The increase of the pulmonary blood flow inhigh-risk hypoxic patients with a bidirectional Glenn anastomosis

Jacek Kołcz[1], Mirosława Dudyńska[2], Aleksandra Morka[3], Sebastian Góreczny[4], Janusz Skalski[1]

[1]Department of Pediatric Cardiac Surgery, Jagiellonian University Medical College, Kraków, Poland
[2]Department of Pediatric Cardiac Surgery, University Children's Hospital in Krakow, Kraków, Poland
[3]Faculty of Health Sciences, Jagiellonian University Medical College, Kraków, Poland
[4]Department of Pediatric Cardiology, Jagiellonian University Medical College, Kraków, Poland

Correspondence to:
Jacek Kołcz, MD, PhD,
FECTS,
Department of Pediatric
Cardiac Surgery,
Jagiellonian University
Medical College,
Wielicka 265,
30–663 Kraków, Poland,
phone: +40 12 658 20 11,
e-mail:
jacek.kolcz@uj.edu.pl

ABSTRACT

Background: An additional shunt in single ventricle patients with Glenn anastomosis may increase pulmonary flow at the expense of ventricle volume overloading. The performance of the modification depends on pulmonary resistance, indicating better results in favorable hemodynamic conditions.

Aims: The study aims at analyzing the influence of precisely adjusted pulsatile shunt in borderline high-risk Glenn patients on early and late results.

Methods: The study involved 99 patients (including 21 children) with the bidirectional Glenn and accessory pulsatile shunt (BDGS group), and 78 patients with the classic bidirectional Glenn anastomosis (BDG group).

Results: There was 1 death in the BDGS group and 4 deaths in the BDG group. No difference in mortality ($P = 0.71$) was found. The Fontan completion was achieved in 69 (88.5%) children in the BDG group and 18 (85.7%) patients in the BDGS group, without fatalities. No intergroup differences in postoperative pulmonary artery pressure ($P = 0.10$), ventilation time ($P = 0.12$), the McGoon ratio ($P = 0.9$), or chylothorax frequency ($P = 0.14$) were observed. Intensive care unit ($P = 0.28$) and hospitalization ($P = 0.05$) times were comparable. Echocardiography revealed no significant differences in the ventricle and atrioventricular valve function between groups. In the BDGS group, higher blood oxygen saturation ($P = 0.03$) and increase of the McGoon index ($P = 0.002$) were noted.

Conclusions: Bidirectional Glenn anastomosis with precisely adjusted accessory pulmonary blood flow provides stable hemodynamics and adequate oxygen saturation in borderline, profoundly hypoxic patients. An advantageous pulmonary artery development before Fontan completion was observed.

Key words: bidirectional Glenn anastomosis, single ventricle, accessory pulmonary flow

INTRODUCTION

The main concerns of staged treatment of single ventricle type congenital heart defects are low pulmonary artery (PA) resistance, adequate pulmonary microvasculature maturation, and the pulmonary arteries' growth [1]. Unfortunately, after initial palliative procedures some patients do not meet the criteria for successful Glenn or hemi-Fontan surgery and eventual Fontan completion, which is the treatment goal. Low energy non-pulsatile blood flow through the cavo-pulmonary connection significantly increases pulmonary resistance over that seen in pulsatile flow. It can cause preoperative underestimation of postoperative pulmonary resistance in borderline cases, leading to profound hypoxia and circulatory failure immediately after the Glenn proce-

dure. In the long-term prognosis, non-pulsatile flow can contribute to the underdevelopment of pulmonary arteries and thromboembolic issues. Elimination of the hepatic bloodstream through the lungs contributes to developing pulmonary arteriovenous malformations and severe hypoxia [2, 3]. Lack of optimal preoperative risk stratification may extend the ultimate decision on the intraoperative period. Patients approaching borderline criteria are frequently disqualified from surgery. We present a group of high-risk borderline patients with hypoxia, increased pulmonary resistance, and marginal-sized pulmonary arteries in whom the lungs accessory blood flow was established and precisely adjusted during the Glenn procedure. The group of patients with pulsatile Glenn (BDGS) is compared to pa-

WHAT'S NEW?

The study presents the results of assisted Glenn anastomosis in high-risk single ventricle patients. An additional pulsatile pulmonary blood flow source was precisely constructed and adjusted intraoperatively in patients in whom otherwise it was impossible to win from by-pass. The results show that bidirectional Glenn anastomosis with an accessory pulsatile blood flow source can assure safe hemodynamics and satisfactory development of the pulmonary arteries as a preparation for Fontan completion. This option may be considered as a solution in borderline Fontan candidates or definitive palliation instead of Fontan completion.

tients with classic bidirectional Glenn anastomosis (BDG) as preparation for Fontan surgery. Although the concept has been known for decades, there is no evidence-based ground for routine leaving an additional pulmonary blood flow at Glenn surgery in all patients. The advantages and disadvantages of the modification are still debated, and the exact role of the procedure unknown [4–7].

METHODS

The study involved patients with single ventricle physiology who underwent the Glenn procedure at the Department of Pediatric Cardiac Surgery, Jagiellonian University, between 2008 and 2019. Jagiellonian University Ethics Committee approved the project, and the informed consent for the study was obtained from the patients' parents.

The BDG and BDGS groups were identified and compared (Table 1, Table 2). All children with Glenn anastomosis and biventricular physiology (e.g., Ebstein anomaly, one

and a half ventricle repairs) were excluded from the study. Also, patients who needed extensive PA patch plasty treated with the hemi-Fontan procedure were excluded from the study (Table 1).

All surgeries were carried out using the previously described technique and methodology. During surgery, the superior vena cava was anastomosed to the PA in the end–to–side manner. All accessory sources of pulmonary blood flow were closed (including tightening of the native PA, if present) (Figure 1). An additional pulmonary blood flow source was created based on preoperative data, size of pulmonary arteries, and lung disease history. In patients in whom preoperative pulmonary resistance was higher (above 1.8 WU/m^2), a mean PA pressure elevated (13–15 mm Hg), or pulmonary arteries small-sized (z score −1.5 to −1.8), and/or there was no possibility of weaning from cardiopulmonary bypass (CPB) because of hypoxia (e.g., blood oxygen saturation below 70%, despite 20 ppm

Table 1. Procedures carried out in patients with single ventricle physiology in the 12 years. The numbers in brackets indicate patients who died

Year	No. of hemi-Fontas	No. of BDG	No. of BDGS	No. of Fontans after hemi-Fontan	No. of Fontans after BDG	No. of Fontans after BDGS
2008	12	5	2	15	0	0
2009	20 (3)	8 (1)	1	9	2	2
2010	18	9	3	13	8	1
2011	25 (1)	5	2	27	11	2
2012	15 (2)	3	1	18	6	3
2013	21	4	2	13	5	2
2014	28	5	2	7	6	2
2015	32 (2)	2	0	19	3	1
2016	17	13 (1)	0	25	4	0
2017	31 (2)	6 (1)	3	14	5	2
2018	12 (1)	8 (1)	3	26	12	2
2019	3	6	2 (1)	8	7	1
Total	234 (11)	74 (4)	20 (1)	194	69	18

Abbreviations: BDG, bidirectional Glenn; BDGS, bidirectional Glenn and shunt

Table 2. Patient's characteristics

Characteristics	BDGS (n = 21)	BDG (n = 78)	*P*-value
Age, months, mean (SD)	6.68 (3.93)	5.92 (4.40)	0.240
Body weight, kg, mean (SD)	7.12 (4.3)	8.3 (6.2)	0.34
Left ventricle morphology, n (%)	14 (66.7)	30 (38.4)	0.02
Right ventricle morphology, n (%)	7 (33.3)	48 (61.5)	
HLHS, n (%)	2 (9.5)	43 (55.1)	0.033
Tricuspid atresia, n (%)	7 (33.3)	20 (25.6)	0.012
DORV, n (%)	4 (19.0)	6 (7.6)	0.42
Pulmonary atresia, n (%)	3 (14.2)	7 (8.9)	0.38
Others, n (%)	5 (23.8)	2 (2.6)	0.43

Abbreviations: DORV, double outlet right ventricle; HLHS, hypoplastic left heart syndrome; SD, standard deviation. Other abbreviations: see Table 1
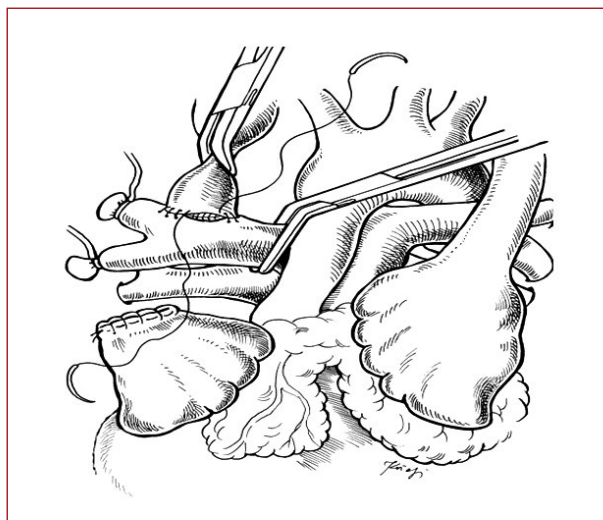
Figure 1. The surgical technique of creating a bidirectional Glenn shunt. The superior vena cava is cut of the right atrium and anastomosed to the pulmonary artery in the end to side

Figure 2. The technique of creation of additional pulmonary blood flow source. **A.** Pulmonary artery banding by narrowing of a distal portion of the pulmonary trunk with polytetrafluoroethylene (PTFE) band. **B.** Modified Blalock–Taussig shunt (diameter of 3.5–3.0 mm) with narrowing of distal part with vascular clip to 3.0 mm

of nitric oxide and FiO_2 1.0, appropriate pharmacologic support with catecholamines and milrinone), either a 3.5 Blalock–Taussig shunt (BTS) was created or a native pulmonary outflow tract was adjusted. The invasive measurement of the pressure in PA was done and, based on the measurements, the BTS was narrowed at the pulmonary end with a vascular clip (to the diameter of approximately 3 mm), or the native outflow tract was banded to a diameter of approximately 3 mm (Figure 2) to maintain mean PA pressure below 15 mm Hg by FiO_2 0.7, $ETCO_2$ 35–40, hemoglobin level 13–14 g/dl, and systemic oxygen saturation 75%–85%. The Fontan procedure was performed before 4 years of age. The total cavopulmonary connection was completed using an extracardiac or intra-extracardiac conduit with fenestration. Any residual accessory pulmonary blood flow source was eliminated at the time of Fontan surgery.

Details concerning preoperative data, diagnostic procedures (echocardiography, hemodynamic assessment), laboratory tests, early postoperative results, and follow-up data, including pre-Fontan clinical data, were gathered and statistically analyzed. Pulmonary artery size was analyzed using the McGoon ratio [8].

Systemic ventricular contractility and atrioventricular valve function were assessed with echocardiography by two experienced echocardiographers, and graded as normal, mildly decreased, moderately decreased, or severely decreased. Two different, previously described quantitative echocardiographic assessment methods of right ventricular function were consequently applied in all patients: the biplane pyramidal approximation method [9] and apical area fractional shortening [10]. The data concerning clinical characteristics and numbers of patients are presented in Table 1 and Table 2.
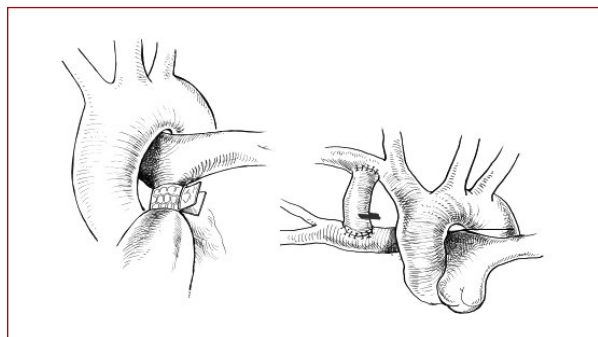
Statistical analysis

For statistical analysis, standard statistical methods were used. The nominal data were described using the following frequency measures: number count and percent group. Normally distributed quantitative variables were presented as the mean and standard deviation (SD). Non-normally distributed data were presented using the median and interquartile range (IQR). The normality of distribution of quantitative data was tested using the Shapiro–Wilk's test. The differences between the groups concerning normally distributed quantitative data were assessed using a paired or an unpaired t-test. Non-normally distributed data were compared using the Mann–Whitney test. The Fisher exact test was used to determine the differences between the groups concerning categorical data. The P-value <0.05 was considered statistically significant using STATISTICA data analysis software system, version 13.

RESULTS

Bidirectional Glenn anastomosis was carried out in 99 patients. In 21 (21.3%) of them, an accessory pulsatile shunt was created (the BDGS group) (Table 1). One (4.7%) patient in the BDGS group died after the procedure because of sepsis. In 78 patients the only pulmonary blood flow source was Glenn anastomosis (the BDG group). Four (5.1%) patients died in the BDG group. Two of them died because of thromboembolic complications and neurologic damage. One child died of sepsis, and one because of the single ventricle's severe dysfunction. There was no difference in the mortality rate between groups ($P = 0.71$).

The Fontan completion was achieved in 69 (88.5%) children in the BDG group and in 18 (85.7%) patients in the BDGS group (Table 1) without fatalities.

There were no differences in mean age (6.68 [3.93] vs 5.92 [4.40] years; $P = 0.24$) and mean weight of the patients (7.12 [4.3] vs 8.3 [6.2] kg; $P = 0.34$) before surgery. In the BDGS group, there was a prevalence of patients with a single left ventricle (14 [66.7%] vs 30 [38.4%]; $P = 0.02$)

and, consequently, a lower rate of hypoplastic left heart syndrome (2 [9.5%] vs 43 [55.1%]; *P* = 0.03; Table 2).

There were no differences in a mean value of preoperative blood oxygen saturation (67.52% [5.66] vs 68.19% [4.65]; *P* = 0.58) or mean value of McGoon index (1.57 [0. 11] vs 1.68 [0.19]; *P* = 0.30). Before surgery, the mean value of PA pressure was higher (14.3 mm Hg [1.33]) in the BDGS group than in the BDG group (12.48 mm Hg [1.20]; *P* = 0.04). Also, a tendency was observed towards higher mean value of PA resistance (1.8 [0.9] vs 1.4 [0.70] WU/m^2; *P* = 0.09) before surgery and higher mean value of postoperative PA pressure (14.72 mm Hg [3.36] vs 13.10 mm Hg [1.26]; *P* = 0.09) in the BDGS group. There was no significant difference concerning median of postoperative time of respiratory support (5.62 h [IQR 3.6–12.8]) vs 7.23 h [IQR 4.8–18.5]; *P* = 0.12), mean McGoon ratio (1.59 [0.72] vs 1.64 [0.66]; *P* = 0.90), or chylothorax frequency (3 [14.2%] vs 4 [5.1%]; *P* = 0.16). A median of intensive care unit time (4.1 days [IQR 2.7–5.8] vs 5.83 days [IQR 3.2–8.42]; *P* = 0.28) and hospitalization time (7.20 days [IQR 5.3–16.7] vs 12.03 days [IQR 6.8–20.3]; *P* = 0.05) were comparable (Table 3). The mean value of postoperative blood oxygen saturation was higher in the BDGS group (81.72% [1.97] vs 78.32% [2.34]; *P* = 0.032).

Postoperative echocardiography revealed no significant differences in ventricular function or atrioventricular valve regurgitation (Table 4). There was no difference in the McGoon ratio and PA pressure between groups in pre-Fontan catheterization (Table 3). Patients from the BDGS group had a higher mean value of blood oxygen saturation (85.2% [4.3] vs 82.5% [3.9]; *P* = 0.03). There were no significant differences in the mean value of McGoon index within BDGS group (1.57 [0.11] vs 1.59 [0.72]; *P* = 0.9; 1.59 [0.72] vs 1.98 [1.62]; *P* = 0.3) and within BDG group (1.68 [0.19] vs 1.64 [0.66]; 1.64 [0.66] vs 1.91 [2.14]; *P* = 0.3). Looking however, at the rate of change of the McGoon index within groups (ΔMcGoon), a significant difference of the median of the increment was noted comparing the BDGS group and the BDG group (0.35 [IQR 0.29–0.42] vs 0.16 [IQR 0.11–0.25]; *P* = 0.002).

DISCUSSION

The bidirectional Glenn shunt or hemi-Fontan anastomosis are well-established, integral steps in a single ventricle treatment strategy. As a second step, these procedures are preceded by neonatal palliations such as Norwood surgery, PA banding, or systemic-to-PA shunt. Both stages aim to

Table 3. Comparison of data concerning clinical and laboratory characteristics of the patients in the investigated period

Characteristics	BDGS (n = 21)	BDG (n = 78)	*P*-value
Pre-operative PA pressure, mean (SD)	14.3 (1.43)	12.48 (2.20)	0.04
Pre-operative PA resistance, WU/m^2, mean (SD)	1.8 (0.9)	1.4 (0.7)	0.09
Pre-operative McGoon index, mean (SD)	1.57 (0.11)	1.68 (0.19)	0.29
Pre-operative O$_2$ saturation, mean (SD)	67.52 (5.66)	68.19 (4.65)	0.58
Duration of ventilation, hours, median (IQR)	5.62 (3.6–12.8)	7.23 (4.8–18.5)	0.124
Chylothorax, postoperative, n (%)	3 (14.2)	4 (5.1)	0.16
ICU stay, days, median (IQR)	4.1 (2.7–5.8)	5.83 (3.2–8.42)	0.28
Hospitalisation time, days, median (IQR)	7.20 (5.3–16.7)	12.03 (6.8–20.3)	0.05
Postoperative PA pressure, mm Hg, mean (SD)	14.72 (3.36)	13.10 (1.26)	0.09
Postoperative McGoon index, mean (SD)	1.59 (0.72)	1.64 (0.66)	0.90
Postoperative O$_2$ saturation, mean (SD)	81.72 (1.97)	78.32 (2.34)	0.032
Pre-Fontan PA pressure, mm Hg, mean (SD)	14.4 (2.8)	13.2 (3.8)	0.18
Pre-Fontan PA resistance, WU/m^2, median (IQR)	1.8 (1.4–2.6)	1.5 (1.3–1.8)	0.23
Pre-Fontan McGoon index, mean (SD)	1.98 (1.6)	1.91 (2.14)	0.91
Pre-Fontan O$_2$ saturation, mean (SD)	85.2 (4.3)	82.5 (3.9)	0.035
Δ of McGoon index, median (IQR)	0.35 (0.29–0.42)	0.16 (0.11–0.25)	0.002

Abbreviations: ICU, intensive care unit; IQR, interquartile range; PA, pulmonary artery; SD, standard deviation; WU, Wood unit. Other abbreviations: see Table 1

Table 4. Postoperative echocardiographic characteristic of heart and valve function

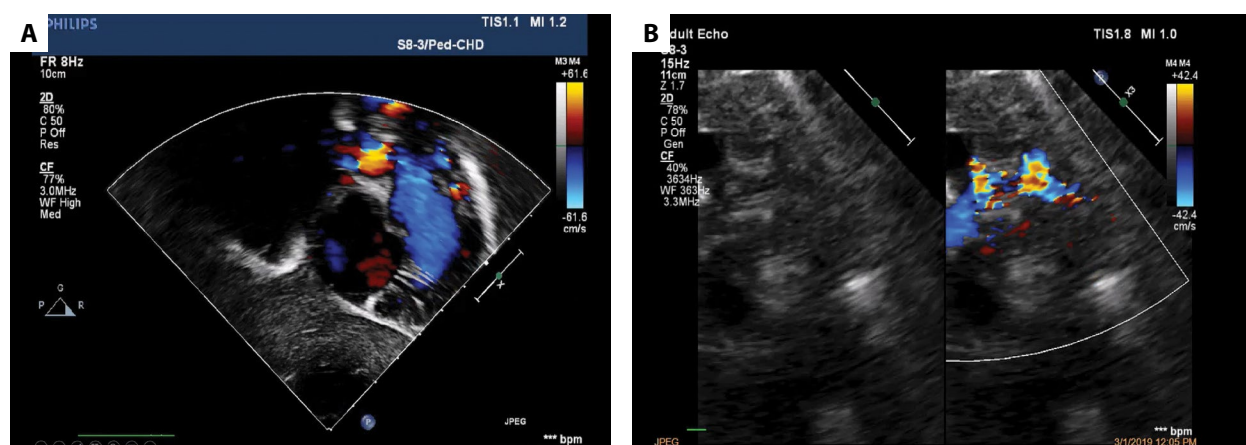| Parameters	BDGS (n = 21)	BDG (n = 78)	*P*-value
Ventricular function			
Normal, n (%)	14 (66.7)	51 (65.3)	0.56
Mildly depressed, n (%)	5 (23.8)	14 (17.9)	
Moderately depressed, n (%)	1 (4.7)	8 (10.2)	
Severely depressed, n (%)	1 (4.7)	5 (6.4)	
AV regurgitation			
None, n (%)	12 (57.1)	48 (61.5)	0.54
Mild, n (%)	3 (14.2)	16 (20.5)	
Moderate, n (%)	3 (14.2)	9 (11.5)	
Severe, n (%)	2 (9.5)	5 (6.4)	

Abbreviations: see Table 1

Figure 3. Echocardiographic presentation of flow through bidirectional anastomosis and accessory blood flow source. **A.** Residual flow through banded main pulmonary artery. **B.** Flow through Blalock–Taussig shunt

optimize the circulatory system for the third step, the Fontan procedure. After several decades of developing such a strategy, 2 of the initial 10 [11] necessary conditions of successful creation of Fontan circulation remained: the good functioning single ventricle and well-developed pulmonary arteries. These are the main goals of the initial stages of treatment. They ensure volume unloading, stepwise remodeling of the single ventricle, and PA development [12, 13]. Unfortunately, a group of patients in whom the criteria of creating cavo-pulmonary anastomosis are borderline imposes significantly increased risk on the second-stage procedure. Lack of perfect preoperative risk stratification causes disqualification of many of them from further treatment. In the present study, we looked at the borderline cavo-pulmonary anastomosis candidates in whom an additional blood flow source was created during surgery. The pulsatile shunt's influence on early and late postoperative results was shown compared to patients with classic BDG.

The population of single ventricle patients with hemodynamics not necessarily suited for creating Fontan circulation is growing. The elevated PA pressure and resistance, small PA branches, accessory vascular or lung defects, chronic lung disease, or single ventricle dysfunction may contribute to intolerance of Fontan physiology [11, 14]. Regrettably, there is no good alternative for such patients. Following neonatal palliative procedures, our approach was not to disqualify borderline patients, however, at the expense of higher perioperative risk. After weaning from CPB, all patients in the BDGS group experienced severe desaturation, despite appropriate pharmacological support. The alternative was to start extracorporeal membrane oxygenation support without a realistic perspective for a successful outcome. The ultimate decision to create an accessory pulsatile shunt was reached intraoperatively. Such an approach ensured a stable, reasonably safe clinical conditions with optimal systemic oxygen saturation and ventricular function. It also created additional possibility of long-term palliation if Fontan completion would be contraindicated [15].

The pulsatile shunt was constructed under the precise invasive pressure measurement within the cavo-pulmonary connection, putting accessory banding on the native pulmonary trunk or a vascular clip on the distal end of the BTS. Such a narrowing can significantly reduce pressure transition to the superior vena cava (SVC) and cause the "ejector pump effect". This approach was based on experimental hemodynamic studies and computational simulations indicating that optimal conditions were reached with the clipped distal shunt, anastomosed to the SVC. This model provided evidence that the energy of the systemic flow is partly transferred to the SVC flow and that it works as the ejector pump. It can increase pulmonary flow without significantly increasing SVC pressure [16, 17].

The reported mortality and morbidity in patients with BDGS differ in previous reports. A higher mortality rate in comparison to classic BDG was reported [18, 19]. In our group of higher-risk patients, only one patient died in the postoperative period because of sepsis, and the mortality rate did not differ between groups. Also, respiratory support time, intensive care time, and hospitalization time were not significantly different. The chylothorax frequency was higher in the BDGS group, although not significantly. Additionally, in the BDGS group, the systemic blood oxygen saturation was significantly higher than in the BDG group, which seems to be the most crucial benefit for patients' quality of life and physical efficiency.

Although there was no difference in the McGoon ratio before the second stage and before the third stage ($P = 0.91$, Table 3), there was a significant difference in the change (Δ) of the McGoon ratio with a substantial increment in the BDGS group ($P = 0.002$). The pulmonary branches' diameter, expressed as the McGoon ratio, is an important risk factor of creating Fontan circulation [20]. Although the time between the first and second stage coincides with intensive PA growth, classical Glenn physiology with a non-pulsatile blood flow through the lungs can profoundly affect PA development. In our material, it ensured significantly better development of pulmonary arteries. It contradicted

previous studies that revealed the absence of development or even regression of PA indices [21–23]. In most published works, the comparison between matched groups (classic Glenn anastomosis vs assisted Glenn shunt) and case-control studies, the comparison of absolute diameters, z-scores, and PA indices between groups were unable to reveal the increase of their size. In our study, the paired comparison of the McGoon index's mean values within matched groups between the surgical treatment stages also did not reveal significant differences. However, the comparison of the mean inside group increments (the mean Δ, the mean change) of the McGoon index between matched groups showed a significantly higher increment in the assisted Glenn (BDGS) group between the second and the third stage of treatment. A pulsatile flow in the vascular bed is a well-known factor influencing vascular development by appropriate shear stress regulation, the release of endothelium-derived factors (nitric oxide, endothelin), and reducing vascular resistance [24]. The additional advantage of such an approach is perfusion of the lungs supplied with blood containing angiogenesis inhibitors of the liver (e.g., endostatin, angiostatin), which were shown to regulate normal development and prevent the formation of arteriovenous fistulas [25–27].

Our data show higher blood oxygen saturation after BDGS than following the BDG ($P = 0.03$). It is related to slightly increased pulmonary blood flow, increased PA pressure, and increased ventricle volume load [28]. Before the second stage surgery, the PA resistance and pressure were higher in the BDGS group (Table 3). However, there was no difference in PA pressure and PA resistance in pre-Fontan catheterization. At the same time, the oxygen saturation and increase in the McGoon ratio were significantly higher in the BDGS group. The ventricular function and atrioventricular valve performance were comparable in both groups (Table 4). Given that the BDGS group contained borderline candidates for Glenn surgery, the results indicate a positive influence of pulsatile blood flow on central pulmonary arteries development in these high-risk patients by maintained atrioventricular valve and ventricle function.

CONCLUSIONS

In summary, bidirectional Glenn with precisely adjusted accessory pulmonary blood flow provides stable hemodynamics in the early postoperative period in borderline cavo-pulmonary anastomosis candidates. Adequate pulmonary blood flow and preserved ventricular function can provide appropriate PA development before Fontan completion with results comparable to outcomes in the group of low-risk patients.

Article information

Conflict of interest: None declared.

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