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Original Article

Transcatheter Fenestration Closure after Fontan Surgery

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Abstract

Background: *Although several studies have examined patients who have undergone transcatheter fenestration closure, comprehensive evaluations of its long-term outcomes remain scarce. Therefore, this study aimed to evaluate the clinical status of these patients after a long-term follow-up period.*

Methods: *This cross-sectional analytical study evaluated the records of all children with congenital heart diseases admitted for transcatheter fenestration closure at Rajaie Cardiovascular Medical and Research Center, a tertiary care hospital specializing in congenital heart diseases in Tehran, Iran. We included patients with a history of fenestration following Fontan surgery who required fenestration closure between January 2012 and August 2020. Cardiac function data, such as ejection fraction (EF), pulmonary artery pressure (PAP), and O_2 saturation, were extracted from electronic medical records.*

Results: *We assessed 26 patients (11 female and 15 male) with a mean age of 13.88±3.73 years. Comparing EF before and after fenestration closure revealed a significant difference (P=0.011), with only 2 patients (7.7%) experiencing a slight reduction (5.0%) in EF. No significant difference was observed in PAP before and after closure (P=0.068), although most patients (n=16, 61.5%) had a postprocedural reduction. Our results demonstrated a significant difference before and after the procedure (P<0.001), with all patients exhibiting increased O_2 saturation after closure.*

Conclusion: *Our study demonstrated improvements in cardiovascular function and desirable organ function among patients. These findings suggest that transcatheter fenestration closure could serve as a beneficial complementary approach for patients with patent fenestration.*

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Introduction

In 1971, Fontan and Baudet first described an atriopulmonary connection to address tricuspid atresia. The pro-cedure aims to prevent the mixing of venous and oxygenated blood, thereby improving systemic oxygenation and reducing cyanosis. Over time, the Fontan procedure has undergone numerous technical revisions and is now considered the primary planned palliation in the single-ventricle pathway.[1]

Surgical fenestration of the atrial baffle has been introduced to improve Fontan surgery outcomes by

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alleviating circuit burdens and augmenting cardiac output. This opening facilitates blood flow through the heart by permitting some O_2-poor blood to mix with O_2-rich blood, enhancing cardiac pumping efficiency. Nonetheless, this improve-ment is accompanied by a drawback of reduced blood O_2 levels.[2] Moreover, fenestration can lead to systemic de-saturation and long-term complications such as cyanosis and systemic thromboembolic events resulting from continuous right-to-left shunting. Additionally, an increased risk of thrombosis is associated with stagnant systemic flow and hypercoagulability.[3-5]

Currently, some clinicians perform fenestration closure following Fontan surgery, while others advise limiting fenestration closure to specific patients. This cautious approach aims to reduce the risks of paradoxical cerebral embo-lism, persistent hypoxemia, and increased ventricular preload resulting from the development of aortopulmonary collateral arteries.[6] While some previous studies have examined patients who underwent transcatheter fenestration closure,[3-8] there is a lack of comprehensive evidence on the long-term outcomes of the procedure. Accordingly, this study aimed to assess the clinical status of this group of patients after extended follow-up (3–5 y) in a referral cen-ter. We hypothesized that our findings would contribute valuable insights into this subject, assisting clinicians in managing patients more effectively.

Methods

This cross-sectional analytical study analyzed the records of children with congenital heart diseases admitted for transcatheter fenestration closure at Rajaie Cardiovascular Medical and Research Center (RCMRC), a tertiary care hospital specializing in congenital heart diseases in Tehran, Iran.

Patients included in the study had a history of Fontan surgery with fenestration between January 2012 and August 2020 and required fenestration closure. Inclusion criteria comprised at least 3 years post-Fontan surgery, mean arterial pressure below 15 mm Hg, suitable pulmonary artery anatomy, and mild-to-moderate valve regurgitation. Written informed consent was obtained from all participants. The study protocol was approved by the Ethics Committee of RCMRC (No: IR.IUMS.FMD.REC.1402.270. Date: 2023-09-02).

A single interventionist performed the closure procedure following the inclusion criteria for patients experiencing persistent systemic desaturation. Transthoracic echocardiography was utilized to detect potential thrombi and as-sess patent fenestration. Angiograms were employed to evaluate arterial and venous collaterals. Before closure with the atrial septal defect (ASD)-Amplatzer, an occlusion test of the fenestration was conducted using an ASD-sizing balloon. If pressure changes were deemed acceptable (right atrial pressure <18 mm Hg and increased right atrial pressure <4 mm Hg), and cardiac output was within normal limits, a suitable device was implanted.

Data collection was performed using a form that included demographic characteristics (eg, age and sex) and clin-ical outcomes. The primary diagnosis of congenital cardiac disease before Fontan surgery was verified, and the specific surgical procedure type was documented from patient records. Additionally, the duration of patent fenestra-tion was recorded.

Laboratory findings post-fenestration closure, including platelet count, liver function tests (aspartate aminotransferase [AST], alanine transaminase [ALT], albumin, and total protein), and bilirubin levels, were measured to assess liver function. Ejection fraction was determined by echocardiography and reported as a percentage before and af-ter closure. Further, pulmonary artery pressure (PAP) and O_2 saturation were evaluated immediately before and after closure in the catheterization laboratory. Following closure, the Nakata index was evaluated to assess the growth of pulmonary artery branches, and the New York Heart Association (NYHA) functional class was determined. Additionally, complications such as systemic emboli resulting from fenestration and mortality were documented.

Data were presented as mean ± standard deviation (SD) and median (Q1–Q3) for numerical variables and frequencies (percentages) for categorical variables. The normality distribution of quantitative variables was assessed using the Kolmogorov-Smirnov test. Considering the non-normal distribution of the quantitative data, before-after results were compared using the Wilcoxon signed-rank test. A P value of less than 0.05 was deemed statistically significant. Statistical analysis was conducted using IBM SPSS Statistics 24 for Windows (IBM In., Armonk, NY).

Results

Our study assessed 26 patients, comprising 11 females (42.3%) and 15 males (57.6%). The mean age of the study population was 13.88±3.73 years (age range =7–20 y), and the mean age at the time of Fontan surgery was 5.42±1.83 years. The mean Nakata index was 241.46±105.48. As shown in Table 1, the primary diagnosis leading to Fontan surgery for most patients was pulmonary atresia (n=9, 34.6%), and the left ventricle was dominant in 76.9% of cases. The majority of patients underwent extracardiac Fontan surgery. Regarding the NYHA functional class, 18 patients (69.2%) were classified as class II, and 8 (30.8%) were classified as class III. As shown in Table 2, all laboratory results were within the normal range, and no cases of liver encephalopathy were observed during fol-low-up. No adverse events were reported during the follow-up period.

Given the non-parametric distribution of EF, a comparison of the median and interquartile range of EF before and after fenestration closure revealed a significant difference (P=0.011). Moreover, our results indicated that only 2 patients (7.6%) experienced a slight decrease in EF. Furthermore, no significant difference was noted in PAP before and after closure (P=0.068), with most patients (n=16, 61.5%) showing a reduction post-procedure.

Concerning O_2 saturation, our results demonstrated significant differences before and after the procedure (P<0.001). Notably, all patients experienced increased O_2 saturation following closure (Table 3). Detailed individual patient characteristics are presented in Table 4.

Table 1. Cardiac findings before fenestration closure.

Diagnosis before Fontan surgery	Frequency (%)
CAVSD	1 (3.8)
DILV	3 (11.5)
DILV, TGA	2 (7.7)
DORV	4 (15.4)
MA	1 (3.8)
PA	9 (34.6)
TA	6 (23.1)
Dominant ventricle before Fontan surgery	
Right	3 (11.5)
Left	20 (76.5)
Unknown	3 (11.5)
Type of Fontan surgery	
Lateral tunnel	6 (23.1)
Extracardiac	20 (76.9)
Atrioventricular Regurgitation before Fontan surgery	
Mild	12 (46.2)
Moderate	14 (53.8)

CAVSD, Complete atrio-ventricular septal defects; DILV, Double inlet left ventricle; TGA, Transposition of the great arteries; DORV, Double outlet right ventricle; MA, Mitral Atresia; PA, Pulmonary Atresia; TA, Tricuspid Atresia;

Table 2. Laboratory results (n=26)*

Tests	Mean ±SD
AST (IU/L)	48.30±32.06
ALT (IU/L)	21.03±10.65
Bilirubin (mg/dL)	1.37±0.44
Total protein (mg/dL)	55.65±9.16
Albumin (mg/dL)	38.07±5.99
Platelets (µL)	281000.01± 103000.05

*Data are presented as mean±SD.
AST, Aspartate aminotransferase; ALT, Alanine transaminase.

Table 3. Cardiovascular function indices and their changes*

	Baseline Median (interquartile range)	Last Follow-up Median (interquartile range)	P**
EF (%)	50.0 (45.0 – 50.0)	50.0 (50.0 – 50.0)	0.011
PAP (mmHg)	13.5 (12.0 – 16.0)	12.0 (12.0 – 14.0)	0.068
O2 Saturation (%)	77.0 (68.7 – 80.0)	90 (85.0 – 90.0)	<0.001

*Data are presented as median (interquartile range).
**Mann-Whitney U test
EF, Ejection fraction; PAP, Pulmonary Artery Pressure.

Table 4. The detailed characteristics of each patient.

No	Sex	Age (year)	Diagnosis	Type of Fon-tan	dominant ventricle	Age at opera-tion (years)	Before-after change			Naka-ta index	Functional class
							EF (%)	PAP (mmHg)	O_2 Satu-ration (%)		
1	M	17	PA	EC	left	11	0.0	-6	13.0	279	mild
2	M	13	DILV	EC	left	6	-5.0	4	34.0	200	mild
3	F	10	DORV	EC	unknown	7	5.0	6	25.0	196	mild
4	M	16	TA	LT	unknown	4	0.0	2	10.0	218	mod
5	F	18	MA	EC	right	2	0.0	6	27.0	119	mild
6	M	8	TA	EC	left	8	5.0	0	16.0	311	mild
7	M	9	PA	EC	left	6	0.0	0	7.0	128	mild
8	M	13	DILV,TGA	EC	left	6	0.0	10	22.0	577	mod
9	F	20	PA	EC	left	5	-5.0	-1	8.0	199	mild
10	M	15	PA	EC	unknown	4	0.0	-6	15.0	191	mild
11	F	13	DILV	LT	left	6	0.0	0	10.0	140	mod
12	F	16	DORV	EC	right	5	5.0	3	20.0	100	mild
13	F	7	CAVSD	EC	left	3	5.0	3	27.0	200	mild
14	M	7	TA	EC	left	3	10.0	1	23.0	191	mod
15	M	17	PA	EC	left	5	0.0	0	10.0	279	mild
16	F	12	PA	EC	left	7	0.0	3	15.0	200	mild
17	F	13	TA	LT	left	7	0.0	2	0.0	190	mod
18	F	14	DORV	EC	left	6	5.0	-2	10.0	310	mild
19	F	12	TA	EC	left	4	0.0	-2	10.0	250	mild
20	M	10	DORV	EC	right	4	0.0	-5	15.0	300	mod
21	M	14	PA	EC	left	6	10.0	2	5.0	420	mild
22	M	17	PA	EC	left	6	5.0	5	10.0	200	mild
23	M	17	DILV,TGA	LT	left	4	10.0	1	10.0	150	mild
24	M	20	TA	EC	left	6	0.0	3	10.0	320	mod
25	M	17	PA	LT	left	6	5.0	3	5.0	400	mild
26	F	16	DILV	LT	left	4	5.0	2	10.0	210	Mod

CAVSD, Atrioventricular septal defect; DILV, Double-inlet left ventricle; DORV, Double-outlet right ventricle; EC, Extracardiac; EF, Ejection fraction; LT, Lateraltunnel; MA, Mitral atresia; PA, Pulmonary atresia; PAP, Pulmonary artery pressure; TA, Tricuspid atresia; TGA, transposition of the great vessels

Discussion

This study evaluated the clinical status, including cardiovascular function, O_2 saturation, liver function, and protein levels, in 26 patients who underwent transcatheter fenestration closure following Fontan surgery. Our findings demonstrated significant improvements in cardiac function indices such as EF, PAP, and O_2 saturation. No significant complications were observed post-procedure.

In the 1970s, Fontan and colleagues pioneered surgical techniques to bypass the right ventricle in univentricular heart anomalies. Their initial approach involved connecting the superior vena cava to the right pulmonary artery and closing the ASD, effectively repurposing the right atrium as a pumping chamber. Early iterations of the Fontan surgery were characterized by high initial mortality rates and prolonged ICU stays. Over time, modifications to the procedure have led to improved outcomes. While earlier Fontan surgery variants were associated with increased complications, the contemporary staged procedure involving fenestration has reduced these issues. Key complications include arrhythmias, obstructed Fontan pathways, cyanosis, paradoxical emboli, thrombus formation, development of collateral vessels, and protein-losing enteropathy.[9-10]

A meta-analysis found that fenestration was associated with lower PAP, more stable O_2 saturation levels, and diminished pleural effusion.[2] Nevertheless, conflicting results have been reported in other studies. A recent propensity score-matched study from the Australia and New Zealand registry analyzed data from 1443 patients (621 fenestrated and 822 non-fenestrated) with a median follow-up of 10.6 years. After matching, fenestration was not associated with survival, hospital stay, protein-losing enteropathy, prolonged pleural effusion, or severe dysfunction symptoms. Conversely, Fontan circuit thromboembolism occurred more frequently in fenestrated patients. The study concluded that fenestration in Fontan surgery did not yield long-term benefits.[11]

Long-term O_2 desaturation resulting from fenestration, along with associated complications such as cyanosis and thromboembolism, necessitates shunt closure years post-surgery. Transcatheter closure using an ASD closure device[12] is a safe and effective minimally invasive procedure for addressing surgically created fenestrations in Fontan heart pathways, successfully improving blood O_2 levels.[13] Still, the ideal timing and indications for closure remain subjects of ongoing debate. Closure device benefits include increased O_2 levels, maintaining stable O_2 during physical activity, and potentially diminishing the risk of stroke, although there is currently no definitive evidence supporting this claim. While shunt closure does not appear to have an immediate

impact on exercise capacity, concerns have been raised about potential adverse effects. Closing the shunt may lead to increased congestion in the venous system, particularly affecting the abdomen and liver, which could increase the risk of complications such as protein-losing enteropathy and liver fibrosis.[5]

To our knowledge, no previous studies have comprehensively examined transcatheter fenestration closure following Fontan surgery. Thus, we have referenced earlier investigations that focused specifically on the effects of closure on cardiopulmonary organs. A systematic review and meta-analysis of 12 studies, encompassing 505 patients who underwent transcatheter closure with a mean follow-up period of 34 months, demonstrated that fenestration closure using a catheter-based approach was associated with improved O_2 levels both at rest and during physical activity, lower maximum heart rate during exercise, and increased exercise duration. These benefits were observed despite a slight increase in pulmonary artery pressure. Findings demonstrated an average increase of 7.9% in systemic O_2 levels, accompanied by a slight elevation of 1.4 mm Hg in pulmonary pressure. Exercise tolerance also showed improvement; however, this aspect was evaluated in only 2 studies and over a short duration.

A 10-year study involving 181 patients who underwent catheter closure (with 154 successful procedures) demonstrated a 9.4% rise in O_2 saturation, reduced diuretic and digoxin requirements, and rare adverse events. Children also exhibited desirable growth patterns.[8]

In a separate retrospective study comparing 42 patients with successful transcatheter closure to 160 patients with unsuccessful procedures (median follow-up of approximately 47 months), a significant increase in O_2 saturation was observed post-closure. Nonetheless, no significant differences in mortality and morbidity were found between the 2 groups.[5]

Another study on 51 patients with a median follow-up time of about 1 year also showed an increased O_2 saturation.[3]

Transcatheter fenestration closure following Fontan surgery has been practiced in Iran since the early 2000s. In 2007, Meraji et al[6] reported 3 patients who underwent transcatheter closure of fenestration with an ASD-Amplatzer device due to severe cyanosis and significant intracardiac shunts. The patients, with an average age of 8 years (range =6–12 y), underwent the procedure approximately 15 months post-Fontan operation. After closure, aortic O_2 saturation rose by an average of 17.6% (range =9%–26%). During a follow-up period of over 2 years (mean =27 mon), echocardiography revealed complete closure in 2 patients, while 1 patient had a small residual opening. Atrial flutter occurred in 1 patient during the follow-up period.[6]

Our study successfully assessed a suitable number of patients during long-term follow-up at our tertiary referral center. Nevertheless, it is essential to acknowledge some limitations. The retrospective nature of the study may have influenced our results. Furthermore, previous research has demonstrated the predictive value of certain biomarkers, such as brain-type natriuretic peptides, for morbidity and mortality in patients with congenital heart diseases following surgery.[13,14] Given the safety and promising findings of this procedure, future prospective studies involving larger sample sizes and incorporating these vital markers are recommended.

Conclusion

Our study demonstrated improvements in patients' cardiovascular function and organ health, suggesting that transcatheter fenestration closure can be a beneficial complementary approach for patients with patent fenestration. To further validate these findings, prospective studies with extended follow-up periods and multicenter data registry systems are warranted. Incorporating relevant biomarkers for patient risk assessment should also be considered in future studies.

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