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Risk Factors for Thrombosis, Overshunting and Death in Infants after Modified Blalock-Taussig Shunt

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Background: The Modified Blalock-Taussig shunt procedure can provide increased flow of blood to the lungs for babies born with certain congenital heart defects. We evaluated 44 subjects under 2 years of age who had a Modified Blalock-Taussig shunt (MBTS) procedure performed from 2009-2013, to investigate risk factors for thrombosis, overshunting and death.

Methods: The study subjects included in our investigation were severely cyanotic newborns with pulmonary stenosis or atresia and duct dependent circulation, and infants having Tetralogy of Fallot with small pulmonary arteries who underwent a MBTS procedure in our facility from 2009-2013. We duly noted patient preoperative characteristics such as hemoglobin, hematocrit, mean platelet volume, prothrombin time and partial thromboplastin time. Our study investigated the risk factors for post-operative overcirculation, thrombosis and death.

Results: The age and weight of patients in our study at the time of procedure ranged from 1 day to 20 months old (median 12 days), and 2.4 kg to 12 kg (mean 4.6 kg), respectively. A total of 8 patients died following surgery, and. 4 (9.1%) had shunt thrombosis, of which one died during shunt revision. Partial thromboplastin time was 28.7 seconds in patients with thrombosis, and 35 in all other patients ($p = 0.04$). Overcirculation was detected in 5 patients; shunt size/body weight was 1.25 in patients who had overcirculation, and 1.06 in all other patients.

Conclusions: It is important to assess risk factors associated with the MBTS operation. The results of our study suggest that a preoperative low aPTT value may be an indicator for thrombosis in infants who have undergone MBTS surgery.

Key Words: Activated partial thromboplastin time • Risk factors • Shunt thrombosis

INTRODUCTION

Early complete repair of cyanotic congenital heart diseases has become a preferable treatment option, even in the neonatal period, due to improved surgical experience, techniques and post-operative intensive care. Nevertheless, the use of a palliative shunt operation in cyanotic infants still stands out as a good option when total correction is not possible.[1-3] In developing countries especially, given the frequent lack of experience and resources, the Modified Blalock-Taussig shunt (MBTS) appears to be the treatment of choice for infants who have cyanotic congenital heart defects with restricted pulmonary artery flow.[4] Factors associated with mortality and morbidity still remain to be characterized despite the available published data. In this study, we aimed to evaluate 44 subjects under two years of age, who underwent a MBTS procedure between 2009 and

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2013, in order to investigate the risk factors for thrombosis, overshunting and death.

MATERIALS AND METHODS

Forty-four patients under 2 years of age who underwent a MBTS procedure in our hospital between 2009 and 2013 were included in this observational study. The age and weight of the patients at the time of the procedure ranged from 1 day to 20 months (median 12 days), and 2.4 kg to 12 kg (mean 4.6 ± 2.3 kg), respectively. Of the 44 patients diagnosed, either by echocardiography (40 patients) or angiography (4 patients), 14 (31.8%) were diagnosed with Tetralogy of Fallot (TOF), 8 (18.2%) with atrioventricular septal defects with pulmonary stenosis (PS), 7 (15.9%) with transposition of great arteries with PS, 5 (11.4%) with pulmonary atresia (PA) with ventricular septal defect (VSD), 3 (6.8%) with PA with intact ventricular septum, and 7 (15.9%) with miscellaneous complex cardiovascular anomalies. Severely cyanotic newborns with pulmonary stenosis, atresia, duct-dependent circulation and infants with TOF with small pulmonary arteries were recommended for surgery. Prostaglandine E1 infusion was given until the procedure for patients with duct dependent circulation. A 3.5 mm or 4 mm gore-tex shunt (4 mm was often the smallest available shunt in our instutition) was used on patients weighing less than 5 kg, and a 5 mm shunt was used for the rest of the patients. MBTS procedures were performed through a lateral thoracotomy in 18 patients. However, median sternotomy was preferred in premature, low-birth weighted newborns or small infants.

All procedures were performed with no cardiopulmonary bypass. Patent ductus arteriosus (PDA) was ligated in 32 patients, and left open in 12. Subsequently, prostaglandin E1 infusion was terminated after the procedure. Modified Blalock-Taussig shunts were anastomosed to the left pulmonary artery in 30 patients, and to the right in 14; all were anastomosed end to side. The preoperative mean O_2 saturation was 77.5% ± 5.0%, and the postoperative mean O_2 saturation was 86.2% ± 4.7%.

After the procedure, patients were sent to either the newborn or pediatric intensive care unit (ICU), and mechanical ventilation was discontinued as early as possible. Patients were reintubated if significant respiratory distress was observed, or a change in the blood gas parameters was indicated. A therapeutic heparin infusion was administered in 32 subjects, according to the preferences of each unit and/or physician. Dopamine (5 μg/kg/min) and milrinone (0.6 μg/kg/ min) infusion were commenced during the procedure and then slowly reduced in the ICU if the target blood pressure was maintained. All patients were transfused with 1 to 6 packs of red blood cells to maintain a hematocrit level above 40%. Additionally, all patients were given oral acetylsalicylic acid starting on the first postoperative day at 3-5 mg/kg/day.

Overcirculation was diagnosed using the following criteria: 1) structures on the left side of the heart were dilated; 2) the velocity of the diastolic component of continuous flow through the shunt was below 2.5 m/sec; 3) the presence of a prominent pulmonary vasculature on a chest X-ray; 4) the presence of retrograde flow in the descendent aorta; and 5) extubation failure or prolonged intubation.

Preoperative characteristics (12 hours before procedure), hemoglobin (Hb), hematocrit (Hct), mean platelet volume (MPV), prothrombin time (PT), activated partial thromboplastin time (aPTT) and post-operative medication were noted for each patient. Thereafter, risk factors for post-operative overcirculation, thrombosis and death were investigated.

Statistical analysis

Statistical analysis was performed using the SPSS 17.0 package. Continuous variables were shown as mean and standard deviation (SD), or median with range. Categorical variables were shown as number and rate. The Kalmogorov-Smirnov test was used to assess the normality of distribution. The homogeneity of variance was examined in groups with normal distribution. To compare the means of the two groups, the Student's t-test or the Mann-Whitney U test was used. Multivariate analyses was performed to compare the parameters of those patients who did and did not experience shunt thrombosis. Receiver-operating characteristic (ROC) curve was applied to detect the significant predictor values for the occurrence of shunt thrombosis.

RESULTS

Mortality

Of the 44 patients in our study, 8 died after surgery at a median of 8 days (1-31 days), 4 were diagnosed with TOF, 2 patients with PA and IVS, 1 patient with PA and VSD and 1 patient with complex congenital heart disease and severe PS. Overall, the mortality rate was 18.2%. Additionally, 3 patients died due to cardiac decompensation (low cardiac output state) in the early postoperative period (within 48 hours), 2 due to sepsis, 2 due to pneumonia, and 1 due to thrombotic occlusion of the shunt. Risk factors associated with death are depicted in Table 1. Low body weight, presence of preoperative acidosis and a high shunt size/body weight ratio were found to be significant risk factors for mortality.

Thrombosis

Four patients (9.1%) had shunt thrombosis, from which 1 died during shunt revision. Pulmonary arteries were hypoplastic in all four patients (Z-score < –2 SD). However, the sizes of the pulmonary arteries were not statistically different in patients who experienced shunt thrombosis as compared to those who did not. Of the 4 patients, 3 did not receive heparin infusion after the procedure, while 1 had shunt thrombosis on post-operative day 6, despite the immediate 20 U/kg/h heparin infusion given for 24 hours.

The mean aPTT was 28.7 seconds in patients with thrombosis, and 35 seconds for all other patients. Only the aPTT value was significantly lower in patients with shunt thrombosis than in the normal group (p = 0.04). We could not find an association between aPTT and shunt thrombosis in multivariate analysis however, although a aPTT value of < 34,95 predicted the occurance of shunt thrombosis with a sensitivity of 100% and a specificity of 52.5%. Patient characteristics associated with thrombosis are shown in Table 2 and Table 3. Analysis of the ROC curve for the aPTT value revealed an AUC of 0.809 (p = 0.04).

Table 1. Risk factors for death after MBTS procedure

	Death	Alive	p value
Age (months)*	1.04	4.6	0.34
Weight (kg)*	3.3	4.9	**0.005**
Shunt/weight ratio*	1.3	1.03	0.05
MV stay (days)*	10.9	14.1	0.87
Hospital stay (days)*	12.1	23	0.17
ICU stay (days)*	12.1	18.2	0.43
Preoperative acidosis (%)	3/8 (38)	2/36 (6)	0.04
Shunt thrombosis (%)	1/8 (13)	3/36 (8)	0.56
Overcirculation (%)	0/8 (0)	5/36 (14)	0.57
Biventricular hearts (%)	3/8 (38)	16/36 (44)	0.51
Single ventricular hearts (%)	5/8 (63)	20/36 (56)	
Total	8	36	

ICU, Intensive care unit; MV, mechanical ventilation.
* Depicted as mean values.

Table 2. Risk factors for thrombosis after MBTS procedure

	Patients with thrombosis (n: 4)	Others (n:40)	p value
Hemoglobin (gr/dl)*	13.5	14.2	0.54
Hematocrit (%)*	40.5	42.5	0.70
Mean platelet volume (fL)*	8.8	8.07	0.20
aPTT (sec)*	28.7	35.7	0.04
PT (sec)*	13.5	14.2	0.65
Shunt/weight ratio*	1.15	1.08	0.65
Platelet count (/mm^3)*	272000	299000	0.51
Age (months)*	2.72	4.08	0.89
Weight (kg)*	4.7	4.6	0.59
Shunt size (mm)*	4.25	4.33	0.82

* Depicted as mean values.

Table 3. Characteristics of patients with thrombosis

Case	Age (Days)	Weight (kg)	Diagnosis	Time to occlusion (Days)	Size (mm)	ASA after surgery	Heparine infusion after surgery	PDA ligated/not	Intervention	Death
1	3	3.6	PA with VSD	17	4	+	-	not	Evacuation of thrombus	-
2	10	2.7	PA with VSD	10	4	+	-	ligated	Shunt revision	-
3	16	3	AVSD, DORV, PS	2	4	+	-	not	Shunt revision	+
4	300	10	Fallot Tetralogy	6	5	+	+	ligated	Medical therapy	-

AVSD, atrioventricular septal defect; DORV, double outlet right ventricle; PA, pulmonary atresia; PDA, patent ductus arteriosus; PS, pulmonary stenosis; VSD, ventricular septal defect.

Overcirculation

Ultimately, we detected overcirculation in 5 patients. No major aorticopulmonary collateral artery was observed before the shunt procedure, and PDA was ligated in all 5 patients. Two of the patients needed a shunt reduction (banding of the shunt), and inotrope and decongestive therapy was successful in the other three patients. No death was noted due to overcirculation.

Further observation showed that the shunt size/body weight was 1.25 in patients who had overcirculation, and 1.06 in the other patients. However, the difference was not statistically significant.

Follow-up

The median follow-up period for patients in this study was 19 months (1 day-47 months). Of those patients, 5 had early reoperation (3 due to thrombosis and 2 due to overcirculation), and 30 patients underwent a subsequent stage palliative operation or a total repair. The median time between the shunt procedure and a subsequent operation was 10 months (2 days-20 months).

DISCUSSION

In developing countries, systemic and pulmonary shunts are still important palliative procedures for infants with restrictive pulmonary blood flow. Therefore, it is essential to gain more knowledge about the risk factors associated with morbidity and mortality.[4,5]

Our overall mortality rate was 18.4%, which seemed relatively high compared to the existing literature. A review of the literature indicated that published mortality rates vary from 2.3% to 16%.[5] There are several studies that have evaluated outcomes of the procedure. Gladman et al., Rao et al. and Ahmad et al. reported mortality rates of 8.3%, 10.9% and 13.6%, respectively.[9-11] The mean patient age in these studies was a little higher than that in our study, involving the same or smaller number of cases. Williams et al., over the 60-year period of their study, showed an overall mortality rate of 14%, where 2000 cases were examined having a relatively high mean age of 8.3 years.[8] When we analyzed the deaths that occurred in our study, we realized that these cases involved low weight, late and were associated with patients inappropriately transferred with acidosis who otherwise needed urgent surgical intervention. In addition, we believe that common problems in developing countries such as a lack of resources (4 mm was the smallest graft most of the time) and the lack of unity in postoperative management were also factors that affected the mortality rate.[1]

Aortopulmonary shunt operations performed on low weight infants, particularly neonates, are shown to have greater mortality risks.[5,7,9] Similarly, in our study, the mean age was 1.04 months in the mortality group and 4.6 months for all other patients. Among the infants that died, 6 out of 8 were neonates. However, the difference was not statistically significant, probably because of the small case number ($p = 0.34$).

The optimal shunt size for each patient is undecided, and remains to be identified. Dirks et al. associated bigger shunt size with post-operative mortality.[7] Odim et al. reported on the need for a postoperative shunt size reduction, indicating that overcirculation is related to higher mortality rates.[14] In our study, even though the elevated shunt size/weight ratio was associated with mortality, overcirculation was not. This discrepancy prompted us to contemplate that diastolic run off, which caused impaired coronary and systemic circulation in particular cases, was the primary underlying pathophysiology for death rather than overcirculation.

Shunt thrombosis is a fatal complication following MBTS procedure with an unknown etiology. In this study, we did not ascertain any relationship between shunt size and shunt thrombosis. Several studies have shown similar findings,[15,16] while others have reported that small shunt size is associated with a higher risk of shunt thrombosis.[6,12,13]

In our study, we investigated whether or not there is a link between shunt thrombosis and hemoglobin, hematocrit, platelet count, PT, aPTT, age, weight, MPV, shunt/weight ratio and shunt size (Table 2). We found that only low aPTT was associated with shunt thrombosis. Some reports showed that young age and smaller shunt size are associated with shunt thrombosis,[12,17] while others concluded that young age is not related to shunt occlusion.[6] In our study, 3 out of 4 patients with thrombosis were neonates; however, we could not find an association between young age, shunt size and thrombosis, which was possibly due to the small number of cases.

Mean platelet volume is generally known to be an important determinant of thrombotic state.[18,19] We could not find any report that examined the relationship between preoperative MPV and shunt thrombosis. In our study, we investigated whether MPV was higher in patients who had shunt thrombosis. We ultimately found that MPV was higher in patients with shunt thrombosis, but the difference was not statistically significant.

A low aPTT or PT can be a sign of a hypercoagulable state. Guzzeta et al. found preoperative and postoperative aPTT values lower in patients who had shunt thrombosis than in those who did not.[6] In our study, the mean aPTT was 28.7 seconds in patients with thrombosis, and 35 seconds in the rest. The aPTT value was significantly lower in patients who experienced shunt thrombosis than in those who did not ($p = 0.04$). We could not find an association between aPTT and shunt thrombosis in the multivariate analysis. However, we believe this would be due to the small number of patients who experienced shunt thrombosis. Interestingly, an aPTT value < 34.95 predicted the occurrence of shunt thrombosis with an excellent level of sensitivity (100%).

Today, there are no tests employed that assess patients' preoperative coagulation state. Therefore, our study suggests that aPTT could be used as a screening test. When a patient is determined to have low aPTT, more sophisticated coagulation tests or specific gene mutation analyses (factor V Leiden, prothrombin 20210 mutation, etc.) could be performed. For example, classic central shunts could be utilized instead of polytetrafluoroethylene (PTFE) grafts in patients with a risk of hypercoagulation, or these patients could receive long-term anti-aggregant and anticoagulant therapeutic regimens after the MBTS procedure.

CONCLUSIONS

MBTS operation is generally considered to be a good option when total correction is impossible in infants with cyanotic heart disease. Therefore, it is important to assess risk factors associated with the procedure. A preoperative low aPTT value may be an indicator for thrombosis in infants who have undergone MBTS surgery. Accordingly, further investigation is necessary in order to better define the relationship between MPV and shunt thrombosis.

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