graft between the pulmonary and subclavian arteries to increase the blood flow in the pulmonary circulation. This palliative procedure is used extensively in the treatment of cyanotic congenital heart disease. However, the mortality rate is high at 4% to 13%[1-3]. The factors that are associated with mortality are still inconclusive. Low bodyweight at time of operation, ductal patency, preoperative ventilator support, shunt thrombosis, and pulmonary overcirculation due to a "too large" shunt have been reported previously[2,4,5]. Shunt thrombosis is one of the most lethal complications that can occur in this treatment and occurs in 3% to 11% of patients[1,2,4]. Predictive factors associated with shunt thrombosis are inconclusive. Therefore, the aim of the present study was to identify the predictors for shunt thrombosis in the early postoperative period and prognostic factors for in-hospital mortality.

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Materials and Methods

A retrospective medical chart review was performed. All infant patients diagnosed with cyanotic heart disease who underwent isolated mBTs at Chiang Mai University Hospital between March 1, 2011 and April 30, 2015, were enrolled onto the

present study. Individuals with missing important data relevant to the study including bodyweight, size of pulmonary artery, graft size, operative data, or postoperative length of stay were excluded from the cohort. Patients who underwent cardiac procedures other than ductal closure and pulmonary arterioplasty were also excluded.

The operation for the patient with a septic condition was postponed until the sepsis was completely treated. Two standard operative approaches were employed, the median sternotomy and the thoracotomy approach. The choice of approach was determined by the informed preference of the surgeon, considering factors such as pulmonary artery anatomy and the hemodynamic status of the patients. Intraoperatively, all patients were heparinized systemically with an unfractionated heparin bolus at a dose of 100 units/kg. The interposition shunt was created using an expanded polytetrafluoroethylene vascular graft (Gore-Tex, W.L. Gore & Assoc, Flagstaff, AZ). The arterial inflow in either the subclavian artery or brachiocephalic artery was dependent on the size of the vessels and the surgeon's decision accordingly. The pulmonary outflow was consistently defined as the pulmonary artery proximal to the first bifurcation on either side. The size of the shunt varied depending on the surgeon and patient. Typically, surgeons selected the shunt size proportionate to the patient's weight, adhering to standard recommendations as 5-mm graft for neonates weighing 5 to 15 kg, 4-mm graft for neonates weighing between 3 and 5 kg, 3.5-mm for neonates weighing between 2 and 3 kg, and 3.0-mm shunt for infants weighing less than 2 kg). The authors determined shunt appropriateness and divided the patients into three categories, under-, proper-, and over-size of shunt according to bodyweight at time of surgery, using the standard recommendations[6]. Cardiopulmonary bypass (CPB) was used if there was severe desaturation, impending cardiac arrest or severe hemodynamic instability. The heparin effect was not reversed by protamine or partially reversed if there was a need for CPB or significant bleeding was observed. After bleeding had subsided, a continuous heparin infusion at rate of 10 unit/kg was given in the case of the patient with a graft size of less than 4-mm. for 48 hours. All patients were prescribed daily aspirin at a dose of 6 mg/kg via orogastric tube within 24 hours after the operation. The transthoracic echocardiography was performed on all patients after surgery, and in case of any adverse events before discharge.

Shunt patency was determined by postoperative echocardiographic results and intraoperative finding during shunt revision. Early shunt thrombosis was defined as shunt thrombosis within 30 days after surgery. In-hospital mortality was defined as any death occurring before hospital discharge. The primary outcome was early shunt thrombosis. The secondary outcome was in-hospital mortality.

This retrospective study was approved by the Institutional Review Board and Ethic Committee of the Faculty of Medicine (166/2016), Chiang Mai University, Chiang Mai, Thailand.

Statistical analysis

Statistical analysis was performed using Stata, version 14 (StataCorp LP, College Station, TX, USA). Categorical variables were presented as numbers with percentages and comparison between groups was analyzed using Fisher's exact test. Continuous variables were presented as median and interquartile range (IQR) or mean and standard deviation (SD) and comparison among groups was made using a t-test or a Wilcoxon rank-sum test. Factors associated with early shunt thrombosis and in-hospital mortality were determined by univariable and multivariable risk regression analyses with a step backward elimination method. Statistical significance was established at the p-value less than 0.05.

Results

Sixty-five patients had undergone primary mBTs during the study period. Sixteen patients were excluded as nine patients did not have complete data and seven patients underwent cardiac procedures other than ductal closure and pulmonary arterioplasty. Therefore, 49 out of the 65 patients were enrolled in the present study. Twenty-eight patients were neonates and twenty-one patients were infants. Twenty-six patients (53.06%) were male and six patients (12.24%) were preterm. Demographic and operative data are described in Table 1. One third of the patients needed preoperative mechanical ventilator support. Only one patient (0.04%) needed CPB during the operation.

Eight patients (16.33%) suffered from early shunt thrombosis and five patients (10.2%) died in hospital from multiple complications. All seven out of eight patients with shunt thrombosis needed shunt reintervention that included a central shunt in four cases, additional contralateral mBTs in one case, ductal stenting in one case, and a thrombectomy in one case. The mean onset of shunt thrombosis was

Table 1. Demographic and operative data

Variables	Shunt thrombosis (n=8)	No shunt thrombosis (n=41)	p-value
Age (month); median (IQR)	0.88 (0.47 to 1.17)	0.70 (0.27 to 3.23)	0.221
Birth status; n (%)			0.047
Term	5 (62.50)	38 (92.68)	
Preterm	3 (37.50)	3 (7.32)	
Birth weight (g); mean±SD	2.60±0.51	2.89±0.52	0.153
Weight at surgery (kg); n (%)			0.094
<3 kg	5 (62.50)	11 (26.83)	
≥3 kg	3 (37.50)	30 (73.17)	
Sex; n (%)			1.000
Female	4 (50.00)	19 (46.34)	
Male	4 (50.00)	22 (53.66)	
Diagnosis; n (%)			
TOF			0.693
• Yes	2 (25.00)	16 (39.02)	
• No	6 (75.00)	25 (60.98)	
Single ventricle			0.151
• Yes	3 (37.50)	6 (14.63)	
• No	5 (62.50)	35 (85.37)	
Pulmonary atresia with IVS			0.522
• Yes	1 (12.50)	3 (7.32)	
• No	7 (87.50)	38 (92.68)	
Pulmonary atresia with VSD			0.421
• Yes	1 (12.50)	2 (4.88)	
• No	7 (87.50)	39 (95.12)	
DORV with PS			1.000
• Yes	0 (0.00)	4 (9.76)	
• No	8 (100)	37 (90.24)	
Tricuspid atresia			1.000
• Yes	1 (12.50)	7 (17.07)	
• No	7 (87.50)	34 (82.93)	
Size of PA (mm); mean±SD	3.61±1.27	4.37±1.21	0.092
Creatinine (mg/mL); mean±SD	0.33±0.13	0.47±0.17	0.044
O2 saturation (%); mean±SD	75.13±6.85	78.93±6.14	0.122
Pre-operative intubation; n (%)			0.015
Yes	6 (75.00)	11 (26.83)	
No	2 (25.00)	30 (73.17)	
Pre-operative PGE1 administration; n (%)			0.406
Yes	7 (87.5)	27 (65.85)	
No	1 (12.50)	14 (34.15)	

IQR=interquartile range; SD=standard deviation; TOF=tetralogy of Fallot; IVS=intact ventricular septum; VSD=ventricular septal defect; DORV=double outlet of right ventricle; PS=pulmonary stenosis; PA=pulmonary atresia; PGE1=prostaglandin E1

13.38 days, with a range of 0 to 30 days. The most common graft size was 3.5- and 4-mm occurring in 19 cases in both sizes (38.78%). Postoperative complications included pneumonia in 12 out of 49 cases (24.49%), sepsis in nine out of 49 cases

Table 2. Pre-operative and operative variables related to predictors associated with early shunt thrombosis

Intra operative variable	Shunt thrombosis (n=8)	No shunt thrombosis (n=41)	p-value
Operation time (hours); mean±SD	1.86±1.12	1.33±0.56	0.046
Incision; n (%)			0.144
Right thoracotomy	5 (62.50)	33 (80.49)	
Left thoracotomy	3 (37.50)	4 (9.76)	
Median sternotomy	0 (0.00)	4 (9.76)	
Size of MBT (mm); mean±SD	3.75±0.60	4.04±0.56	0.199
MBT shunt size; n (%)			0.211
3 mm	1 (12.50)	0 (0.00)	
3.5 mm	4 (50.00)	15 (36.59)	
4 mm	2 (25.00)	17 (41.46)	
5 mm	1 (12.50)	9 (21.95)	
Shunt appropriateness; n (%)			1.000
Proper size	5 (62.50)	25 (60.98)	
Under size	2 (25.00)	10 (24.39)	
Over size	1 (12.50)	6 (14.63)	
PDA management; n (%)			1.000
No PDA	1 (12.50)	7 (17.07)	
Left untouched	7 (87.50)	33 (80.49)	
PDA ligation	0 (0.00)	1 (2.44)	
Cardiopulmonary bypass use; n (%)			1.000
Yes	0 (0.00)	1 (2.44)	
No	8 (100)	40 (97.56)	

SD=standard deviation; MBT=modified Blalock-Taussig; PDA=patent ductus arteriosus

(18.37%), pleural effusion in four out of 49 cases (8.16%), and ipsilateral diaphragmatic paralysis. No patient needed reoperation due to bleeding.

From the univariable analysis, being preterm baby (p=0.047) and patients who needed preoperative intubation (p=0.015) were significant predictive factors for early shunt thrombosis as shown in Table 1. The patients suffered from shunt thrombosis had statistically significant longer operation time, lower postoperative O2 saturation, longer intensive care unit (ICU) stay and ventilator support, a higher incidence of pneumonia, sepsis, reintubation, and higher in-hospital mortality as shown in Table 2 and 3. However, only postoperative sepsis was determined as being a significant predictive factor for early shunt thrombosis from the multivariable risk regression analysis using stepwise elimination method analysis as shown in Table 4. Age at surgery, diagnosis, size of pulmonary artery, size of shunt or shunt appropriateness were not significantly associated with early shunt thrombosis.

Table 5 shows the results of the univariable analysis

Table 3. Post-operative outcomes associated with early shunt thrombosis

Postoperative variable	Shunt thrombosis (n=8)	No shunt thrombosis (n=41)	p-value
O2 saturation (%); mean±SD	76.75±7.78	84.02±4.52	0.001
Creatinine (mg/mL); mean±SD	0.58±0.21	0.44±0.17	0.057
ICU stay (days); median (IQR)	43 (19 to 60)	6 (4 to 12)	<0.001
Time on ETT (hours); median (IQR)	23 (10 to 49)	2 (1 to 4)	<0.001
Inotrope use >48 hours; n (%)			1.000
Yes	4 (50.00)	23 (56.10)	
No	4 (50.00)	18 (43.90)	
Heparin use in 24-hour; n (%)			1.000
Yes	8 (100)	38 (92.68)	
No	0 (0.00)	3 (7.32)	
Pneumonia; n (%)			0.015
Yes	5 (62.50)	7 (17.07)	
No	3 (37.50)	34 (82.93)	
Pleural effusion; n (%)			0.120
Yes	2 (25.00)	2 (4.88)	
No	6 (75.00)	39 (95.12)	
Chylothorax; n (%)			-
Yes	0 (0.00)	0 (0.00)	
No	8 (100)	41 (100)	
Sepsis; n (%)			0.003
Yes	5 (62.50)	4 (9.76)	
No	3 (37.50)	37 (90.24)	
Re-intubation; n (%)			0.023
Yes	5 (62.5)	8 (19.51)	
No	3 (37.50)	33 (80.49)	
In hospital mortality; n (%)			0.002
Yes	4 (50.00)	1 (2.44)	
No	4 (50.00)	40 (97.56)	

IQR=interquartile range; SD=standard deviation; ICU=intensive care unit; ETT=endotracheal tube

Table 4. Multivariable risk regression analysis for predictors of shunt thrombosis*

Variables	RR	95% CI	p-value
Inotrope use within 24 hours	0.62	0.15 to 2.53	0.509
Sepsis	7.93	1.86 to 33.69	0.005

RR=risk ratios; CI=confidence interval

* Stepwise elimination method analysis

for the prognostic factors for in-hospital mortality. Prematurity (p=0.010), lower body weight (p=0.014), bodyweight less than 3 kg. (p=0.002), smaller size of pulmonary artery (p=0.033), preoperative intubation (p=0.043), lower postoperative saturation (p=0.031), longer ICU stay (p=0.036), longer intubation time (p=0.038), reoperation for shunt revision (p=0.014), postoperative sepsis and early shunt thrombosis (p<0.001) were identified as significant prognostic

Table 5. Univariable analysis of prognostic factors for in-hospital mortality after the modified Blalock-Taussig shunt procedure

Variables	In-hospital death (n=5)	Survived (n=44)	p-value
Birth status; n (%)			0.010
Term	2 (40.00)	41 (93.18)	
Preterm	3 (60.00)	3 (6.82)	
Birth weight (kg); mean±SD	2.30±0.36	2.91±0.51	0.014
Weight at surgery; n (%)			0.002
<3 kg	5 (100)	11 (25.00)	
≥3 kg	0 (0.00)	33 (75.00)	
Size of PA (mm); mean±SD	3.2±0.67	4.37±1.16	0.033
Pre-operative intubation; n (%)			0.043
Yes	4 (80.00)	13 (29.55)	
No	1 (20.00)	31 (70.45)	
O2 saturation (%); mean±SD	77.60±5.61	83.43±5.61	0.031
ICU stay (days); median (IQR)	21 (18 to 60)	7 (4 to 16)	0.036
Time on ETT (hours); median (IQR)	10 (5 to 60)	3 (2 to 6)	0.038
Re-operation for revising shunt; n (%)			0.014
Yes	4 (80.00)	9 (20.45)	
No	1 (20.00)	35 (79.55)	
Sepsis; n (%)			0.037
Yes	3 (60.00)	6 (13.64)	
No	2 (40.00)	38 (86.36)	
Re-intubation; n (%)			0.014
Yes	4 (80.00)	9 (20.45)	
No	1 (20.00)	35 (79.55)	
Shunt thrombosis; n (%)			0.002
Yes	4 (80.00)	4 (9.09)	
No	1 (20.00)	40 (90.91)	

IQR=interquartile range; SD=standard deviation; PA=pulmonary atresia; ICU=intensive care unit; ETT=endotracheal tube

Table 6. Multivariable risk regression analysis with step backward elimination method of risk factors for in-hospital mortality after neonatal Blalock-Taussig shunt procedure

Variables	RR	95% CI	p-value
Preterm vs. Term	7.43	0.60 to 91.55	0.118
Preoperative O2 saturation	0.81	0.60 to 1.09	0.167

RR=risk ratios; CI=confidence interval

factors for in-hospital mortality. Shunt size or shunt appropriateness did not associate with in-hospital mortality. However, multiple risk regression analyses with step backward elimination method failed to identify any significant predictor of in-hospital mortality as shown in Table 6.

Discussion

The classic Blalock Taussig shunt was introduced by Blalock & Taussig in 1945[7]. The modification was performed by de Leval et al. in 1975 using a

polytetrafluoroethylene interposition graft instead of native subclavian artery and became known as the mBTs[8]. The mBTs became one of standard palliative procedures for treating cyanotic congenital heart disease until a definite operation could be performed. This procedure was often performed in neonates and infants because of the small bodyweight and high risk for definite surgery. Therefore, a considerable risk of mortality and morbidities still remained.

Shunt thrombosis is one of the most catastrophic complications after mBTs that causes profound desaturation and even cardiac arrest from a severe decrease of pulmonary blood flow. From previous studies, the incidence of thrombotic occlusion of mBTs was between 3% to 11.8% of infants[2,4,9,10]. In the present study, the overall incidence of early shunt thrombosis was 16.33% (8 out of 49 cases), which was higher than previously published data. Previous studies[9,11,12] have been conducted to clarify the factors associated with this critical complication. Tamisier et al. found that younger age at surgery and the lower weight of patients were significantly associated with shunt thrombosis[12]. Bove et al. demonstrated that the weight of less than 3.6 kg at surgery was a significant predictive factor for shunt thrombosis[11]. Guzzetta et al. who conducted a specific study about in-hospital shunt thrombosis in infants also found that weight less than 3 kg was related to shunt thrombosis[9]. Consistent with the previous studies[9,11,12], the present study data indicated a trend towards lower body weight as the predictor of shunt thrombosis. However, due to the small sample size, this association did not reach statistical significance. The authors found no correlation between age at surgery and shunt thrombosis as found by Tamisier et al[12]. Prematurity was also identified as a predictor for shunt thrombosis (p=0.047). This factor could have an effect on thrombotic risk by increasing pulmonary vascular resistance in a premature lung condition, which may cause intermittent pulmonary hypertension, and a low flow state would be the result. Prematurity has never been identified as a predictor of shunt thrombosis in previous studies and this finding may be camouflaged by the effect of the preexisting low bodyweight of these small babies. Petrucci et al.[13] did observe a propensity toward a higher mortality rate with prematurity, however, their results did not reach statistical significance.

From the present study data, preoperative intubation is significantly related to shunt thrombosis (p=0.015). However, this could also be explained by the emergency status of the patients that forced the surgeons to operate in critical conditions or small bodyweight and hence be a confounding variable.

Guzzetta et al. also reported the smaller the size of the pulmonary artery being shunted as one of the predictors of shunt thrombosis[9]. The present study data also suggested the same, but the data did not reach the level of statistical significance (p=0.092), possibly because of the small population. This finding may reflect the point that smaller patients also have smaller pulmonary artery sizes. Three studies[4,14,15] have reported that shunt size was the predictive factor for shunt thrombosis, but in the present study analysis, the shunt size did not relate to shunt thrombosis or the mortality rate.

The present study also showed adverse effects of shunt thrombosis to overall outcomes. Four out of five deaths (80%) occurred as a result of shunt thrombosis. In the thrombotic group, patients had a lower O2 saturation, poorer renal function, and a higher incidence of sepsis. Sepsis could be the cause or the result of the shunt thrombosis. Five out of eight cases of shunt thrombosis occurred after the onset of sepsis and septic shock, which could be the cause of thrombosis due to the low flow state. Significant longer ventilator support and ICU stay were observed in the thrombotic group. However, the results of the multivariable analysis only indicated that sepsis was a statistically significant predictor for shunt thrombosis. As mentioned earlier, the authors are reluctant to conclude that sepsis is the cause of thrombotic complications.

The overall mortality of mBTs is recorded as being between 3.7% and 14% with many risk factors being suggested in previous publications[1-3,13]. The present study data showed an acceptable overall in-hospital mortality rate of 10.2% (5 out of 49 patients), which is comparable to other studies. There have been factors put forward as identifying predictors of mortality after mBTs including low bodyweight, larger shunt size/bodyweight ratio, preoperative intubation, and specific diagnosis such as pulmonary atresia with an intact ventricular septum and univentricular heart. The most commonly suggested risk factor amongst this wide variety of factors is low bodyweight. Dirks et al. reported low body weight and bigger shunt size/bodyweight ratio as risk factors associated with in-hospital mortality[2]. Inconsistent cut off-value of what constitutes a low bodyweight was found among previous publications, the range being from 2 to 3.6 kg[2,5,11]. The authors also found that a body weight surgery of less than 3 kg as the greatest risk of in-hospital mortality. This

does not include the shunt size. The data suggests that shunt thrombosis is a strong predictor of mortality (p=0.002). The four deaths in the present series were the result of shunt thrombosis and its resulting complications. Prematurity was also found to be a significant predictor of mortality, which was similar to the findings in the Society of Thoracic Surgeons Congenital Heart Surgery Database review, but the results did not show statistical significance[13]. Two previous studies[5,14] showed that preoperative ventilation was a risk factors of mortality, but the present study results did not reach statistical significance. The diagnosis also does not relate to mortality. However, only five cases in the cohort died, which could lead to the misreading of the statistical analysis. The authors also performed multivariable analysis for the mortality aspect, however, no statistically significant predictor was found.

There are limitations to the present study. First, this is a retrospective study with small population, thus, it cannot gain enough statistical power to identify the possible risk factors contributing to both shunt thrombosis and mortality. The retrospective design means that some important data such as ductal patency, which was found as significant predictor of shunt thrombosis[1], and coagulogram data were not available. The authors focused on in-hospital mortality and extended this to 30 days after surgery if the patient was discharged earlier. Three patients died suddenly at home or in the emergency room after experiencing sudden cyanosis over the 30-day period but within three to four months after surgery. The cause of the sudden cyanosis may be explained partially by an acute shunt thrombosis but an autopsy or an echocardiogram were not performed. A longer study until the next stage of operation should be conducted to identify the exact number of inter-stage mortality in the patients. Finally, the study warrants further investigation with a larger population to ascertain whether a larger sample would achieve adequate statistical power or whether the present study findings are correct as they stand.

Conclusion

From the present study data, predictors of early shunt thrombosis from the univariable analysis included prematurity, weight at surgery of less than 3 kg, preoperative intubation, and sepsis, but after using the multivariable analysis, only sepsis was identified as a significant predictor. Shunt thrombosis has adverse effects including lower postoperative saturation, worsening renal function, higher incidence of sepsis and mortality and increased length of ventilator support and ICU stay. These findings would imply that the occurrence of shunt thrombosis also results in an increase in use of health resources. Prematurity, weight at surgery of less than 3 kg, and incidence of a shunt thrombosis are the predictors of mortality according to the univariable analysis of the data. The size of the shunt does not relate to either an early shunt thrombosis or mortality. Nevertheless, further study with a larger sample size should be conducted to warrant the level of significance and a longer study will answer the true inter-stage mortality in this “not so simple” procedure.

What is already known on this topic?

Shunt thrombosis is identified as one of the most catastrophic complications following mBTs, leading to profound desaturation and even cardiac arrest due to a severe decrease in pulmonary blood flow. Previous studies have reported the incidence of thrombotic occlusion of mBTs to be between 3% to 11.8% of infants. Various factors have been proposed as predictors of shunt thrombosis after mBTs, including younger age at surgery, lower weight, prematurity, and preoperative intubation. Previous studies have also suggested that low body weight, shunt size/body weight ratio, preoperative intubation, and specific diagnoses are risk factors for mortality after mBTs. The overall mortality rate after mBTs is reported to be between 3.7% and 14%.

What does this study add?

It provides updated data on the incidence of early shunt thrombosis following mBTs, with an observed incidence of 16.33% in the study population. This study identifies specific factors associated with shunt thrombosis, including prematurity, preoperative intubation, and longer operative time. These factors were found to be significant predictors of shunt thrombosis in univariable analysis. However, sepsis may be a significant predictor of shunt thrombosis, based on multivariable analysis results.

Overall, this study contributes valuable insights into the risk factors, complications, and outcomes of mBTs, which can inform clinical practice and improve patient care in this population.

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Authors' contributions

All authors have contributed to the conception, design, article review, result interpretation, manuscript drafting, critical intellectual input, and final approval for publication. Collectively, they hold full responsibility for ensuring the integrity and accuracy of all aspects of this work.

Conflicts of interest

The authors declare no conflict of interest.

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