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ORIGINAL ARTICLE

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Incidence and factors influencing the spontaneous closure of Fontan fenestration

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Abstract

Introduction: The Fontan operation is the final stage of single ventricle palliation in patients with complex congenital heart disease. Fenestration in the Fontan conduit, providing an atrial level right to left shunt, has been shown to reduce early postoperative morbidity. However, there is limited data on the long-term fate of this fenestration. The aim of this study is to define the rate of spontaneous closure of the fenestration in the Fontan conduit and factors predictive of the fate of the fenestration.

Methods: This was a retrospective study reviewing the medical records of the patients who underwent fenestrated Fontan operation at our center. Preoperative, intraoperative and postoperative variables including the status of the Fontan fenestration were extracted and analyzed.

Results: Of 67 patients included in the study, 15 (22%) had spontaneous closure of the fenestration. Of the remaining 52 patients, 11 (20%) had procedural closure of this fenestration (10 via cardiac catheterization and 1 via surgery) at a median duration of 3 months after the Fontan operation. Patients with higher preoperative pulmonary vascular resistance and a history of postoperative systemic venous thromboembolism had higher likelihood of having persistence of the fenestration with *P* value of .045 and .037, respectively.

Conclusions: The rate of spontaneous closure of the Fontan fenestration was 22% in our study. Elevated preoperative pulmonary vascular resistance and history of systemic venous thromboembolism are predictive of persistent Fontan fenestration.

KEYWORDS
fenestrated Fontan, Fontan operation, single ventricle, spontaneous closure

1 | INTRODUCTION

The Fontan operation is the final stage of single ventricle palliation in patients with complex congenital heart disease (CCHD). In most patients, this operation is preceded by bidirectional superior cavopulmonary anastomosis. The Fontan operation was first described by Fontan and Baudet in 1971 as a palliative procedure for patients with tricuspid atresia.[1] Later it was expanded to include a wide spectrum of CCHD with single ventricle physiology. Over time, it has undergone modifications which included intracardiac lateral tunnel, followed later by extracardiac conduit Fontan. The latter modification is the most widely used surgical technique in the current era of single ventricle palliation.[2] A fenestration is often placed in the Fontan conduit to provide a systemic to pulmonary venous connection at the atrial level to reduce the morbidity and mortality following this procedure.[3,4]

It is well known that in some patients, the fenestration closes spontaneously over time, whereas in others it remains patent. Despite contributing to improved early postoperative outcomes following Fontan operation, it has been reported that persistence of this fenestration is associated with increased long term morbidity.[5,6] Long term patency of the Fontan fenestration has been reported to be associated with higher likelihood of lower oxygen saturation and paradoxical embolism.[5] It has also been shown that patients with persistent fenestration have a greater decrease in oxygen saturation and increase in physiological dead space during a cardiopulmonary stress test[6] and that long-term persistence of the fenestration is a marker of poor Fontan outcomes.[7] Given this background, we aim to define the incidence of and factors influencing spontaneous closure of the Fontan fenestration.

2 | METHODS

2.1 | Study population

This was a retrospective chart review of all patients who underwent fenestrated extracardiac conduit Fontan palliation surgery at the Holtz Children's/Jackson Memorial Hospital during the period of January 2000 through June 2016. Patients who had no postoperative follow up care at our center were excluded from the study. This review was approved by the Institutional Review Board of Human Subjects Research at the University of Miami and Holtz Children's Hospital.

2.2 | Surgical technique

Following a redo median sternotomy, total cardiopulmonary bypass with mild hypothermia was initiated. The surgery was typically performed on the beating heart without cardioplegia. Cardioplegia was utilized only if there was a need for concomitant intracardiac procedures. The inferior vena cava at the atriocaval junction was mobilized and amputated after placing a vascular camp at the atrial end of atriocaval junction. An end to end anastomosis was made between the inferior vena cava and the Gore-Tex (WL Gore and Associates, Flagstaff, Arizona) tube graft. Following this, a 4 mm fenestration was made in the anteromedial aspect of the tube graft and a side to side anastomosis was constructed 2-3 mm around the fenestration in the tube graft and a small right atriotomy. The distal end of the tube graft was then cut to approximate length and an end to side anastomosis was made between the tube graft and the branch pulmonary artery completing the extracardiac conduit fenestrated Fontan operation.

2.3 | Data collection

The following preoperative variables were collected from a pre-Fontan cardiac catheterization: mean pulmonary artery pressures, transpulmonary gradient, pulmonary vascular resistance (PVR), systemic ventricular end diastolic pressure, presence of significant aorta to pulmonary artery collaterals (requiring closure preoperatively), Nakata index and McGoon's ratio. The other variables collected include preoperative cardiac rhythm, and prior pulmonary artery interventions (balloon angioplasty, stenting of the pulmonary arteries, and surgical pulmonary arterioplasty). Immediate postoperative variables reviewed were: pleural effusion persisting for more than 2 weeks and new onset rhythm disorders. Most recent follow-up visit documentation was reviewed to identify ventricular function, atrioventricular valve function, NYHA class, cardiac rhythm disturbances, cardiac-related hospitalizations, and the presence of any postoperative morbidity. Most recent clinical encounter documentation was also reviewed for: oxygen saturation, NYHA class, arrhythmia history, cardiac rhythm, type of thromboprophylaxis, history of postoperative systemic venous thromboembolism, protein losing enteropathy, fenestration patency, and Fontan pathway obstruction. In patients who had no evidence of a patent fenestration, prior data were reviewed to define the time in months from Fontan operation to the closure of the fenestration, spontaneously or due to transcatheter intervention.

2.4 | Statistical analysis

Descriptive statistics included median ± SEM (range) time in months from the surgery. Continuous variables were compared with the status of fenestration using ANOVA test. Chi-square test was used to analyze the association between categorical variables and the status of fenestration. A P value of $< .05$ was considered statistically significant. Statistical analysis was performed using IBM SPSS 22 statistical software, version 22 (Armonk, New York).

3 | RESULTS

A total of 105 patients underwent Fontan operation at our institution between January, 2000-June, 2016 (Figure 1). Of these, 38 patients were

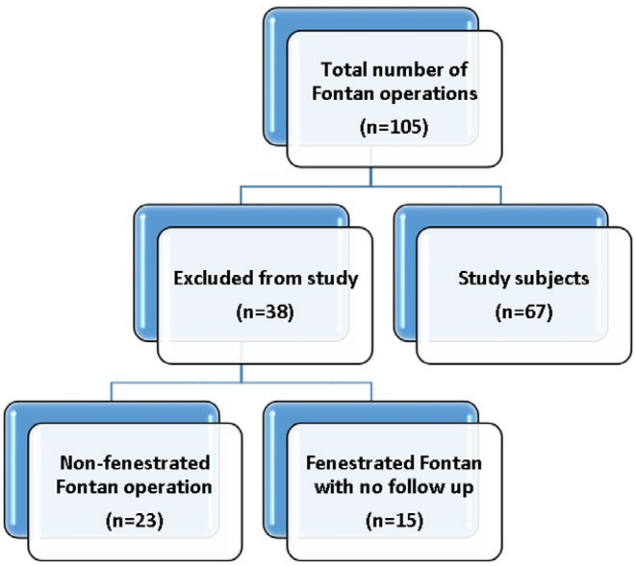

FIGURE 1 This figure represents the flow of patients in this study [Colour figure can be viewed at wileyonlinelibrary.com]

excluded: 23 who underwent non-fenestrated Fontan; 15 who had no follow up at our institution and therefore had no additional data following the Fontan operation. Among the study subjects, 36 (54%) were male and the median age at the time of Fontan operation was 3.9 ± 0.8 years (range: 2-44.8). Demographic data of the patients in the study is shown in Table 1. Among the 67 patients included in this study, 15 (22%) had spontaneous closure of the fenestration. The median duration from the Fontan operation for spontaneous closure of the fenestration was 3 ± 6 months (range: 0.5-84 months). During the study period, 13 patients underwent cardiac catheterization 37 ± 8 months (range: 8-96 months) after the Fontan operation with an intent to close the fenestration. In 12 of these patients, the indication was lower oxygen saturation with exercise and/or exercise intolerance and in 1 it was concern for increased risk for systemic thromboembolism following thrombus formation in the SVC. Of these 13 patients, 10 underwent successful device closure of the fenestration. In 3, fenestration closure was abandoned due to unfavorable hemodynamics. During the study period, 1 patient underwent surgical closure of the fenestration in the immediate postoperative period for significant desaturation. Figure 2 shows the most recent status of Fontan fenestration among the study subjects. Patients who had spontaneous closure of the fenestration had a trend toward lower mean age at the time of their Fontan operation when compared to the group without spontaneous closure (4.13 vs 6.25 years $P = .25$).

Table 2 shows the association between the variables assessed in the study and the status of the Fontan fenestration. Patients with an elevated PVR (>2 Wum^2) had a lower likelihood of spontaneous closure ($P = .045$). Also those with a history of systemic venous thromboembolism had a higher likelihood of persistent fenestration ($P = .037$). Presence of aortopulmonary collaterals and abnormal pre-Fontan rhythm had near statistical significance in predicting the persistence of fenestration ($P = .06$).

TABLE 1 Demographic data

		Spontaneous closure (group 1): n = 15	Without spontaneous closure (group 2): n = 52	*P* value
Age at surgery, mean (SEM)		4.13 (0.56)	6.25 (0.96)	.25
Sex	Male	5	31	.07
	Female	10	21	
Diagnosis	Heterotaxy	2	6	
	HLHS	4	14	
	DORV	2	11	
	DILV	2	2	
	Unbalanced AVSD	2	5	
	Others	3	14	

Abbreviations: AVSD, atrioventricular septal defect; DILV, double inlet left ventricle; DORV, double outlet right ventricle; HLHS, hypoplastic left heart syndrome; SEM, standard error of mean.

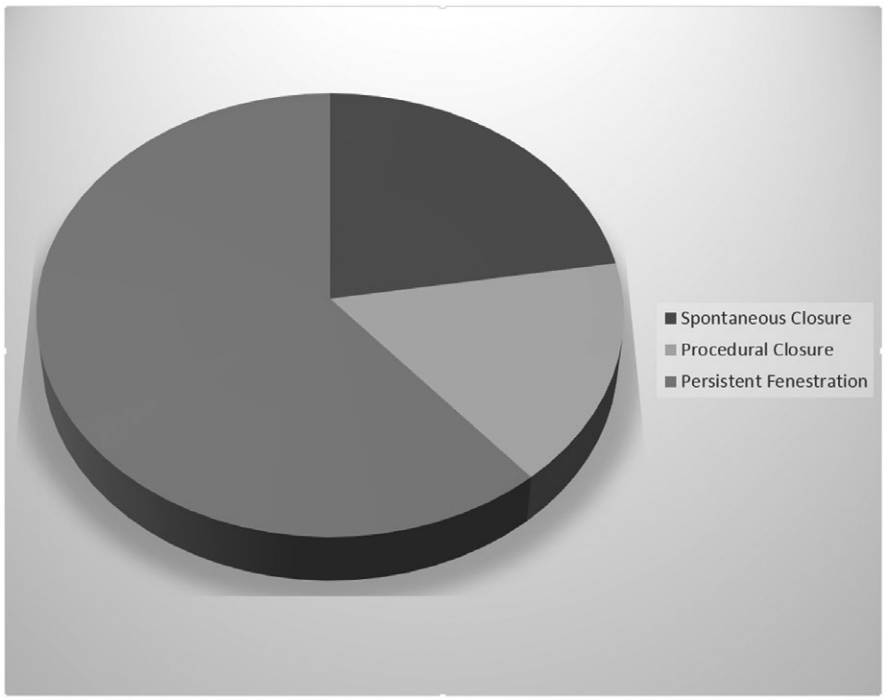

FIGURE 2 Pie chart representing the proportion of patients with spontaneous closure, transcatheter closure and patent fenestration

TABLE 2 Association between the study variables and the Fontan fenestration status

Variable	Status of Fontan fenestration		
	Closed spontaneously	Not closed spontaneously	*P* value
Pulmonary vascular resistance > 2	1/11	11/48	.045*
Mean PAP (>15 mm Hg)	1/13	2/50	.34
TPG > 5 mm Hg	4/13	10/50	.28
End diastolic pressure > 10 mm Hg	2/13	4/50	.28
Nakata Index < 200	3/6	13/31	.38
McGoon Ratio < 1.9	7/10	24/45	.14
Significant AP collaterals	6/13	13/51	.06
Non-sinus rhythm preoperatively	0/14	7/51	.06
Prior pulmonary artery interventions	7/15	25/52	.9
Postoperative effusion > 14 days	6/12	16/52	.5
Reduced postoperative ventricular function	1/15	5/40	.72
AV valve regurgitation: Mild and above	5/15	17/52	.97
NYHA class: Class II and worse	3/10	17/46	.12
Coumadin use	5/15	7/51	.19
History of thromboembolism	0/11	5/49	.037*
Non–sinus rhythm postoperative rhythm	4/15	17/52	.66
Pacemaker	0/14	7/52	.06
SpO_2 < 90%	0/8	1/28	.14
PLE	1/11	3/47	.22

Abbreviations: AP, aortopulmonary; AV, atrioventricular; NYHA, New York Heart Association; PAP, pulmonary artery pressure; PLE, protein losing enteropathy; SpO2, transcutaneous oxygen saturation; TPG, transpulmonary gradient.
*$P < .05$

4 | DISCUSSION

With the advancements in the surgical techniques and management of patients with single ventricular physiology, the incidence of early and late Fontan failure has decreased significantly over the past 2 decades. Early postoperative mortality rates have decreased from 9%-15%[8,9] in the 80 s to under 3% in the current era.[10] A large number of patient and operative variables have been attributed to as risk factors for Fontan failure. Some of the patient factors include- presence of heterotaxy syndrome, systemic right ventricle, reduced systemic ventricular function, cardiac rhythm abnormalities, higher pre-Fontan mean pulmonary artery pressure and systemic ventricular end diastolic pressure. Operative variables associated with Fontan failure include, the need to perform additional concomitant procedures, prolonged cardiopulmonary bypass time, and prolonged cross clamp time.[11] A combination of these risk factors further increases the risk of Fontan failure.

Fenestration of the Fontan circuit was first described in 1990 to overcome the potential for low cardiac output state in the immediate postoperative period by providing an atrial level right to left shunt.[3] It was originally introduced for higher risk patients, which included the patients with ventricular dysfunction, elevated PVR and distal pulmonary artery anatomical abnormalities. In addition to reducing postoperative mortality, other positive effects of fenestration include, a reduction in chronic postoperative pleural effusion and a reduction in the number of hospital days after the Fontan operation.[12] At our center, we currently perform a fenestrated extracardiac Fontan operation in all patients. The placement of fenestration in standard risk patients remains a topic of debate. Some studies have demonstrated improved postoperative recovery, even in standard risk patients, by having a fenestration in the Fontan circuit,[13,14] whereas others did not show added benefits of Fontan fenestration postoperatively.[15] Currently, there is limited data on medium and long term effects and the rate of spontaneous closure of the fenestration. In the literature, there is a wide variation in the rate of spontaneous closure of the fenestration ranging from 8% to 29%.[16,17] Consistent with this, the rate of spontaneous closure in our patients was 22%.

Transcatheter closure of the Fontan fenestration has been well described in the literature. In some institutions, patients with persistently persistent fenestration undergo elective transcatheter closure 1-3 years following the Fontan operation.[16] Test occlusion of the fenestration is performed in the catheterization laboratory with a balloon catheter in order to assess the feasibility and success of device closure, by simulating post-occlusion hemodynamics. At our center, we perform balloon test occlusion of the fenestration for 15 minutes. Presence of one or more of the following factors precluded fenestration closure: decrease in cardiac output by >10%, increase in Fontan pressure by >10% from baseline, both with balloon test occlusion, and presence of significant venovenous collaterals.

In our study, 20% of patients with a persistent fenestration underwent fenestration closure, all but one via transcatheter device closure. We pursue elective closure of the fenestration only in patients with baseline resting desaturation (SpO_2 < 90%) and/or complaint of fatigue with mild to moderate exertion secondary to desaturation which was present in 10 out of 11 patients in our study.

Persistent fenestration is also associated with increased risk of systemic thromboembolism. It is well known that patients with CCHD are at higher risk for thromboembolism due to alteration in the hemodynamic and coagulation protein profile.[18,19] Right to left shunt across the fenestration in Fontan patients increases the risk of systemic embolism. Given this risk, one patient in our study who had a thrombus in the SVC, underwent elective transcatheter closure of the fenestration in order to prevent systemic embolism. In our study, patients with a history of thromboembolic episodes were noted to be at increased risk of having persistence of the fenestration (P = .037). We hypothesize, that the patients with thromboembolic episodes might have additional subclinical thrombi in the Fontan conduit and pulmonary arteries. These might alter the Fontan hemodynamics, elevating the pulmonary vascular resistance and thereby preventing spontaneous closure of the fenestration. We also noted that elevated PVR of > 2 Wum^2 predicted a higher likelihood of persistence of the fenestration (P = .045). The higher PVR in patients with patent fenestration was not related to lower Qp in this study. Presence of significant aortopulmonary collaterals and abnormal pre-Fontan cardiac rhythm were associated with higher incidence of persistent Fontan fenestration, almost achieving statistical significance (P = .06). Use of warfarin (versus aspirin) for thromboprophylaxis had no influence on the patency of Fontan fenestration in this study.

Kotani et al showed that persistence of the Fontan fenestration 6-12 months after the surgery is indicative of physiological intolerance of the Fontan pressures, as noted by a significantly high incidence of Fontan failure and mortality. Therefore, higher PVR and a history of systemic venous thromboembolism, factors which are predictive of patency of Fontan fenestration, could in turn may help us identify those patients who are at risk for Fontan failure.

5 | LIMITATIONS

Our study is limited by the small sample size and its retrospective nature. Loss of few patients to follow up at our institution and lack of all data in those who are included in the study, were other major limitations of our study.

6 | CONCLUSIONS

The rate of spontaneous closure of the fenestration following Fontan palliation surgery is 22% with a median duration from surgery to spontaneous closure of 3 months. Elevated pulmonary vascular resistance and history of systemic venous thromboembolism were predictive of persistence of the Fontan fenestration.

CONFLICT OF INTEREST

The authors have no conflicts to disclose.

AUTHOR'S CONTRIBUTION

Dr Gorla performed data collection and drafted the initial manuscript and approved the final manuscript as submitted. Dr Jhingoeri, Dr Chakraborty, Dr Garg, Dr Raja, and Dr Rosenkranz critically reviewed and approved the final manuscript as submitted. Dr Swaminathan conceptualized and designed the study, drafted the protocol, supervised data collection and statistical analysis, edited, approved, and revised the final manuscript as submitted. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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REFERENCES

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. *Thorax*. 1971;26(3):240-248.
2. Raj S, Rosenkranz E, Sears B, Swaminathan S. Intermediate-term results after extracardiac conduit Fontan palliation in children and young adults with single ventricle physiology-a single-center experience. *Pediatr Cardiol*. 2016;37(6):1111-1118.
3. Bridges ND, Lock JE, Castaneda AR. Baffle fenestration with subsequent transcatheter closure. Modification of the Fontan operation for patients at increased risk. *Circulation*. 1990;82(5):1681-1689.
4. Bridges ND, Mayer JE Jr, Lock JE, et al. Effect of baffle fenestration on outcome of the modified Fontan operation. *Circulation*. 1992;86(6):1762-1769.
5. Quinones JA, Deleon SY, Bell TJ, et al. Fenestrated fontan procedure: evolution of technique and occurrence of paradoxical embolism. *Pediatr Cardiol*. 1997;18(3):218-221.
6. Heal ME, Jackson LB, Atz AM, Butts RJ. Effects of persistent Fontan fenestration patency on cardiopulmonary exercise testing variables. *Congenit Heart Dis*. 2017;12(4):399-402.
7. Kotani Y, Chetan D, Saedi A, et al. Persistent fenestration may be a marker for physiologic intolerance after Fontan completion. *J Thorac Cardiovasc Surg*. 2014;148(6):2532-2538.
8. Cetta F, Feldt RH, O'Leary PW, et al. Improved early morbidity and mortality after Fontan operation: the Mayo Clinic experience, 1987 to 1992. *J Am Coll Cardiol*. 1996;28(2):480-486.
9. Stewart RD, Pasquali SK, Jacobs JP, et al. Contemporary Fontan operation: association between early outcome and type of cavopulmonary connection. *Ann Thorac Surg*. 2012;93(4):1254-1260; discussion 1261.
10. Petrossian E, Reddy VM, Collins KK, et al. The extracardiac conduit Fontan operation using minimal approach extracorporeal circulation: early and midterm outcomes. *J Thorac Cardiovasc Surg*. 2006;132(5):1054-1063.
11. Murphy MO, Glatz AC, Goldberg DJ, et al. Management of early Fontan failure: a single-institution experience. *Eur J Cardiothorac Surg*. 2014;46(3): 458-464; discussion 464.
12. Mavroudis C, Zales VR, Backer CL, Muster AJ, Latson LA. Fenestrated Fontan with delayed catheter closure. Effects of volume loading and baffle fenestration on cardiac index and oxygen delivery. *Circulation*. 1992;86(5 Suppl):II85-II92.

13. Airan B, Sharma R, Choudhary SK, et al. Univentricular repair: is routine fenestration justified? *Ann Thorac Surg*. 2000;69(6):1900-1906.
14. Lemler MS, Scott WA, Leonard SR, Stromberg D, Ramaciotti C. Fenestration improves clinical outcome of the fontan procedure: a prospective, randomized study. *Circulation*. 2002;105(2):207-212.
15. Thompson LD, Petrossian E, McElhinney DB, et al. Is it necessary to routinely fenestrate an extracardiac fontan? *J Am Coll Cardiol*. 1999;34(2):539-544.
16. Imielski BR, Woods RK, Mussatto KA, Cao Y, Simpson PM, Tweddell JS. Fontan fenestration closure and event-free survival. *J Thorac Cardiovasc Surg*. 2013;145(1):183-187.
17. Sommer RJ, Recto M, Golinko RJ, Griepp RB. Transcatheter coil occlusion of surgical fenestration after Fontan operation. *Circulation*. 1996;94(3):249-252.
18. Nowak-Gottl U, Kotthoff S, Hagemeyer E, et al. Interaction of fibrinolysis and prothrombotic risk factors in neonates, infants and children with and without thromboembolism and underlying cardiac disease. A prospective study. *Thromb Res*. 2001;103(2):93-101.
19. Firdouse M, Agarwal A, Chan AK, Mondal T. Thrombosis and thromboembolic complications in fontan patients: a literature review. *Clin Appl Thromb Hemost*. 2014;20(5):484-492.

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