MedCrave
Step into the World of Research
International Journal of Pregnancy & Child Birth

Research Article
Open Access
CrossMark

Clinical profile, surgical approach and outcomes of children with Fontan procedure in a country with limited resources

Abstract

Background: For more than five decades, the Fontan or Fontan-Kreutzer procedure has been the mainstay treatment for congenital heart disease with a single functioning ventricle. Data concerning epidemiological profiles are poor, especially in countries with limited resources. Here, we present the cases of children with complex congenital heart disease (CHD) born in Kosovo who underwent some forms of Fontan palliation measuring the renal resistive index (RRI) to assess ventricular function and renal complications after the Fontan procedure.

Objectives: This study aimed to describe the primary pathology, age, place of surgical intervention, and outcomes of children in Kosovo, a country with limited resources, who underwent the Fontan procedure in different countries.

Results: from January 2018 to December 2021, 40 patients (28 male and 12 female) aged 6 to 19 years (mean 6.03 years) after a total Cavo-pulmonary connection were examined for renal insufficiency and thrombotic complications. The renal resistive index (RRI) and hematological parameters were analyzed as criteria for possible early and late complications. Two patients only developed complications in the cohort group. In both cases, the second and third stages of surgery were performed late, at the ages of 12 and 9 years. The first patient manifested a severe form of protein-lousing enteropathy, renal insufficiency, and plastic bronchitis, while the other patient presented with initial signs of protein-lousing enteropathy and recurrent ventricular tachycardia.

Conclusion: Survival after Fontan operation in our group was excellent. Survival is closely dependent on the primary diagnosis, associated anomalies, age at palliation, and place of surgery.

Keywords: single ventricle, tricuspid atresia, hypoplastic left heart syndrome, fontan procedure

Volume 9 Issue 3 - 2023

Arlinda Maloku,[1,2] Ramush Bejiqi,[2,3] Aferdita Mustafa,[2] Naim Zeka,[1,2] Rinor Bejiqi[2]
[1]University of Prishtina, Kosova
[2]University Clinical Center of Kosovo, Kosovo
[3]Visiting Professor, Texas Health Science Center, USA

Correspondence: Ramush Bejiqi, University Clinical Center of Kosovo, Pediatric Clinic, Prishtina, Kosovo
ramush.bejiq@outlook.com

Received: June 20, 2023 | **Published:** July 5, 2023

Introduction

The Fontan procedure was initially introduced in 1971 as a treatment for patients with tricuspid atresia, representing a milestone in congenital heart surgery.[1,2] It provides a means for congenital heart disease (CHD) patients with a single functional ventricle (e.g., tricuspid atresia, heterotaxy syndrome, hypoplastic left heart syndrome (HLHS), and single ventricle) to separate the pulmonary and systemic circulations with fair systemic oxygen saturation.[2] With advancements in perioperative care, the surgical survival rate of first-stage palliation prior to the Fontan procedure and Fontan procedure percentage reach 80%-90%.[3]

Therefore, the number of patients who underwent the Fontan procedure (Fontan patients and post-Fontan patients) will increase over time. Prior to the Fontan operation or in early follow-up during childhood, Fontan patients are already at risk of many complications, such as protein-lousing enteropathy, plastic bronchitis, several thromboses, and arrhythmia from the associated conduction system abnormalities.[4,5] Thromboembolic complications are a major cause of early and late mortality in children with single-ventricle congenital heart defects who have undergone the Fontan procedure.[6]

Thrombosis is an important and unpredictable complication, not only after the Fontan operation, but also associated with each stage of single-ventricle palliation.[7] It is an important cause of morbidity, particularly when it leads to pulmonary embolism or stroke, and contributes to mortality. However, the impact of arrhythmias and relevant treatment strategies remain unclear.[8] The medical needs of the Fontan and post-Fontan population are likely to become a formidable challenge; however, it remains still defined.[2] This far, only 1 study, based on a database from a tertiary care hospital, has estimated the incidence of the Fontan procedure from the served population at 0.10/1000.

Results

Patients and surgical procedures

From January 2018 to December 2021, 40 patients (28 male and 12 female), aged 0 to 19 years (mean 6.03 years) after a total Cavo-pulmonary connection were examined for renal insufficiency and thrombotic complications. All children underwent one form of total Cavo-pulmonary connection, including the Fontan procedure, using an internal or external PTFE conduit plus a bidirectional Cavo-pulmonary connection during 2002–2018. Survival and late adverse events were also analyzed. Risk factors for early and late mortality were examined using the hazard function methodology. The renal resistive index (RRI) and hematological parameters were analyzed as criteria for possible early and late complications. The primary reasons for Fontan palliation are summarized in Table 1. Only three patients had mitral atresia; two had previously undergone Blalock-Hanlon septectomy and had a thin-walled right atrium. 22 patients had tricuspid atresia (TA), seven patients had pulmonary atresia with

ventricular septal defect (PA+VSD), and eight had double outlet right ventricle (DORV), of which two had hypoplastic right ventricle). In 38 of them, one other heart defect was present, mostly atrial and ventricular septal defects, in 32 children Table 2.

Table 1 Primary diagnosis before the surgery

Primary diagnosis	With thrombotic therapy		Without thrombotic therapy		Total	
	N	%	N	%	N	%
PA atresia	5	17.2	2	18.2	7	17.5
MV atresia	2	6.9	1	9.1	3	7.5
TV atresia	14	48.3	8	72.7	22	55
L-TGA	1	3.4	-	-	1	2.5
Single ventricle	7	24.1	-	-	7	17.5
Total	29	100	11	100	40	100

PA, pulmonary artery; MV, mitral valve; TV, tricuspid valve; L-TGA, left transposition of the great arteries

Table 2 Associated heart anomalies

ASD/VSD	With thrombotic therapy		Without thrombotic therapy		Total	
	N	%	N	%	N	%
ASD	3	10.3	-	-	3	7.5
ASD+VSD	22	75.9	10	90.9	32	80
VSD	2	6.9	1	9.1	3	7.5
(blank)	2	6.9	-	-	2	5
Total	29	100	11	100	40	100

ASD, atrial septal defect;VSD, ventricular septal defect

Seven of them, five with tricuspid atresia, were diagnosed in utero (from 18 to 32 weeks of gestation) and as a leak of cardio surgery services in Kosovo, in utero transport has been realized. In all of them, some forms of palliation, Glenn or Fontan, were performed. As a consequence of missing cardio-surgical services in Kosovo, surgical intervention has been performed in different European countries, in the USA, Italy, and Turkey (Table 3).

Table 3 Age of patients at the third surgery

Age at the 3rd surgery	N	%
4 years	3	33.3
6 years	3	33.3
8 years	1	11.1
15 years	1	11.1
Total	9	100

We measured RRI in both kidneys and in terminal renal arteries using ultrasonography methods (2-D, pulls, and color Doppler) and compared the results with those of 30 healthy children from the control group. As a standard, we performed three measurements on both sides and a median value from the results was used as a parameter. In addition, a few other hematological and urine analyses were included in the study as a parameter to assess renal complications after these procedures. Data were statistically analyzed using Fisher's test, Kruskal Wallis, and Dunn's Multiple Comparison test, and are presented in tables and graphics (Table 4–6).

Table 4 Country were the children had surgical intervention

Place of surgical intervention				Total surgery by place%
	first surgery	second surgery	third surgery	%
USA	0%	0%	3%	3%
Czech Republic	3%	0%	0%	3%
Italy	26%	34%	34%	94%
Germany	10%	3%	14%	27%
Turkey	54%	40%	40%	134%
Israel	3%	3%	3%	9%
Austria	2%	3%	3%	8%
Switzerland	-	3%	3%	6%
France	2%	14%	0%	16%

Table 5 Resistive renal index value in the left kidneys

IRR left	Study group					
	Group with antithrombotic therapy		Group without antithrombotic therapy		Total	
	N	%	N	%	N	%
<0.5	3	10.3	-	-	3	7.5
0.5 - 0.9	9	31	3	27.3	12	30
>0.9	17	58.6	8	72.7	25	62.5
Total	29	100	11	100	40	100
Fisher test	P = 0.486					
OR (95% CI)	1.882 (0.412 - 8.599)					

Table 6 Resistive renal index value in the right kidneys

IRR right	Study group					
	Group with antithrombotic therapy		Group without antithrombotic therapy		Total	
	N	%	N	%	N	%
<0.5	4	13.8	-	-	4	10
0.5-0.9	11	37.9	3	27.3	14	35
>0.9	14	48.3	8	72.7	22	55
Total	29	100	11	100	40	100
Fisher test	P = 0.286					
OR (95% CI)	2.857 (0.628 - 12.986)					

Discussion

Choussat's "Ten Commandments," which describes the components of an ideal Fontan candidate, was first published in 1977. These guidelines, modified slightly by various centers, have served clinicians in the past 33 years by helping determine which patients could safely be staged toward Fontan palliation with a high probability of success. Despite the wisdom in these commandments, it is clear from a historical perspective that total compliance with all criteria does not necessarily portend excellent long-term survival because Kaplan-Meier survival curves demonstrate a disturbing attrition trend.[9] Given the advancements made in catheter/interventional techniques and in surgical and hybrid techniques, as well as advancements in imaging modalities to guide invasive techniques and newer pacing technologies, we believe that the endpoint of the original commandments should be modified to include improvements in long-term survival.[10–15]

Our cohort group of patients after the Fontan procedure is perhaps unique in the world and in Europe, since, in the absence of cardiac surgery services in Kosovo, all children were sent to different countries worldwide, such as the USA, the different countries of Europe and Turkey, and in different cities within a country, as well as different hospitals within a city. The situation is further complicated when a patient undergoes three cardio-surgical interventions in three different cardiac surgery centers. It is worth mentioning that despite this variation in cardio-surgical treatment, we did not note any deaths after cardio-surgical intervention. Complications after the Fontan procedure are numerous and can be divided into early and late complications. Early complications include heart failure, malignant rhythm disturbances that lead to heart failure, and protein-lousing enteropathy.[10] Late complications are more frequent and can present as plastic bronchitis, various types of heart rhythm disturbances, protein lousing enteropathy, heart failure, and kidney failure.[14]

In our study, we analyzed only late complications and found them in 7 children. Five children had rhythm disorders, two them developed complete atrioventricular block, and a permanent pacemaker was implanted. Regular tests showed good function and both children had normal physical activities. Three other patients with rhythm disturbances developed episodes of ventricular tachycardia that were well-controlled with drug therapy.

From the analyzed group of patients, only two children had increased renal resistance index (RRI) values, where in one child the values were moderately increased, whereas in the other patient, we found very high values of RRI. Furthermore, in the other patient with complications after Fontan, all interventions were performed in three different cardio-surgical centers in European countries.

Both patients had other late complications associated with the Fontan procedure: the first patient had mild signs of protein-lousing enteropathy but with good ventricular function, while the other patient had all the complications seen in patients with Fontan: signs of functional ventricular insufficiency classified by NYHA III, plastic bronchitis, severe signs of protein-losing enteropathy, and high values of the renal resistance index (Table 7).[11]

Table 7 Renal resistance index

No	Age	Sex	Primary diagnosis	Time of diagnosis	I operation/ place	II operation/ place	III operation / place	Age/ I operation	Age /II operation	Age /III operation
1	13	m	Atresio VT	postnatal	Italy	Italy	Italy	3 months	6 months	3 years
2	19	m	L-TGA	postnatal	Italy	Italy		3 months	9 months	
3	19	m	Atresio VT	prenatal	Austria	Austria	Austria	after birth	9 months	8 years
4	7	m	Atresio AP	postnatal	Italy	Italy		1.5 years	2 years	
5	7	f	Atresio VT	prenatal	Turkey	Turkey	Turkey	5 months	1 year	3 years
6	19	f	Atresio VT	postnatal	Italy	Italy		9 months	2 years	
7	19	m	Single ventricule	postnatal	France	Swiss	Swiss	after birth		15 years
8	4	f	Atresio VT	postnatal	Turkey			2.5 months		
9	12	m	Atresio VT	postnatal	Italy	Italy	Italy	1 month	6 months	3 years
10	4	m	Atresio VT	postnatal	Turkey			4 months		
11	3	m	Atresio AP	postnatal	Turkey	Turkey		1 month	3 months	
12	4	f	Single ventricule	prenatal	Italy	Italy		after birth	8 months	
13	6	m	Single ventricule	postnatal	Germany	Germany		after birth	2 months	
14	19	m	Atresio VT	postnatal	Check Republic	SHBA		after birth	4 months	
15	18	m	Single ventricule	postnatal	Germany	Germany		1 month	7 months	
16	6	m	Atresio VM	postnatal	Turkey	Turkey		after birth	5 months	
17	9	f	Atresio VM	postnatal	Italy	Turkey		2 years	3 years	
18	10	m	Single ventricule	postnatal	Israel	Israel	Israel	after birth	4 years	5 years
19	11	m	Atresio AP	postnatal	Italy	Italy	Italy	5 months	6 months	4.5 years
20	2	f	Single ventricule	postnatal	Turkey			after birth		
21	7	f	Atresio AP	prenatal	Italy	Italy		after birth	1 month	
22	11	f	Atresio AP	postnatal	Turkey			4 months		
23	5	m	Atresio VT	prenatal	Turkey	Turkey	Turkey	after birth	6 months	4 years
24	3	m	Atresio VT	postnatal	Turkey			after birth		
25	7	m	Atresio VT	prenatal	Italy	Italy		after birth	10 months	
26	3	m	Atresio VT	postnatal	Turkey			4 months		
27	6	m	Single ventricule	postnatal	Germany	Germany		after birth	3 months	

Table 7 continued.....

No	Age	Sex	Primary diagnosis	Time of diagnosis	I operation/ place	II operation/ place	III operation / place	Age/ I operation	Age /II operation	Age /III operation
28	9	m	Atesio VT,	postnatal	Turkey	Turkey		after birth	3 months	
29	4	f	Atresio VT	postnatal	Turkey			after birth		
30	3	f	Atresio VT	postnatal	Turkey			1 month		
31	2	f	Atresio VT	postnatal	Turkey	Turkey		2 months	6 months	
32	2	m	Atresio VT	prenatal	Turkey	Turkey		1 month	9 months	
33	18	m	Atresio VM	postnatal	Germany	Germany		1 month	2 years	
34	4	m	Atresio VT	postnatal	Turkey	Turkey		after birth	4 months	
35	3	m	Atresio AP	postnatal	Turkey	Turkey		after birth	4 months	
36	8	f	Atresio VT	postnatal	Italy	Italy	Italy	1 month	4 months	3.5 years
37	3	m	Atresio VT	postnatal	Turkey	Turkey		1 month	6 months	
38	2	m	Atresio VT	postnatal	Turkey	Turkey		after birth		
39	2	m	Atresio AP	postnatal	Turkey			after birth		
40	5	m	Atresio VT	postnatal	Turkey	Turkey		after birth	4 months	

Based on the criteria for the Fontan procedure described in 1977 by Choussat and the criteria revised by Dr. Wilkinson (2010), one of the criteria was the age at which the intervention was performed.[12]

In patients with severe complications, it is interesting that the first intervention was performed in Paris, at the age of 6 months, while the second intervention was performed very late, in Lausanne, Switzerland, at the age of 15 years, when clinical and echocardiographic findings showed heart failure and mild-severe AV valve regurgitation.

Therefore, we recommend that cardio-surgical interventions should be performed at the ideal age, according to the primary congenital heart defect and hemodynamic status, based on the revised criteria of Choussat.

Conclusion

In patients with a functionally univentricular heart, the Fontan strategy achieves separation of systemic and pulmonary circulation and reduction of ventricular volume overload.[13]

Contemporary modifications to surgical techniques have significantly improved survival rates. However, the resulting Fontan physiology is associated with a high morbidity. In this review, we discuss the state of the art of the Fontan strategy by assessing survival and risk factors for mortality and complications of the Fontan circulation, such renal resistance index and thromboembolism are discussed. The common surgical and catheter-based interventions following Fontan completion are outlined. We describe functional status measurements, such as quality of life and developmental outcomes, in contemporary Fontan patients. The current role of drug therapy in Fontan patients has also been explored. Furthermore, we assessed the current use and outcomes of mechanical circulatory support in the Fontan circulation and novel surgical innovations. Despite large improvements in outcomes for contemporary Fontan patients, a large burden of disease exists in this patient population, especially in countries with limited resources. Continued efforts to improve outcomes are warranted. Several remaining challenges in the Fontan field have been identified.

Total Cavo-pulmonary connections have the following advantages: (1) they are technically simple and reproducible in any atrioventricular arrangement and are away from the atrioventricular node; (2) most of the right atrial chamber remains at low pressure, which reduces the risk of early or late arrhythmias; (3) reduction of turbulence prevents energy losses and minimizes the risk of atrial thrombosis; and (4) postoperative cardiac catheterization performed in 10 patients confirmed these favorable flow patterns with minimal gradients throughout the connections. These encouraging early results support the continuing use of a total Cavo-pulmonary connection, at least for patients with a non-hypertrophied right atrium.

Acknowledgements

Author contributions: Each author contributed substantially to the conception and design of the acquisition, analysis, and interpretation of data for this article. Each author drafted and revised the article critically for important intellectual content. All authors have accepted responsibility for the entire content of this submitted manuscript and have approved its submission.

Consent: Written informed consent was obtained from the patient's parents for publication of this case report and accompanying images.

Honorarium: None declared.

Competing interests: The funding organization(s) played no role in the study design, collection, analysis, and interpretation of data, in the writing of the report, or in the decision to submit the report for publication.

Ethical approval: This report was approved by the Institutional Review Board at the University Clinical Center of Kosovo, Prishtina, Kosovo, Nr 16/22.

Conflicts of interest

The authors alone are responsible for the content and writing of this article. The authors declare no conflict of interest with respect to the authorship and/or publication of this article.

References

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. *Thorax*. 1971;26(3):240–248.
2. Lee MC, Wu MH, Lin MT, et al. Incidence and postnatal profile of fontan patients by adolescence from a nationwide birth cohort. *Acta Cardiologica Sinica*. 2020;36(4):367.
3. Dabal RJ, Kirklin JK, Kukreja M, et al. The modern Fontan operation shows no increase in mortality out to 20 years: a new paradigm. *The*

Journal of Thoracic and Cardiovascular Surgery. 2014;148(6):2517–2524.

4. Wu MH, Wang JK, Lin JL, et al. Supraventricular tachycardia in patients with right atrial isomerism. *Journal of the American College of Cardiology.* 1998;32(3):773–779.
5. Epstein MR, Saul JP, Weindling SN, et al. Atrioventricular reciprocating tachycardia involving twin atrioventricular nodes in patients with complex congenital heart disease. *Journal of cardiovascular electrophysiology*. 2001;12(6):671–679.
6. Odegard KC, McGowan Jr FX, DiNardo JA, et al. Coagulation abnormalities in patients with single–ventricle physiology precede the Fontan procedure. *The Journal of Thoracic and Cardiovascular Surgery*. 2002;123(3):459–465.
7. Kay WA, Moe T, Suter B, et al. Long term consequences of the Fontan procedure and how to manage them. *Progress in cardiovascular diseases.* 2018;61(3–4):365–376.
8. Peretto G, Durante A, Limite LR, et al. Postoperative arrhythmias after cardiac surgery: incidence, risk factors, and therapeutic management. *Cardiology research and practice*. 2014.
9. Stern HJ. Fontan "Ten Commandments" revisited and revised. *Pediatric cardiology*. 2010;31(8):1131–4.
10. Marcelletti CF, Hanley FL, Mavroudis C, et al. Revision of previous Fontan connections to total extracardiac cavopulmonary anastomosis: a multicenter experience. *The Journal of Thoracic and Cardiovascular Surgery*. 2000;119(2):340–346.
11. Mackie AS, Veldtman GR, Thorup L, et al. Plastic Bronchitis and Protein–Losing Enteropathy in the Fontan Patient: Evolving Understanding and Emerging Therapies. *Canadian Journal of Cardiology*. 2022.
12. Choussat A. Selection criteria for Fontan's operation. Pediatric cardiology. New York: Churchill–Livingstone; 1977:559–560.
13. Van der Ven JP, Van den Bosch E, Bogers AJ, et al. State of the art of the Fontan strategy for treatment of univentricular heart disease. *F1000Research*. 2018;7.
14. Deal BJ, Mavroudis C, Backer CL. Arrhythmia management in the Fontan patient. *Pediatric cardiology*. 2007;28(6):448–456.
15. Jacobs JP, Mayer Jr JE, Mavroudis C, et al. The society of thoracic surgeons congenital heart surgery database: 2016 update on outcomes and quality. *The Annals of thoracic surgery*. 2016;101(3):850–862.

Citation: Maloku A, Bejiqi R, Mustafa A, et al. Clinical profile, surgical approach and outcomes of children with Fontan procedure in a country with limited resources. *Pregnancy & Child Birth.* 2023;9(3):104–108. DOI: 10.15406/ipcb.2023.09.00286