General Thoracic and Cardiovascular Surgery (2021) 69:451–457
https://doi.org/10.1007/s11748-020-01461-9

ORIGINAL ARTICLE

Risk factors for morbidity and mortality after a bidirectional Glenn shunt in Northern Thailand

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Received: 26 December 2019 / Accepted: 4 August 2020 / Published online: 11 August 2020

Abstract

Objectives Owing to the evolution of surgical techniques, the survival rate of patients undergoing a bidirectional Glenn shunt has improved. However, the morbidity and mortality are still high. The aims of this study were to determine the survival rate and risk factors influencing the morbidity and mortality in patients with a functional univentricular heart after a bidirectional Glenn shunt.

Methods One hundred and fifty-one patients who had undergone a bidirectional Glenn operation were enrolled. Early worse outcomes were defined as postoperative death within 30 days and a hospital stay ≥ 30 days.

Results The median age was 7.1 years (range 0.3–26 years). The median age at the time of the Glenn operation was 2.2 years (range 0.2–15.9 years). The survival rates of patients at 1-, 5-, 10- and 15-year after the Glenn operation were 89%, 79%, 75%, and 72%, respectively. The predictors for the mortality were preoperative mean pulmonary artery pressure ≥ 17 mmHg, preoperative pulmonary vascular resistance index ≥ 3.1 Wood Units·m^2 and atrioventricular valve regurgitation. In addition, the independent predictors of an early worse outcome included preoperative mean pulmonary artery pressure ≥ 17 mmHg and diaphragmatic paralysis.

Conclusion The presence of preoperative atrioventricular valve regurgitation, preoperative mean pulmonary artery pressure ≥ 17 mmHg, preoperative pulmonary vascular resistance index ≥ 3.1 Wood Units·m^2, or diaphragmatic paralysis were found to be independent risk factors requiring the good patients' selection for the Glenn operation and early aggressive management of the diaphragmatic paralysis for reducing morbidity to ensure successful candidature for Fontan completion.

Keywords Glenn operation · Atrioventricular valve regurgitation · Pulmonary artery pressure · Worse outcome · Mortality

Introduction

The bidirectional Glenn shunt, alternatively named bidirectional cavopulmonary shunt or hemi-Fontan procedure is recognized as the standard intermediate palliative procedure before the completion of the Fontan operation in patients with solely a functional single ventricle [1]. The first successful cavopulmonary shunt creating an end-to-end superior vena cava to the pulmonary artery was performed by Glenn in 1958 [2]. The advantages of the bidirectional Glenn operation is the reduced volume loading of the single ventricle resulting in the improvement in the diastolic function, decreasing atrioventricular regurgitation. In addition, this operation permits correction of the residual anatomical defects in patients such as an enlarged atrial septum, also facilitating atrioventricular valve repair, pulmonary artery plasty, and aortic arch repair prior to the final stage of the palliative Fontan operation. Several previous reports have shown that a pulsatile Glenn shunt could be a useful long-term palliative procedure replacing the Fontan operation especially in high-risk Fontan candidates [3–5]. Due to modified surgical techniques, this operation can improve early postoperative outcomes and reduce the morbidity and mortality related to the Fontan operation. Several previous studies reported that age at the time of the Glenn operation, dominance of the right ventricle, heterotaxy syndrome,

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atrioventricular valve regurgitation, high central venous pressure, high transpulmonary gradient, increased pulmonary vascular resistance, single ventricular dysfunction, pulmonary artery stenosis, anomalous pulmonary venous drainage, and prolonged cardiopulmonary bypass time all affected the survival rate after a bidirectional Glenn operation [6–15]. The aims of this study were to determine the survival rate and risk factors influencing the morbidity and mortality of patients following a bidirectional Glenn shunt.

Methods

One hundred and fifty-one patients who underwent a bidirectional Glenn operation between January 1999 and December 2018 were recruited onto this retrospective cohort study. The medical data collected included diagnosis, echocardiography, cardiac catheterization, previous surgery associated with the Glenn operation, age at the time of the Glenn shunt, the type of Glenn procedure and associated complications. Echocardiographic data consisted of dominant ventricular morphology and degree of atrioventricular valve regurgitation. Cardiac catheterization data included mean pulmonary artery pressure, pulmonary vascular resistance index (PVRi), Nakata index and systemic ventricular end-diastolic pressure. The primary outcome was the death of the patient. The secondary outcome was an early worse outcome including postoperative death within 30 days and a hospital stay ≥ 30 days.

Statistical analysis

The data were analyzed in the form of descriptive statistics with categorical data and quantitative data using SPSS version 23 (SPSS Inc., Chicago, IL, USA). Kaplan–Meier was used for estimating the survival curve and the log-rank test provided a statistical comparison of the two curves. The evaluation of the predictor for mortality was assessed using univariate and multivariate Cox proportional regression analysis. Assessment of the predictors for an early worse outcome was done using the binary logistic regression analysis. All of the statistical tests used for analysis were 2-sided with significance being accepted with a p value of < 0.05.

Results

One hundred and fifty-one patients (53% female) underwent the bidirectional Glenn operation. The median age was 7.1 years (range 0.3–26 years). The median age at the Glenn shunt was 2.2 years (range 0.2–15.9 years). The median follow-up time after the Glenn shunt was 4.1 years. The diagnoses included tricuspid atresia, 44 cases (29%); heterotaxy syndrome, 38 cases (25%); double inlet left ventricle, 14 cases (10%); pulmonary atresia/intact ventricular septal defect, 13 cases (9%); mitral atresia, 6 cases (4%); unbalanced atrioventricular septal defect, 9 cases (6%); hypoplastic left heart syndrome, 2 cases (1%) and other, 25 cases (16%). Echocardiography and cardiac catheterization data before the Glenn operation are shown in Table 1. The dominant ventricular anatomy was a morphologic left ventricle in 90 patients (60%) and a morphologic right ventricle in 61 patients (40%). Thirty-four patients (23%) had mild to severe atrioventricular valve regurgitation. The surgery prior to the Glenn operation was as follows: modified Blalock-Taussig shunt, 66 cases (44%); pulmonary artery banding, 11 cases (7%); PDA ligation, 5 cases (3%); pulmonary artery plasty 5 cases (4%); Norwood operation, 4 cases (3%); coarctation repair, 2 cases (1%); unifocalization, 2 cases (1%) and TAPVR repair, 1 case (1%). The most common surgical procedures associated with the Glenn shunt were a taken down shunt (30%), atrial septectomy (19%), pulmonary artery plasty (18%), and PDA ligation (11%). Eighty-three patients (55%) had undergone a pulsatile Glenn. The complications included infection, 23 cases (15%); chylothorax, 11 cases (7%); arrhythmia, 7 cases (5%) and diaphragmatic paralysis, 4 cases (3%).

Outcomes were as follows: survival to Fontan operation, 75 cases; waiting for the Fontan operation, 47 cases; not candidate to the Fontan operation, 4 cases; and death 30 cases (Fig. 1). The survival rates 1-, 5-, 10-, and 15-year post the Glenn operation were 89%, 79%, 75%, and 72%, respectively (Fig. 2). Using the univariate Cox regression analysis, the predictors of mortality in patients after the Glenn operation were postoperative mean pulmonary artery pressure ≥ 20 mmHg [hazard ratio 46.5 (95%CI 1.4–1583.7)], cardiopulmonary bypass time ≥ 105 min [hazard ratio 5.5

Table 1 Echocardiography and cardiac catheterization data in patients before Glenn operation

Data	Patients
Ventricular morphology (*n*, %)	
Right ventricular morphology	61 (40)
Left ventricular morphology	90 (60)
Atrioventricular valve regurgitation (*n*, %)	
None	111 (77)
Mild	26 (18)
Moderate	6 (4)
Severe	2 (1)
Mean pulmonary artery pressure (mmHg)	15 ± 4
PVRi (Wood Units·m^2)	2.3 ± 1.1
Nakata index (mm^2/m^2)	324 ± 120
Systemic ventricular end-diastolic pressure (mmHg)	10 ± 4

PVRi pulmonary vascular resistance index

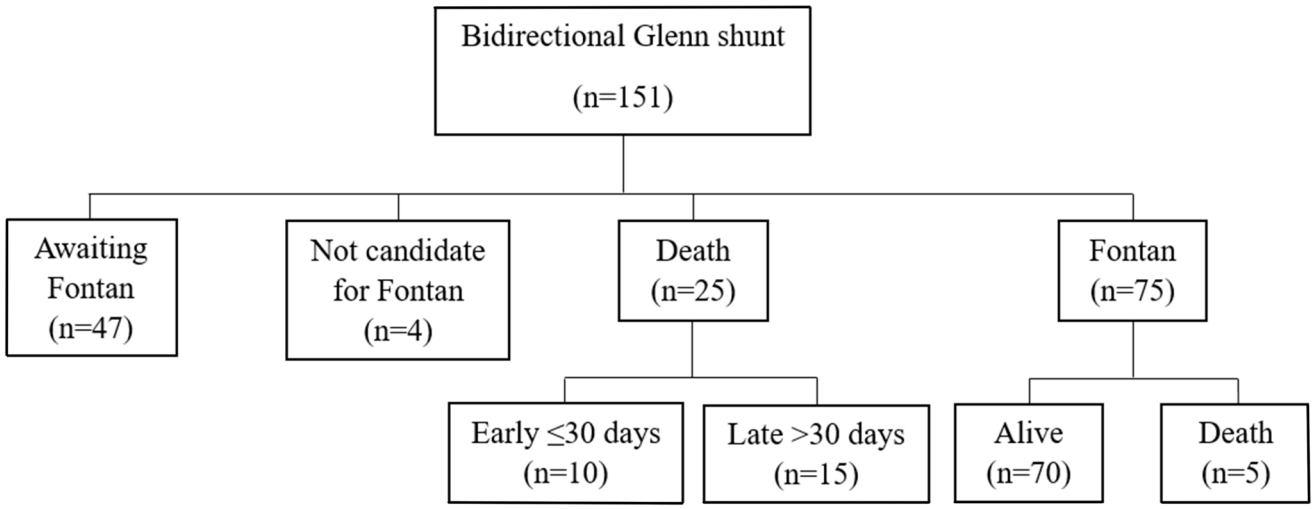

Fig. 1 Flow chart of outcomes in patients after a bidirectional Glenn operation

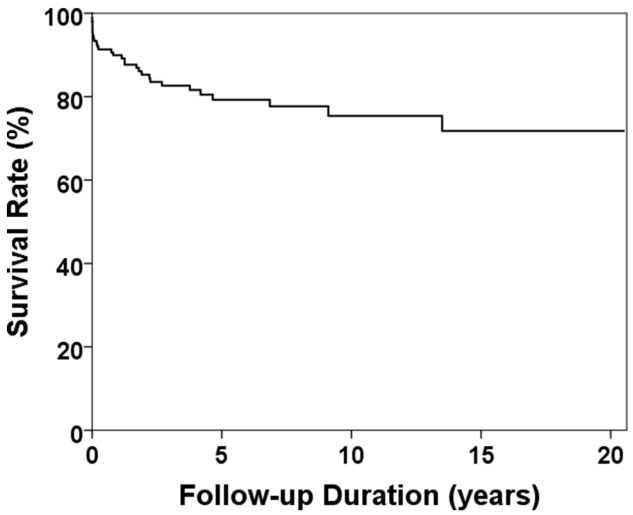

Fig. 2 Kaplan–Meier curve for survival rate in patients after a bidirectional Glenn operation

(95%CI 2.3–13.1)], preoperative mean pulmonary artery pressure ≥ 17 mmHg [hazard ratio 6.7 (95%CI 1.8–24.9)], preoperative PVRi ≥ 3.1 Wood Units·m^2 [hazard ratio 3.6 (95%CI 0.9–13.7)], right ventricular morphology [hazard ratio 3.6 (95%CI 1.7–7.6)], heterotaxy syndrome [hazard ratio 2.9 (95%CI 1.4–6.1)], atrioventricular valve regurgitation [hazard ratio 3.3 (95%CI 1.5–7.4)], and bilateral Glenn shunt [hazard ratio 2.7 (95%CI 1.3–5.6)]. After adjustment for confounding factors by the multivariate Cox regression analysis, the independent predictors for the mortality were preoperative Glenn mean pulmonary artery pressure ≥ 17 mmHg [hazard ratio 36.0 (95%CI 1.5–848.2)], preoperative PVRi ≥ 3.1 Wood Units·m^2 [hazard ratio 16.8 (95%CI 1.5–192.4)], and atrioventricular valve regurgitation [hazard ratio 14.7 (95%CI 1.0–207.4)] (Table 2).

With regard to the predictors of an early worse outcome in patients after the Glenn operation, the patients in the early worse outcome group had higher preoperative mean

Table 2 Univariate and multivariate Cox regression analysis for the predictors of mortality in patients after the Glenn operation

Factors	Univariate		Multivariate	
	Hazard ratio (95%CI)	*p* value	Hazard ratio (95%CI)	*p* value
Heterotaxy syndrome	2.9 (1.4–6.1)	0.004		
Right ventricular morphology	3.6 (1.7–7.6)	0.001		
Bilateral Glenn shunt	2.7 (1.3–5.6)	0.006		
Atrioventricular valve regurgitation	3.3 (1.5–7.4)	0.003	14.7 (1.0–207.4)	0.04
Preoperative mean PA pressure ≥ 17 mmHg	6.7 (1.8–24.9)	0.004	36.0 (1.5–848.2)	0.02
Preoperative PVRi ≥ 3.1 Wood Units·m^2	3.6 (0.9–13.7)	0.06	16.8 (1.5–192.4)	0.02
CBP time ≥ 105 min	5.5 (2.3–13.1)	0.0004		
Postoperative mean PA pressure ≥ 20 mmHg	46.5 (1.4–1583.7)	< 0.0001		

CPB cardiopulmonary bypass; *PA* pulmonary artery; *PVRi* pulmonary vascular resistance index

pulmonary artery pressure than that in the good outcome group. In the case of the post-Glenn shunt data, the early worse outcome group had a longer cardiopulmonary bypass time, greater mean pulmonary artery pressure and more patients with diaphragmatic paralysis than those in the good outcome group. There was no statistically significant difference between the two groups in the case of an atrioventricular valve regurgitation, single ventricular morphology, type of Glenn shunt, pulmonary vascular resistance index, Nakata index and systemic vascular end-diastolic pressure. The univariate logistic regression analysis indicated the predictors of the early worse outcome in patients after the bidirectional Glenn operation included preoperative mean pulmonary artery pressure ≥ 17 mmHg, postoperative mean pulmonary arterial pressure ≥ 26 mmHg, cardiopulmonary bypass time ≥ 66 min and diaphragmatic paralysis. After adjustment for confounding factors using the multivariate logistic regression analysis, independent predictors of an early worse outcome included preoperative mean pulmonary arterial pressure ≥ 17 mmHg [odds ratio 4.8 (95%CI 1.1–21.0)] and diaphragmatic paralysis [odds ratio 33.6 (95%CI 2.7–425.2)] (Table 3). Graphing displays comparing the survival rate in relation to an atrioventricular valve regurgitation, a preoperative mean pulmonary artery pressure and preoperative pulmonary vascular resistance index using the log-rank test are shown in Fig. 3. Graphing display comparing the survival rate in relation to the subgroup analysis of a preoperative mean pulmonary artery pressure and preoperative pulmonary vascular resistance index is shown in Fig. 4.

Discussion

This study showed the survival rate of patients after a bidirectional Glenn shunt between 1999 and 2018 at 1-, 5-, 10- and 15-years was 89%, 79%, 75%, and 72% respectively. In a previous study from 2002 to 2007, Alsoufi et al. found the overall 8-year survival rate following a Glenn shunt was 74% [16]. In a study including data from 1995 to 2005 Scheurer et al. showed that in patients who underwent a bidirectional Glenn shunt survival and lack of transplantation rates were 96% at 1 year and 89% at 5 years [17]. Francois et al. reported that between 1992 and 2012 following the Glenn operation 82% of the patients could undergo the Fontan operation [18]. The predictors of mortality after a bidirectional Glenn shunt in this study were preoperative mean pulmonary arterial pressure ≥ 17 mmHg, preoperative pulmonary vascular resistance index ≥ 3.1 Wood Units·m^2, and atrioventricular valve regurgitation. Several studies reported that high pulmonary artery pressure and PVRi were the risk factors for the Glenn shunt. Alsoufi et al. revealed that the risk factor for death prior to the Fontan operation was PVRi ≥ 3 Wood Units·m^2 [16]. Chacon-Portillo et al. showed that higher PVRi was the predictor for pulsatile Glenn failure [19]. In our study, the age at the Glenn operation was 2.2 years resulting in the need for the adaptation of the pulmonary arteriole. The advantage of the pulsatile Glenn shunt was pulmonary artery growth, prevention of pulmonary arteriovenous malformation, and high oxygen saturation. However, this pulsatile Glenn operation may lead to an increase in pulmonary artery pressure and PVRi. This would therefore require aggressive management for decreasing pulmonary artery pressure and PVRi prior to the Glenn operation. The Glenn shunt usually needs to be performed at a young age. Atrioventricular regurgitation was also found to be a predictor for mortality in this study. In support of this finding Scheurer et al. also found that atrioventricular regurgitation was an independent risk factor for death or transplantation in patients who had undergone a Glenn shunt [17]. In addition, Friedman et al. demonstrated that atrioventricular regurgitation was a factor associated with decreasing successful progression after the Glenn operation [20]. Two further studies, one by Lee et al. which revealed that atrioventricular regurgitation was a significant adverse risk factor for survival after the Fontan operation [12], and one by Chacon-Portillo et al. which showed that atrioventricular regurgitation was a predictor of pulsatile Glenn failure also add weight to our findings [19]. High pulmonary artery pressure and PVRi might be due to several conditions such as hypoplastic pulmonary artery anatomy, pulmonary vascular abnormalities, chronic lung disease, or systemic ventricular dysfunction. Therefore, aggressive evaluation and management of the atrioventricular regurgitation is vital at the time of the bidirectional Glenn operation.

Table 3 Univariate and multivariate logistic regression analysis for predictors of the early worse outcome in patients after the Glenn operation

Factors	Univariate		Multivariate	
	Odds ratio (95%CI)	*p* value	Odds ratio (95%CI)	*p* value
Preoperative mean PA pressure ≥ 17 mmHg	4.5 (1.2–16.8)	0.02	4.8 (1.1–21.0)	0.009
Postoperative mean PA pressure ≥ 26 mmHg	16.3 (4.5–59.4)	< 0.0001		
CPB ≥ 66 min	6.1 (1.6–23.4)	0.006		
Diaphragmatic paralysis	32.5 (3.4–309.0)	< 0.0001	33.6 (2.7–425.2)	< 0.0001

CPB cardiopulmonary bypass; *PA* pulmonary artery

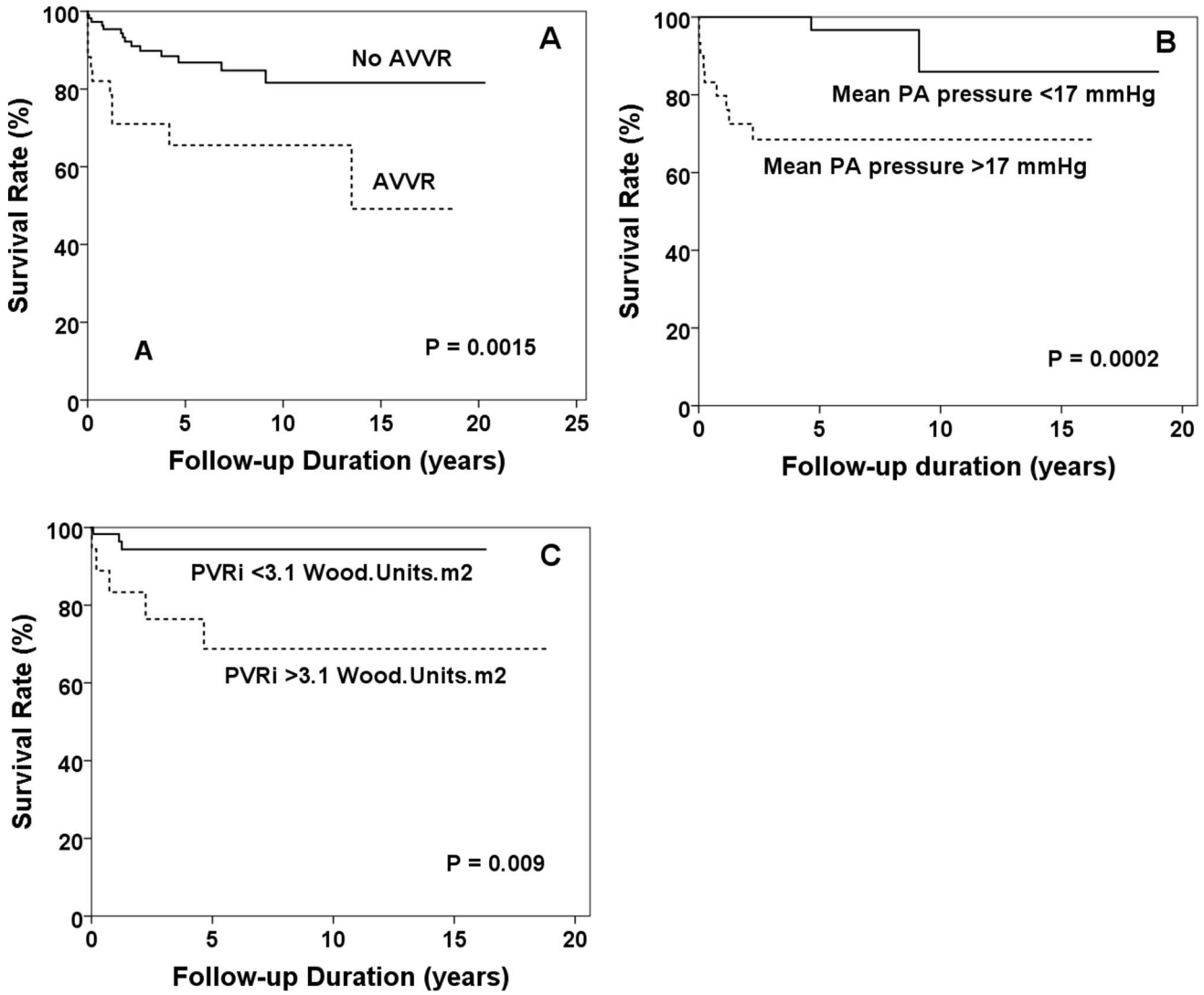

Fig. 3 Graphic displays comparing the survival rate in relation to (**a**) atrioventricular valve regurgitation (AVVR), **b** preoperative mean pulmonary artery (PA) pressure and (**c**) preoperative pulmonary vascular resistance index (PVRi) in patients after a bidirectional Glenn operation

The predictors for an early worse outcome were preoperative mean pulmonary artery pressure ≥ 17 mmHg and diaphragmatic paralysis. The incidence of diaphragmatic paralysis was 0.3% to 2.5% after pediatric cardiac surgery including Blalock-Taussig shunt, Fontan operation, arterial switch procedure and bidirectional Glenn shunt [21–24]. AI-Ebrahim et al. reported that patients with diaphragmatic paralysis after cardiac surgery were successfully weaned from the mechanical ventilation after the diaphragmatic plication [24]. Therefore, early diaphragmatic plication should be performed after the diagnosis of diaphragmatic paralysis using the ultrasonography or fluoroscopy for minimizing prolong hospital stay's complication. The risk factors in other studies for mortality were right ventricular morphology, heterotaxy syndrome, prolonged cardiopulmonary bypass, and bilateral Glenn shunt. In this study, these risk factors were only shown to be significant risk factors in the univariate analysis. Kogon et al. found that right ventricular morphology was a risk factor for an adverse outcome after bidirectional Glenn operation [11]. Keizman et al. showed that the bilateral bidirectional Glenn operation had a tendency for a higher prevalence of a worse postoperative outcome, Fontan failure, and early mortality [25]. It has also been postulated that unequal blood flow arborization to both lungs and segmental hypertension are risk factors in the case of the Glenn shunt. Kogon et al. demonstrated that a prolonged cardiopulmonary bypass time was a factor for an adverse outcome [11]. Talwar et al. showed that inotropic support, duration of ventilation, ICU stay, and hospital stay were significantly less in the off-CPB group [26]. Hussain et al. reported that patients without a cardiopulmonary bypass was a safe procedure and had no neurological

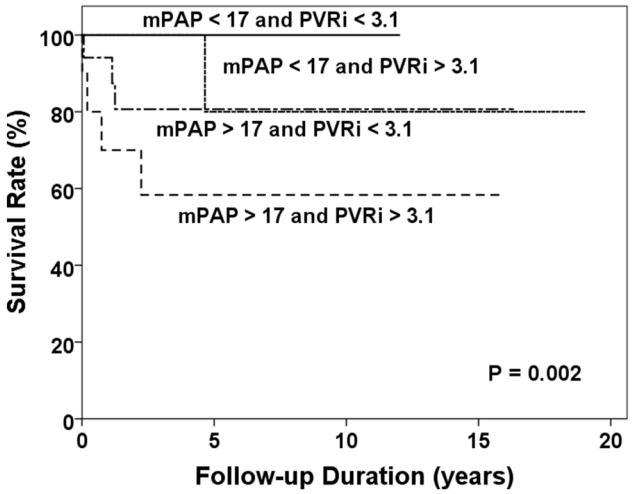

Fig. 4 Graphic displays comparing the survival rate in 4 subgroups based on the preoperative mean pulmonary artery pressure (mPAP) and preoperative pulmonary vascular resistance index (PVRi) in patients after a bidirectional Glenn operation

complications [27, 28]. The retrospective nature of this study is a limitation however the findings are indicative and a prospective study including a large number of post Glenn operation patients is warranted.

Conclusion

The presence of preoperative atrioventricular valve regurgitation, mean pulmonary arterial pressure ≥ 17 mmHg, pulmonary vascular resistance index ≥ 3.1 Wood Units·m^2 and diaphragmatic paralysis were independent risk factors for mortality and an early worse outcome following a bidirectional Glenn Shunt. These factors require an aggressive management for decreasing pulmonary artery pressure and pulmonary vascular resistance prior to the Glenn shunt, the good patients' selection for the Glenn surgery, and early management of the diaphragmatic paralysis to minimize morbidity and mortality of the Glenn operation and facilitate successful candidature for Fontan completion.

Compliance with ethical standards

Conflict of interest The authors have no disclosures to report.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee.

Informed consent There was no informed consent because of the retrospective study design.

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