Outcomes of Primary Bidirectional Glenn in Children with Single Ventricle Physiology and Increased Pulmonary Blood Flow

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ABSTRACT

Background: We reported our experience in managing patients with single ventricle (SV) physiology and increased pulmonary blood flow (PBF), aiming to assess if it is feasible to proceed with primary Bidirectional Glenn (BDG) without a prior operation to limit PBF.

Materials and methods: This is a retrospective study with 51 consecutive patients who underwent BDG operation as a primary operation or a second stage prior to the definitive Fontan operation at King Abdulaziz University Hospital (KAUH) in Jeddah, Saudi Arabia between 2010 and 2018. Patients were categorized into two groups based on their PBF prior to the operation: Patients who had SV physiology and increased PBF (seven patients) vs. patients with SV physiology and restricted PBF (44 patients).

Results: The median age for the increased PBF group was 9.9 months [interquartile range (IQR): 2-16.9 months], and the median age for the restricted PBF group was 15.3 months (IQR: 6.7-42.6 months). Although the length of hospital stay was longer in patients with increased PBF (P = 0.039), we couldn’t find a statistically significant difference in early mortality, duration of mechanical ventilation, length of pleural drainage, and length of intensive care unit (ICU) stay between the groups.

Conclusion: In our experience, we found that primary BDG could be done safely for patients having SV physiology and increased PBF with acceptable short-term outcomes. It might further reduce the morbidity and mortality for those patients by avoiding the risk of initial pulmonary artery banding or aortopulmonary shunts.

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to evaluate the clinical characteristics, the outcomes and the factors affecting the outcomes for all patients who underwent BDG, during the study period at our institution.

MATERIALS AND METHODS

We retrospectively reviewed all patients who underwent BDG operation as a primary operation or a second stage prior to the definitive Fontan operation at King Abdu-laziz University Hospital (KAUH) in Jeddah, Saudi Arabia between 2010 and 2018. Approval of this study was obtained from the Research Ethics Board at our institution, and consent for the surgical procedures was obtained from each patient. The requirement for individual consent was waived for this observational study.

Demographic, clinical, operative, catheterization, echocardiographic and outcome data were collected from hospital medical records and the cardiac surgical database.

The patients were categorized into two groups, based on their PBF prior to the operation: patients who had SV physiology and increased PBF versus patients with SV physiology and restricted PBF. The patients were considered to have increased PBF if they had clinical manifestation of heart failure, chest x-ray was showing pulmonary congestion, and echocardiogram was revealing unobstructed PBF with pressure gradient less than 30 mmHg across right ventricular outflow tract.

The findings from the most recent echocardiogram done before the BDG operation were reviewed. Ativoventricular valve (AVV) regurgitation was graded as severe, moderate, mild, or absent, based on pulse wave tracing and color Doppler mapping.

Data from the most recent cardiac catheterization performed before the BDG operation was reviewed. Measurements included ventricular end-diastolic pressure (VEDP), mean PA pressure, indexed pulmonary vascular resistance (PVRI), and pulmonary venous wedge pressure. Preoperative and postoperative oxygen saturations were noted.

Surgical details were recorded, including cardiopulmonary bypass time (CPB) and aortic cross-clamp time. Also, we documented the procedures that were done prior to BDG procedure, such as the Norwood procedure, patent ductus arteriosus (PDA) stent, PAB, or a previous Blalock-Taussig (BT) shunt and simultaneous procedures done at the time of the BDG procedure, such as PA plasty, AVV repair and atrial septectomy.

Early postoperative hemodynamic data was noted, including superior vena cava (SVC) pressure (through internal jugular or subclavian central lines). Inotropes and vasoactive medications were recorded at an hourly interval during the first 24 hours after admission to postoperative intensive care unit (ICU). In the current analysis, the inotropic score (IS) was calculated as per Wernovsky [Wernovsky 1995] and the Vasoactive-Inotropic Score (VIS) as described by Gaies et al. [Gaies 2014] and Davidson et al. [Davidson 2012].

\[ IS = \text{Dopamine dose (μg/kg/min)} + \text{Dobutamine dose (μg/kg/min)} + 100 \times \text{epinephrine dose (μg/kg/min)} \]

\[ VIS = IS + 10 \times \text{Milrinone dose (μg/kg/min)} + 10,000 \times \text{Vasopressin dose (U/kg/min)} + 100 \times \text{Norepinephrine dose (μg/kg/min)} \]

Postoperative outcome data included the total duration of mechanical ventilation, duration of pleural drainage, ICU stay, total hospital stay, VIS, morbidity, and mortality. The duration of chest tube drainage was determined by the day on which all the intraoperative chest tubes were removed. Morbidity was determined by the existence of a complication, such as early postoperative intervention, delayed chest closure, diaphragmatic paralysis and chylous effusion that required dietary changes to a low-fat diet.

Statistical analysis: Statistical analysis using "IBM SPSS statistics ver. 20.0" and "Excel 2013" was applied to test the hypothesis. Descriptive statistics were done to calculate means, Std. Deviation, median and interquartile range (IQR). Shapiro-Wilk test was used to test the normality of the study sample variables. Pearson’s correlation was used to identify the strength and direction of relationship that present between two or more variables. Independent Sample T-Test / Mann-Whitney tests were applied to find if there was a significant difference between two groups and Chi-square test was used to find the significant association between categorical variables.

RESULTS

Patients characteristics: Fifty-one consecutive patients underwent BDG at KAUH from 2010 to 2018. The median age at the time of BDG was 15.2 months (IQR: 6-41.8 months), and the median weight was 8 kg (IQR: 5.9-11kg). Six patients (11.8%) were less than four months of age and three patients (5.9%) were less than 4 kg at the time of the operation.

Preoperative evaluation: The most common anatomic subtypes were tricuspid atresia in 23.5%, unbalanced atrioventricular septal defect (UAVSD) in 17.6%, double outlet right ventricle (DORV) in 17.6%, double inlet left ventricle (DILV) in 11.8%, hypoplastic left heart syndrome (HLHS) in 5.9%, or other in 23.5%. Patient diagnoses are summarized in Table 1. (Table 1)

Twenty-seven patients (52.9%) had no previous palliation, whereas the remaining 24 patients (47.1%) had a previous palliation, such as PDA stent (N = 12), Norwood operation (N = 6), aortopulmonary shunt (N = 3), PAB (N = 2), and atrial septostomy (N = 1).

Anatomically, 20 patients (39.2%) had a morphologic single left ventricle (LV), 14 patients (27.5%) had a morphologic single right ventricle (RV), and 17 patients (33.3%) had either two ventricles that could not be partitioned or indeterminate SV. Morphology AVV function was normal in 72.5%, whereas insufficiency was identified as mild in 13.7%, moderate in 9.8%, and severe in 3.9%.

Preoperative catheterization was performed in 34 patients (66.7%). Median PA pressure was 18 mmHg, median PVRI

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was 0.9 Woods unit (WU).m² and median VEDP was 15 mmHg (IQR: 10-17 mmHg).

Operative data: Forty patients underwent unilateral BDG, whereas bilateral BDG was performed in 10 patients with bilateral SVC and one patient had Kawashima procedure. The most common additional procedures performed included atrial septectomy (N = 20), pulmonary arterioplasty (N = 14), AVV repair (N = 2), ventricular septal defect (VSD) enlargement (N = 1) and total anomalous pulmonary venous return (TAPVR) repair (N = 3). The operative details for each group are represented in Table 2. (Table 2)

Outcome data: Hemodynamic studies showed a median postoperative SVC pressure of 18 mmHg (IQR: 13-21 mmHg). Arterial oxygen saturation rose from 81% (IQR: 73-87%) preoperatively to 86% (IQR: 84-90%) postoperatively.

The median postoperative VIS was 9.5 on postoperative 24 hours. The median duration of pleural drainage was five days (IQR: 4-7 days). The median duration of mechanical ventilation was 10 hours (IQR: 6-23.75 hours). The median duration of stay in the ICU and hospital was four days (IQR: 2-6.75 days) and eight days (IQR: 6-13 days), respectively.

Three patients needed early postoperative interventional cardiac catheterization, one patient for Glenn stenting, one patient for right pulmonary artery stenting, and another patient for small left SVC coil occlusion. In addition, three patients needed surgical intervention for PAB tightening, plication of the diaphragm, and permanent pacemaker insertion. Two patients had delayed chest closure. Postoperatively, eight patients had chylous effusion (15.7%), and three patients had diaphragmatic paralysis (5.9%). One of the patients needed}

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**Table 1. Preoperative data of patients who underwent bidirectional Glenn**

<table>
<thead>
<tr>
<th></th>
<th>Increased PBF (N = 7)</th>
<th>Restricted PBF (N = 44)</th>
<th>All Patients (N = 51)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)*</td>
<td>9.9 (2 – 16.9)</td>
<td>15.3 (6.7 – 42.6)</td>
<td>15.2 (6-41.8)</td>
<td>0.082</td>
</tr>
<tr>
<td>Weight (kg)*</td>
<td>6.3 (4.5-9.4)</td>
<td>8.4 (6.1-12.5)</td>
<td>8 (5.9-11)</td>
<td>0.232</td>
</tr>
<tr>
<td>Oxygen saturation before BDG (%)*</td>
<td>87 (75-92)</td>
<td>80 (73-86)</td>
<td>81 (73-87)</td>
<td>0.163</td>
</tr>
<tr>
<td>Diagnosis (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TA</td>
<td>3 (42.9%)</td>
<td>9 (20.5%)</td>
<td>12 (23.5%)</td>
<td></td>
</tr>
<tr>
<td>DILV</td>
<td>1 (14.3%)</td>
<td>5 (11.4%)</td>
<td>6 (11.8%)</td>
<td></td>
</tr>
<tr>
<td>DORV, VSD, PS</td>
<td>-</td>
<td>9 (20.5%)</td>
<td>9 (17.6%)</td>
<td></td>
</tr>
<tr>
<td>UAVSD</td>
<td>1 (14.3%)</td>
<td>8 (18.2%)</td>
<td>9 (17.6%)</td>
<td></td>
</tr>
<tr>
<td>HLHS</td>
<td>-</td>
<td>3 (6.8%)</td>
<td>3 (5.9%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2 (28.6%)</td>
<td>10 (22.7%)</td>
<td>12 (23.5%)</td>
<td></td>
</tr>
<tr>
<td>Morphology of the dominant ventricle (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV</td>
<td>4 (57.1%)</td>
<td>16 (36.4%)</td>
<td>20 (39.2%)</td>
<td></td>
</tr>
<tr>
<td>RV</td>
<td>-</td>
<td>14 (31.8%)</td>
<td>14 (27.5%)</td>
<td></td>
</tr>
<tr>
<td>Indeterminate</td>
<td>3 (42.9%)</td>
<td>14 (31.8%)</td>
<td>17 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>Diagnostic catheterization before BDG (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PA pressure (mmHg)**</td>
<td>56 (25-62)</td>
<td>17.5 (5-24)</td>
<td>18 (5-62)</td>
<td>0.002</td>
</tr>
<tr>
<td>PVRI (WU.m²)**</td>
<td>2.3 (1.1-2.9)</td>
<td>0.9 (0.4-2.9)</td>
<td>0.9 (0.4-2.9)</td>
<td>0.025</td>
</tr>
<tr>
<td>VEDP (mmHg)*</td>
<td>15 (15-21)</td>
<td>13 (10-17)</td>
<td>15 (10-17)</td>
<td>0.245</td>
</tr>
<tr>
<td>The patients underwent intervention prior to BDG (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDA Stent</td>
<td>-</td>
<td>12 (27.3%)</td>
<td>12 (23.5%)</td>
<td></td>
</tr>
<tr>
<td>Norwood</td>
<td>-</td>
<td>6 (13.6%)</td>
<td>6 (11.8%)</td>
<td></td>
</tr>
<tr>
<td>BT Shunt</td>
<td>-</td>
<td>3 (6.8%)</td>
<td>3 (5.9%)</td>
<td></td>
</tr>
<tr>
<td>PA Band</td>
<td>-</td>
<td>2 (4.5%)</td>
<td>2 (3.9%)</td>
<td></td>
</tr>
<tr>
<td>Septostomy</td>
<td>-</td>
<td>1 (2.3%)</td>
<td>1 (2.0%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>-</td>
<td>24 (45.4%)</td>
<td>24 (47.1%)</td>
<td></td>
</tr>
</tbody>
</table>

BDG, bidirectional Glenn; BT, Blalock-Taussig; DILV, double inlet left ventricle; DORV, double outlet right ventricle; HLHS, hypoplastic left heart syndrome; PA, pulmonary artery; PBF, pulmonary blood flow; FAD, patent ductus arteriosus; PS, pulmonary stenosis; PVRI, pulmonary vascular resistance index, RV right ventricle; TA, tricuspid atresia; UAVSD, unbalanced atrioventricular septal defect; VEDP, ventricular end-diastolic pressure, WU; Woods unit. *Median (interquartile range); **Median (minimum-maximum)
diaphragmatic placation. Early postoperative mortality following BDG was two patients (3.9%).

The PA pressure had significant positive correlation with the duration of pleural drainage ($P = 0.013$), but it was not correlated with the duration of mechanical ventilation, the length of ICU stay, or hospital stay. VIS at 24 hours postoperatively was positively correlated with duration of mechanical ventilation ($P = 0.013$) and ICU length of stay ($P = 0.029$).

Two group comparison: Among the 51 patients who underwent BDG procedure, seven patients had increased PBF at the time of the surgery and a primary BDG was performed for them. The remaining 44 patients had restricted PBF as an initial congenital cardiac lesion or after previous surgical intervention like PAB, BT shunt or Norwood procedure. (Table 1)

The median age for the increased PBF group was 9.9 months (IQR: 2-16.9 months), the age of three out of seven patients in this group was less than three months at the time of BDG (35, 62 and 78 days). On the other hand, the median age for the restricted PBF group was 15.3 months (IQR: 6.7-42.6 months).

In SV physiology and increased PBF group, four patients had cardiac catheterization before BDG procedure. The other three patients, who were less than three month old, had manifestations of heart failure, high oxygen saturations and lung plethora (in chest x-ray) which indicate low PVR. Accordingly, they underwent primary PBG based on the clinical evaluation without cardiac catheterization.

The PA pressure was significantly higher in patients with increased PBF than those with restricted PBF ($P$-value was 0.002). The median PVRI in the patients with restricted PBF was 0.9 WU.m$^{-2}$ (range from 0.4 to 2.9 WU.m$^{-2}$), and the median PVRI for patients with increased PBF was 2.3 WU.m$^{-2}$ (range from 1.1 to 2.9 WU.m$^{-2}$), which is significantly higher than patients with restricted PBF ($P$-value was 0.025).

We compared the short-term outcome of the two groups, and we found that initial ICU hemodynamic data was very similar. Median postoperative SVC pressure was 17 mmHg (IQR: 10-23 mmHg) in the increased PBF group and 18 mmHg (IQR: 13-21 mmHg) in the restricted PBF group ($P = 0.85$). Median postoperative arterial oxygen saturation was 86% (IQR: 84-94%) and 87% (IQR: 84-90%) in increased PBF group and restricted PBF group, respectively ($P = 0.555$).

The maximum VIS after 24 hours postoperatively was not significantly different in both groups, $P$-value was 0.473. Postoperatively, one patient from each group needed inhaled nitric oxide as a pulmonary vasodilator. In addition, one patient from each group had delayed chest closure. Throughout the hospital stay, two patients (28.6%) from the increased PBF group developed postoperative chylos drainage and six patients (13.6%) from the restricted PBF group.

There was one postoperative mortality from each group; this does not represent a statistical significance. The data for duration of mechanical ventilation, length of ICU stay, length of hospitalization, and length of pleural drainage are presented in Table 3. (Table 3) Although the length of hospital stay was longer in the increased PBF group ($P = 0.039$), we could not find a statistically significant difference between the duration of mechanical ventilation, length of pleural drainage, and length of ICU stay in both groups.

**DISCUSSION**

Patients with various SV anomalies associated with increased PBF require early control with PAB to prevent pulmonary overcirculation and the later development of pulmonary vascular disease [Alsoufi 2015]. Freedom and coworkers
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Table 3. The outcome variables*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Increased PBF (days)</th>
<th>Restricted PBF (days)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of pleural drainage</td>
<td>9.0 (4.0 – 15.0)</td>
<td>5.0 (4.0 – 6.0)</td>
<td>0.060</td>
</tr>
<tr>
<td>Duration of mechanical ventilation</td>
<td>15.5 (7.5 – 92.3)</td>
<td>8.5 (6.0 – 24.0)</td>
<td>0.531</td>
</tr>
<tr>
<td>Length of ICU stay</td>
<td>5.5 (3.5 – 11.0)</td>
<td>4.0 (2.0 – 6.3)</td>
<td>0.207</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>17.0 (9.0 – 22.8)</td>
<td>8.0 (6.0 – 11.0)</td>
<td>0.039</td>
</tr>
</tbody>
</table>

PBF, pulmonary blood flow. *Continuous variables are presented as median (interquartile range).

[Freedom 1987] demonstrated a high incidence of systemic outflow obstruction in patients with SV treated initially with PAB placement [Ilbawi 1991; Franklin 1990; Lee 2014; Lui 1993]. The advantages of this strategy are mainly the avoidance of CPB in the neonatal period and it decreases risk of thrombotic occlusion than might occur with a BT shunt [Alsoufi 2015].

However, there are several disadvantages of PAB due to the difficulty obtaining adequate protection of pulmonary circulation with PAB, the possibility of distortion of PA and damage of the pulmonary valve with subsequent regurgitation. It also increases ventricular hypertrophy that might accelerate bulboventricular foramen rate of narrowing with subsequent early development of systemic ventricle outflow tract obstruction [Alsoufi 2013; Franklin 1991; Fraser 2009; Freedom 1986; Lee 2014; Matitau 1992]. Also, reported hospital mortality after PAB continues to be high; in a recent Society of Thoracic Surgeons harvest, hospital mortality for PAB was 8.9 % [Alsoufi 2015].

Performing an early primary BDG for patients with SV and increased PBF could be an option to provide a low pressure PBF and avoid the risk of steal from the systemic circulation that might happen in patients with parallel circulation such as those with PAB or aortopulmonary shunts [Alsoufi 2012]. In addition, it will help in avoiding the risk of first-stage palliation early in life as PAB or BT shunt.

In this series, we studied the short-term outcome of patients who had SV with increased PBF and underwent a primary BDG in comparison with those who had SV and restricted PBF as an initial congenital lesion or after previous palliative procedure, such as PAB, aortopulmonary shunt, Norwood procedure, or PDA stent. We found that early mortality, mechanical ventilation duration, pleural drainage duration and ICU length of stay were not significantly different in both groups but the length of hospital stay was longer in patients who had SV with increased PBF and underwent a primary BDG (P = 0.039).

Our practice is making a concentrated effort to wean patients off any oxygen supply before hospital discharge, which might result in prolonged hospital stay in the group of increased PBF who may require oxygen supplementation for longer duration due to preoperative congested lungs. The preoperative PA pressure was higher in the patients’ group with increased PBF, which could be flow related. Postoperatively, SVC pressure and oxygen saturation were comparable between both groups.

Taking into consideration that the comparison was made between the outcomes of BDG only and not including the duration of pleural drainage, duration of mechanical ventilation, ICU stay, hospital stay and mortality of the procedures prior to BDG in the restricted PBF group. Therefore, the cost and risk of the first-stage palliation should be considered in comparing the outcomes of both groups, in terms of cost benefit.

We performed further analysis of variables that might affect the outcomes, following the BDG operation for the overall patients’ population. We found that preoperative PA pressure has significant association with the duration of pleural drainage (P = 0.013), but not affecting the other outcomes.

The maximum VIS calculated in the first 24 hours after ICU admission was studied by Gaies et al., and they found it significantly and strongly associated with morbidity and mortality in this multi-institutional cohort of infants after cardiac surgery [Gaies 2014]. In the present study, the maximum VIS at 24 hours postoperatively had significant correlation with duration of mechanical ventilation and ICU stay (P = 0.013 and P = 0.029, respectively). On the other hand, the VEDP, ventricular morphology, degree of AAV regurgitation and CPB time were not associated with BDG outcomes.

The variables associated with surgical outcomes have been addressed mainly by single-center studies with varying and sometimes conflicting results. These studies have identified age, weight-for-age, PA pressure, ventricular morphology, AVV regurgitation, and CPB as factors associated with BDG outcomes [Anderson 2009; Dohain 2020; Ellassal 2020; Jaquiss 2006; Kogon 2008; Petrucci 2010].

Study limitations: The retrospective nature of the study was a limitation to get all the required data. The group of patients who had SV physiology with increased PBF was relatively small, which limits the statistical power of the study. Because of difficulties attributable to vascular access or clinically based decisions, some patients were not catheterized, and catheterization data variables are not available for all patients.

**CONCLUSION**

There is limited published data showing the outcomes of primary BDG for patients with SV physiology and increased...
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PBF. In our experience, we found that it can be done safely with acceptable short-term outcomes. Even more, it may reduce the morbidity and mortality for those patients by skipping the first-stage palliation as initial PAB or aortopulmonary shunts. Although, we did not find much difference in the outcome after BDG between increased PBF group and restricted PBF group, but we cannot always advocate avoiding PAB and proceeding with primary BDG directly due to limited data. We recommend future studies to evaluate short- and long-term outcomes of such patients.

REFERENCES


