MODIFIED BLALOCK-TAUSSIG SHUNT ----IN-HOSPITAL SHUNT OCCLUSION: EXPERIENCE AT NICVD

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Objectives: The clinical variables leading to postoperative thrombotic occlusion of a modified Blalock-Taussig shunt (mBTS) remain obcsure. In this study, we assess several peri-operative variables to determine association with postoperative in-hospital shunt occlusion.

Methods.: We retrospectively reviewed the medical records of children receiving a mBTS as a first operation between January 1, 2010 and December 31, 2013. Numerous perioperative variables were collected, focusing on those that would increase resistance to blood flow through the shunt or alter coagulation.

Results: In all, 207 children fit our criteria. In-hospital shunt occlusion occurred in 14 patients (6.8%); 3 patients (21.4%) subsequently died during their hospitalization. Pulmonary atresia/ventricular septal defect with or without major aortopulmonary collateral arteries was the most common diagnosis associated with shunt occlusion (57.1%). Of the collected perioperative variables, pulmonary artery size was significantly associated with shunt occlusion(p =0.03). Preoperative coagulation values were significantly reduced in those patients who experienced shunt occlusion. Additionally, the immediate postoperative activated partial thromboplastin time was significantly reduced in the occlusion group although values remained well above normal as all were treated postoperatively with a heparin infusion.

Conclusion: We found that a patient's anatomy (pulmonary atresia/ventricular septal defect with or without major aortopulmonary collateral arteries) and the size of the pulmonary artery being shunted had a significant impact in predicting postoperative in-hospital shunt occlusion. These results emphasize that technical skills and a low resistance to blood flow are necessary for successful shunt function. Although some perioperative coagulation values were significantly reduced in those who were destined to experience shunt occlusion, they would be difficult to detect clinically.

Key Words: Modified, Blalock-Taussig shunt, shunt occlusion, cardiac surgery, pulmonary artery.

PJC 2014; 25: 31-39

INTRODUCTION

Systemic-to-pulmonary artery shunts were first described by Blalock-Taussig (BT) in 1945[1] (subclavian to pulmonary artery shunt), Potts in 1946[2] (descending aorta to left pulmonary artery shunt), and Waterston-Cooley in 1962[3] and 1966[4] (ascending aorta to right pulmonary artery shunt).

A modified Blalock-Taussig shunt (mBTS) is a surgically placed graft between the systemic and pulmonary arterial circulations that redirects systemic blood flow into the pulmonary circulation. It is often placed in those with right-sided obstructive cardiac defects to increase pulmonary blood flow. Postoperative shunt patency is critical to adequate systemic oxygenation. Nevertheless, in the immediate hours after placement of a mBTS or before hospital discharge, a child may experience an episode of profound hypoxia and even cardiac arrest as a result of clotting of the shunt and consequent loss of pulmonary blood flow. Even with the use of aggressive postoperative anticoagulation therapy, thrombotic occlusion of a mBTS occurs in 3% to 9%[5-9]. Despite previous studies, the clinical

variables predictive of postoperative shunt occlusion remain elusive[9-11]. In this retrospective investigation, we analyze perioperative variables that might contribute to early postoperative in-hospital shunt occlusion in those receiving a shunt.

METHODS

After Institutional Review Board approval, a retrospective chart review was performed on all patients receiving mBTS as a first operation between January 1, 2010 and December 31, 2013. Patients undergoing a surgical procedure other than pulmonary arterioplasty and ligation or division of a patent ductus arteriosus at the same time as placement of the mBTS were excluded from this study.

Intraoperatively all patients received a heparin bolus of 100 units/kg before shunt placement when performed without cardiopulmonary bypass (CPB). Clamp time was defined as the time from subclavian or innominate artery occlusion to the opening of the shunt and is used as an indication of the surgical time required to place the shunt. Heparin was not neutralized by protamine at the end of the procedure.

Gore-Tex expanded polytetrafluoroethylene (PTFE) grafts (W.L. Gore & Assoc, Flagstaff, AZ) were used on all patients receiving synthetic shunts. Our standard mBTS size (and the smallest size available) is 4mm although deviations occur based on patient size and the surgeon's discretion. A 4.0 mm shunt is often be used for neonates who weigh less than or equal to 4kg and a 5.0 mm shunt if greater than 4.0 kg. Postoperatively, after bleeding subsided, all patients were placed on a heparin infusion at 10 units / kg/ h until transfer from the intensive care unit. Subsequently, all patients received a daily oral dose of 40 mg aspirin.

The primary endpoint of this investigation was postoperative in-hospital shunt occlusion defined by clinical scenario (acute hypoxia and loss of shunt murmur) and echocardiographic evidence of poor shunt flow or angiographic evidence of significant shunt narrowing. Data collection for patients experiencing shunt occlusion ceased at the time of occlusion.

Numerous preoperative, intraoperative, and postoperative variables were recorded (Table I). To direct our search, we considered factors that would either increase the resistance of blood flow through the shunt or contribute to postoperative thrombosis by affecting one or more of the elements of Virchow's triad: stasis, endothelial injury, and hypercoagulability.[8]

Perioperative factors contributing to the resistance of blood flow through the shunt were evaluated by the size of the shunt, size of the vessel being shunted (measured by the preoperative transthoracic echocardiogram), and postoperative hemoglobin levels. Virchow's triad was evaluated by evidence of low cardiac output or perioperative lactate values, endothelial damage by examining operative notes for technical issues encountered during the procedure, and multiple perioperative coagulation values.

Statistical Analysis

All statistical analyses were performed using SAS 9.3 statistical software (SAS Institute, Cary, NC). Statistical significance was assessed using an alpha level of 0.05.

RESULTS

Two hundred seven patients received mBTS as a first operation during the study period. The mean age was 2.7 ± 0.9 years and the mean weight was 4.8 ± 0.9 kg. Fourteen patients (6.8%) experienced shunt occlusion, and 15 (7.2%) died before hospital discharge.

Although cardiac diagnosis was not significantly associated with shunt occlusion ($p = 0.06$), the diagnosis of pulmonary

TABLE-I: PREOPERATIVE, INTRAOPERATIVE, AND POSTOPERATIVE DATA COLLECTION

Preoperative	Intraoperative	Postoperative
Age	BT shunt size	Competitive source of PBF
Weight	Clamp time[b]	C-reactive protein
Sex	Concurrent pulmonary arterioplasty	Lactate
Diagnosis	Need for CPB	pRBCs transfused[c]
Prematurity[a]	pRBCs transfused	
Chromosomal		
abnormalities		
Cardiac		
catheterization		
Presence of CVL		
Size of PA to receive		
shunt		
C-reactive protein		
Lactate		
pRBCs transfused		

[a] Defined as less than 36 weeks. [b] Defined as time from subclavian/innominate artery occlusion to opening of Blalock-Taussig shunt. [c] Packed red blood cells (pRBCs) transfused for the first 24 hours postoperatively or until the time of shunt occlusion.
BT=Blalock-Taussig; CPB=cardiopulmonary bypass; CVL= central venous line; PA= pulmonary artery; PBF= pulmonary blood flow.

atresia/ventricular septal defect with or without major aortopulmonary collateral arteries accounted for 57% of patients experiencing shunt occlusion versus 18.1% in the no-occlusion group. The second most common diagnosis in the occlusion group was tetralogy of Fallot (n = 2; 14%). In 8 of the 14 patients with shunt occlusion, the underlying cause was probably technical because patients responded either to surgical revision in the operating room (n = 5), placement of a stent in the catheterization laboratory (n = 1), conversion to a Sano shunt (n = 1), or a complete repair (n = 1). Of the remaining 6, shunt occlusion may have been more of a primary thrombotic event as 4 responded to stripping the shunt and 2 to angioplasty. Only 3 of the 14 occlusion patients (21.4%) died during their hospitalization. Postoperative outcome data are shown in Table II. Patients who had shunt occlusion had a longer ventilator times and intensive care unit stays and a higher rate of in-hospital mortality.

Of all collected perioperative variables (Tables III, IV, and V), only one showed a statistically significant association with shunt occlusion: the size of the pulmonary artery being shunted (p = 0.03). The postoperative transfusion of RBC, and preoperative C-reactive protein (CRP) levels were all numerically greater in the occlusion group versus the no-occlusion group but did not reach statistical significance (p =0.06,p =0.12, and p = 0.47, respectively). Further analysis of native PA size identified a threshold value of approximately 4.0 mm that maximally separated the two groups.

Preoperative prothrombin time, international normalized ratio (INR), and activated partial thromboplastin time (aPTT) values were significantly reduced in patients whose shunts occluded. The immediate postoperative aPTT was also significantly reduced in these patients. No other significant differences were found.

TABLE-II: POSTOPERATIVE OUTCOME VARIABLES

Variable	No Occlusion (n = 193)	Occlusion (n = 14)	p Value
Ventilator time, hours	71 ±80	139 ± 105	0.02
Intensive care unit stay, days	7±8	11±5	0.001
In-hospital mortality	12 (6.2)	3 (21.4)	0.034

Values expressed as mean±SD or total (%).

TABLE-III: COLLECTED PREOPERATIVE VARIABLES

Preoperative Variable	No Occlusion (n =193)	Occlusion (n = 14)	p Value
Age, years	2.7 ±0.9	3.1 ± 0.5	0.23
Weight, kg	4.5 ± 0.7	5.7 ± 1.0	0.38
Male	111 (57.5)	10 (71.4)	0.31
Prematurity	49 (25.4)	1 (7.1)	0.12
Chromosomal abnormality	18 (9.3)	2 (14.3)	0.54
Cardiac catheterization	75 (38.9)	6 (42.9)	0.77
Presence of central venous line	125 (64.8)	7 (50)	0.27
Size of pulmonary artery shunted, mm	5.3 ±1.0	4.5 ±0.8	0.03
C-reactive protein, mg/dL	1.1 ± 1.5	3.3 ± 3.6	0.47
Lactate, mg/dL	11.2 ± 5.1	9.5 ±5.3	0.32
pRBC transfusion, mL/kg	13 ± 19	19 ± 23	0.23

Values expressed as mean ±SD or total (%). Normal reference ranges: CRP <1.0 mg/dL; lactate 4.5 to 19.8 mg/dL. CRP = C-reactive protein; pRBC = packed red blood cells.

DISCUSSION

Prosthetic shunt obstruction is not uncommon. Causes of ePTFE shunt failures include thrombosis, neointimal proliferation at the anastomosis, and pulmonary artery distortion or stenosis related to the fixed length of a prosthetic tube. Shunt thrombosis is the most common complication associated with pediatric shunts. Incidence of thrombotic occlusions in ePTFE shunts has been reported to range from 0 – 13%, and may occur early (0 – 30 days) or late (> 30 days). Clinical predictors leading to this occurrence remain unclear.

In this investigation, we focused our analysis on clinical variables that either contribute to increased resistance of blood flow through the shunt or affect one of the three components of coagulation as outlined in Virchow's triad (stasis, endothelial injury, hypercoagulability). We

TABLE IV. COLLECTED INTRAOPERATIVE VARIABLES

Intraoperative Variable	No Occlusion (n = 193)	Occlusion (n =14)	p Value
Blalock-Taussig shunt size			
4.0 mm	163 (84.5)	10 (72)	
5.0 mm	23 (12)	2 (14)	0.20
6.0 mm	7(3.6)	2 (14)	
Clamp time, minutes	35±12	35 ± 6	0.93
Concurrent pulmonary arterioplasty	36 (18.7)	5 (35.7)	0.12
Need for cardiopulmonary bypass	20 (10.4)	1 (7.1)	0.7
Packed red blood cell transfusion, mL/kg	41±62	34±25	0.68

Values expressed as mean± SD or total (%).

TABLE V. COLLECTED POSTOPERATIVE VARIABLES

Postoperative Variable	No Occlusion (n = 193)	Occlusion (n = 14)	p Value
Competitive source of pulmonary blood flow	96 (49.7)	7 (50)	0.99
C-reactive protein, mg/dL[a]	6.9 ± 6.5	7.6 ±5.5	0.78
Lactate, mg/dL	20.9 ± 11.4	15.7 ± 5.2	0.12
Packed red blood cells transfusion, mL/kga	22 ± 62	63 ± 99	0.06

Values expressed as mean ± SD or total (%). Normal reference ranges: CRP <1.0 mg/dL; lactate 4.5 to 19.8 mg/dL.
CRP = C-reactive protein.

assessed resistance by considering Poiseuille's Equation: R = lh/r4 (where R =resistance, l = length, h = viscosity, and r = radius). The length of the shunt was dictated by the patient's anatomy and thus not measured in the operating room. Blood viscosity was assessed by analyzing postoperative hemoglobin values and the postoperative transfusion of RBC. Hemoglobin levels measured immediately postoperatively and on postoperative day 1 showed no difference between the occlusion and no-occlusion groups. However, the transfusion of RBC over the first 24 postoperative hours tended to be greater in those whose shunts occluded. To examine the effect of radius, we documented the size of the shunt and measured by preoperative transthoracic echocardiogram the size of the pulmonary artery receiving the shunt. Of these two variables, the size of the pulmonary artery was statistically significantly associated with postoperative occlusion.

PJC Vol 25, No. 1 & 2
January — June 2014

The optimal size for mBTS has been a source of considerable debate. Smaller shunts have been associated with an increased risk of thrombotic occlusion[9,13]. Tsai and associates[9] reported on 86 patients of all ages undergoing mBTS placement. Ten patients had postoperative shunt failure; 4 had confirmed thrombotic occlusion. They found that a younger age and a smaller shunt size were associated with shunt failure. However, other studies have not consistently found this association[10,14]. Our data, too, show no relationship between shunt size and the occurrence of postoperative thrombosis. Pulmonary artery size may be the more important variable as initially the shunt is larger than the size of the native pulmonary artery into which it is sewn. Al Jubair and associates[8] found that shunt failure was more common if the pulmonary artery diameter was less than 4 mm. Our analysis agrees with their conclusion. The optimal material for a shunt has also been debated. Some investigators favor SVG in lieu of the more standard synthetic PTFE material[15,16]. This is a reasonable conclusion because PTFE is a highly electronegative material and coagulation is supported on negatively charged surfaces.

We also attempted to evaluate factors contributing to coagulation by affecting the elements of Virchow's triad. Lactate values, representing low cardiac output and stasis, were similar between the two groups. Endothelial injury is a foregone conclusion during surgery and occurs from arteriotomy and suture lines at either end of the shunt. Technical issues regarding shunt construction are critical. Eight of the 10 patients (80%) in the occlusion group who underwent shunt revision, either in the operating room or cardiac catheterization laboratory, or complete repair immediately after occlusion and were successfully discharged from the hospital. This result suggests that technical issues are an important variable and may coincide with small pulmonary artery size.

Another important fact elucidated by our data is that, in today's environment, postoperative in-hospital shunt occlusion does not necessarily result in mortality. Only 21.4% of the patients who had shunt occlusion subsequently died in the hospital. Surgical revision, the use of extracorporeal membrane oxygenation, and other catheter-based interventions are proving to be lifesaving for these patients when promptly and effectively instituted by a coordinated care team. Regarding hyperviscosity, Sahoo and colleagues[17] showed that hemodilution to a hematocrit of 45% resulted in improved shunt patency in the immediate postoperative period. Our investigation provides some evidence that hyperviscosity is detrimental to shunt flow in that the postoperative transfusion of RBCs tended to be greater in the occlusion group.

Current evidence supports the existence of an intimate relationship between inflammation and thrombosis[18-20] The acute-phase response protein CRP is highly involved in inflammatory processes and possesses substantial prothrombotic properties[21]. In a recent article, Cholette and associates[22] identified an association between elevated preoperative CRP levels and an increased postoperative thrombotic risk in those undergoing initial palliative surgery. In this investigation we, too, found that those whose shunt occluded postoperatively entered the operating room with numerically higher, although not statistically significant, CRP levels. Our data are limited in that CRP levels were not consistently measured preoperatively in all patients. Nevertheless, we believe that the association of elevated preoperative CRP levels with postoperative thrombosis deserves further inquiry.

A hypercoagulable state may occur postoperatively secondary to activation of the coagulation system during surgery. Ahmad and associates[5] suggest that careful monitoring of the coagulation profile should be performed postoperatively to aid in the detection of sudden shunt thrombosis. However, they do not expound on which coagulation values to follow nor do they

provide evidence of abnormal values in those experiencing shunt occlusion. Our study suggests that postoperative monitoring of routinely performed coagulation values does little to help detect, and subsequently prevent, postoperative shunt thrombosis. Although the aPTT measured immediately postoperatively was significantly reduced in children who experienced shunt occlusion compared to those who did not, both groups had abnormally prolonged values because all patients were routinely placed on a heparin infusion postoperatively. Thus it is hard to know the numeric threshold that would indicate a hypercoagulable state or be predictive of shunt thrombosis. Our results suggest that the coagulation tests commonly employed for monitoring these patients postoperatively are too insensitive to be of value. More sophisticated coagulation tests, such as thrombelastography or thrombin generation assays, might prove more useful. Interestingly, the preoperative prothrombin time, INR, and aPTT of those who had postoperative shunt thrombosis were also reduced compared to those who did not. Again, it would prove challenging to accurately identify these patients prospectively because the reduction was minimal.

Limitations of this study include its retrospective design and lack of data regarding late shunt occlusion after hospital discharge. We intentionally eliminated patients undergoing complex reconstructive surgery such as a Norwood stage I palliation at the time of mBTS placement. Early and late shunt occlusion has been extensively examined in these patients[23-25] so we chose to concentrate on patients undergoing a mBTS as a sole procedure. Although we sought to define shunt occlusion with objective evidence, the "true" incidence of shunt occlusion in our patient population is unknown. Additionally, none of the patients who had shunt occlusion underwent formal hypercoagulation testing; thus we are unaware whether there was any genetic predisposition to thrombosis in the occlusion group. A final limitation of this study is the small sample size. The lack of power and the rarity of the primary outcome (only 14 had shunt occlusion) may be responsible for our inability to show a statistically significant difference in many of the collected perioperative variables between the two groups.

CONCLUSION

Current methods to address shunt thrombosis are preventative (anti-platelet or anti-coagulant therapy) and corrective (surgical or catheter-based shunt revisions). Anti-platelet therapy includes long-term postoperative administration of aspirin or clopidogrel. Anti-coagulants such as intravenous heparin has also been used to lower the risk of shunt thrombosis. Despite these preventative strategies, shunt thrombosis remains a significant cause of morbidity and mortality. Corrective procedures for chronic shunt thrombosis may involve a second planned or unplanned intervention with surgery, thrombolysis, mechanical thrombectomy, balloon angioplasty, or stent implantation.

A child's anatomy has an impact on the occurrence of postoperative in-hospital shunt occlusion. The presence of small pulmonary arteries may heighten the incidence of postoperative shunt occlusion either because of technical issues or by increasing the resistance to blood flow through the shunt. Excessive postoperative transfusion of RBC may also contribute to an increased resistance to flow and consequent shunt occlusion. Additionally, although not statistically significant, those who had shunt occlusion had numerically elevated preoperative CRP levels. Preoperative prothrombin time, INR, and aPTT values were reduced in children who had shunt occlusion. Although these values may in theory be capable of detecting at-risk children, they were still within a normal range, making it extremely difficult to prospectively identify these children. Despite a reduction in the aPTT value immediately postoperatively, routine postoperative coagulation values were still prolonged outside of

the normal range and thus unable to reliably aid clinicians in detecting which patients are destined to have occlusion.

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