Received: 22 Feb 2025 | **Accepted:** 15 Apr 2025 **Genel Tıp Derg. Volume** 35/**Issue** 3 (June), 519-529
DOI: 10.54005/geneltip.1644893

ORIGINAL ARTICLE

Analysis of Perioperative Factors in the Development of Early Fontan Failure: A Single-center Experience

Erken Fontan Yetmezliğinin Gelişiminde Perioperatif Faktörlerin Analizi: Tek Merkez Deneyimi

[1]Mustafa Yılmaz, [1]Başak Soran Türkcan, [1]Ata Niyazi Ecevit, [2]Alper Gürsu, [1]Atakan Atalay

[1]Department of Pediatric Cardiovascular Surgery, Ankara Bilkent City Hospital, Türkiye
Cardiovascular Surgery, Türkiye
[2]Department of Pediatric Cardiology, Ankara Bilkent City Hospital, Türkiye

Correspondence

Mustafa Yılmaz, MD, Department of Pediatric Cardiovascular Surgery, Ankara Bilkent City Hospital, Türkiye

E-Mail: mustafayz1983@gmail.com,

How to cite ?

Yılmaz M, Türkcan BS, Ecevit AN, Gürsu A, Atalay A. Analysis of Perioperative Factors in the Development of Early Fontan Failure: A Single-center Experience. Genel Tıp Derg. 2025;35 (3): 519-529

ABSTRACT

Aim: Early Fontan failure (EFF) after Fontan surgery is rarely observed. Examining perioperative factors associated with this complication, which can lead to mortality and morbidity, is crucial for early diagnosis and treatment.
Methods: All pediatric patients undergoing Fontan surgery between 2019 and 2023 were retrospectively analyzed. Preoperative demographic, echocardiographic, and angiographic data were collected. Hospital data related to operative and postoperative variables were retrospectively examined. The relationship between these variables and the development of EFF was investigated.
Results: A total of 21 Fontan patients were included in this study, and 10 of them (47.6%) developed EFF. Postoperatively, three patients (14.2%) died. Of the patients, 52.4% were male, with a median age of 4.5 years. Among the findings, postoperative maximum vasoactive-inotropic score (maxVIS) within the first 24 postoperative hour (p=0.023) and initial blood gas lactate values (p=0,019) were significantly higher in patient developing EFF. Furthermore, the need for renal replacement therapy (p=0.020) and extracorporeal membrane oxygenation (ECMO) (p=0.020) were found to be associated with EFF. Delay in extubation due to hemodynamic instability has been identified as a significant risk factor for the development of EFF.
Conclusions: The postoperative maxVIS value in postoperative 24 hour and initial lactate levels in intensive care unit were found to be associated with EFF development. Delay in extubation due to hemodynamic instability has been identified as a significant risk factor for the development of EFF.

Keywords: Early Fontan failure, Fontan, Pediatric

ÖZ

Amaç: Fontan operasyonu sonrası erken Fontan yetmezliği (EFY) nadir izlenmektedir. Mortalite ve morbiditeyle sonuçlanabilecek bu komplikasyonla ilişkili perioperative faktörlerin incelenmesi erken tanı ve tedavi için önemlidir.
Gereç ve Yöntemler: 2019-2023 yılları arasında Fontan operasyonu geçirmiş tüm pediatrik hastalar retrospektif olarak incelendi.Hastaların preoperative demografik , ekokardiyografik, anjiografik verileri toplandı. Operatif ve postoperatif değişkenlere ait hastane verileri retrospektif olarak incelendi.Tüm bu değişkenler ile EFY gelişimi arasındaki ilişki araştırıldı.
Bulgular: Bu çalışmaya toplam 21 Fontan hastası dahil edilmiştir ve bunların onunda (%47,6) EFY gelişmiştir. Ameliyat sonrası dönemde üç hasta (%14,2) hayatını kaybetmiştir.. Hastaların %52,4'ü erkek olup, medyan yaş 4,5 yıl olarak belirlenmiştir. Bulgular arasında, ameliyattan sonraki ilk 24 saatteki maksimum vasoaktif-inotropik skor (maxVIS) (p=0,023) ve yoğun bakımdaki il arterial kan gazı laktat değerlerinin (p=0,019) EFY gelişen hastalarda anlamlı şekilde daha yüksek olduğu izlenmiştir. Ayrıca, böbrek replasman tedavisi (p=0,020) ve ekstrakorporeal membran oksijenasyonu (EKMO) ihtiyacının (p=0,020) EFY ile ilişkili olduğu saptanmıştır. Hemodinamik instabilite sebebiyle ekstübasyonun ertelenmesi EFY gelişim riskinin artışı ile ilişkili bulunmuştur.
Sonuçlar: Hastaların postoperatif ilk 24 saatteki maxVIS ve yoğun bakımda alınan ilk arter kan gazı laktat değerlerinin yüksek olması EFY gelişimi ile ilişkili bulunmuştur.Hemodinamik instabilite sebebiyle ekstübasyonun ertelenmesi EFY gelişimi için önemli bir risk faktörü olarak belirlenmiştir.

Anahtar Kelimeler: Erken Fontan yetmezliği, Fontan, Pediatrik

Introduction

The Fontan operation was first described in 1971 by Francis Fontan in a patient with tricuspid atresia (1). This surgical method, which has undergone numerous modifications over the years, still maintains its validity as a palliative treatment for patients with a functional single ventricle (2). The basic premise of this surgical technique is to provide patients with a more functional and healthier long-term life by reducing the preload and afterload of a single ventricle that is currently functioning effectively. However, it also has some inherent limitations (3), and these may lead to early and long-term complications, resulting in significant challenges for both patients and clinicians (4, 5). Today, owing to modern surgical techniques, improved services in intensive care unit (ICU), and increasing experience, significant reductions in mortality and morbidity have been observed in patients following the Fontan surgery (5, 6). Clarifying the roadmap that must be meticulously followed from birth to end-stage palliation has enabled the appropriate surgical or endovascular interventions for the right patients (7). Unfortunately, there are still patients experiencing circulatory failure in the acute period following this type of surgery, resulting in early morbidity and even mortality (8). This situation has been particularly influenced by the fact that, in recent years, the Fontan

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

surgery has been performed on high-risk patients with complex malformations, in many high-volume centers worldwide (9). Detailed preoperative evaluation and appropriate patient selection are considered crucial for achieving successful postoperative outcomes in such high-risk patients (7).

This study aimed to compare the preoperative and operative characteristics of patients with and without early Fontan failure (EFF) and to identify any significant variables, if any. In addition, other variables that may be associated with EFF in the early postoperative period have also been analyzed and investigated.

Materials and Methods

Patients were evaluated after approval was obtained Ethics Committee (Decision No: E2-24-6147). The study was conducted under the principles of the Declaration of Helsinki. All patients undergoing extracardiac Fontan (ECF) surgery at our clinic between August 2019 and December 2023 were included in the study. The patients' demographic and echocardiographic data, as well as information on catheterization, previous surgeries or interventions, and data from other imaging methods, were reviewed in the pediatric cardiology and cardiovascular surgery council before the Fontan surgery. Additionally, the patients' current heart rhythms, histories of arrhythmia, and complications experienced during and after previous operations (such as prolonged pleural effusion, chylothorax, and diaphragm paralysis) were also critical factors in the preoperative decision-making process.

Exclusion Criteria for the Fontan Surgery

During the single ventricle palliation pathway, patients developing severe neurological symptoms for any reason and could not be adequately mobilized, as well as those with congenital syndromes that caused significant mobility restrictions, were not subjected to the Fontan surgery, due to the high risk of postoperative morbidity and mortality. As the result of the serious long-term morbidities that may arise, patients with severe (Grade 3 and above) systemic atrioventricular (AV) valve insufficiency, which is deemed unsuitable for repair and whose systemic ventricular ejection fraction is observed to be <50% on echocardiography, were not subjected to the Fontan surgery (10). In our clinic, this patient group is managed with the continuation of Glenn physiology and close medical follow-up, along with maximum medical treatment, due to the high risk of perioperative surgical mortality and morbidity.

During catheterization, we assessed the presence of stenosis in the Glenn anastomosis, the development of the pulmonary artery bed, and the presence of venovenous or arteriovenous collaterals. Major collateral vessels were embolized when possible, and balloon dilation and stent implantation were performed for focal stenoses. The Fontan operation was not recommended for patients with pulmonary lobar artery occlusion and associated lung parenchymal perfusion loss due to any cause, nor for those with a McGoon index <2.0 in invasive measurements and a mean pulmonary artery pressure (mPAB) ≥15 mm Hg, due to the high risk of mortality and morbidity (11).

The surgical data were collected from the operation notes of patients undergoing surgery following the decision for the Fontan operation. Additionally, the clinical data were recorded during the post-operative ICU period. Using this data, we analyzed the preoperative, intraoperative and postoperative information of patients monitored for EFF and those who were not, investigating the risk factors that may contribute to the development of EFF.

Definitions

EFF is defined as a severe clinical condition in which hemodynamic stability cannot be achieved despite intensive fluid replacement and high inotropic support, during the early post-operative follow-up in ICU. This condition may lead to the need for mechanical circulatory support, renal replacement therapy (RPT), Fontan takedown, re-catheterization, or death. Additionally, the clinical scenarios including prolonged pleural effusion, extended stay in ICU and prolonged hospitalization during postoperative period, are accepted as EFF.

Prolonged intubation was defined as the inability to extubate the patient due to hemodynamic instability within 24 hours of arrival at ICU post-operatively. Prolonged ICU need was defined as taking longer than seven days for the patient to be transferred to the ward after the operation, or any patient returning to ICU for any reason after being transferred to the ward, resulting in a total ICU stay of more than seven days. Similarly, prolonged pleural effusion was defined as continuous drainage from the thorax for more than seven days, or the need to reinsert a thoracic tube after its removal. Prolonged hospital stay was defined as hospitalization for more than fourteen days. Patients requiring inotropic support due to hemodynamic instability during the ICU follow-up were evaluated, and

the vasoactive inotropic score (VIS) was calculated as described in the literature (12). Additionally, serum lactate levels were recorded and examined to assess the effectiveness of systemic circulation (13).

Surgical Procedure

The ECF modification was performed on all patients. An 18 to 20 mm expanded polytetrafluoroethylene (ePTFE) tube graft was the primary choice. However, in cases where this graft was unavailable, a handmade 18 to 20 mm tube graft was created using Hegar dilators from a bovine pericardial patch, sized to match the patient's inferior vena cava (IVC) diameter. In rare instances where the entrance of the IVC to the heart was atypical and a long, tortuous graft was required, a Dacron tube graft was preferred. Fenestration was performed in some patients at the discretion of the operating surgeon, utilizing a 4-mm punch for a side-to-side anastomosis between the atrial wall and the graft sidewall.

If present, antegrade pulmonary blood flow was surgically attempted to be closed in all patients. However, due to extensive adhesions and the unsuitable position of the pulmonary artery relative to the aorta for surgical access, this procedure could not be performed in some patients, leading to the presence of residual antegrade pulmonary flow. Since intraoperative pressure measurements did not hinder the Fontan operation, the antegrade pulmonary flows were left open with a plan for endovascular closure in the post-operative period, and the operation was completed.

For patients requiring intracardiac repair, short-term cardiac arrest was applied. For others, the entire procedure was performed with a beating heart under cardiopulmonary bypass (CPB) support. During the post-operative ICU period, patients experiencing severe hemodynamic instability were either imaged with cardiac catheterization or underwent urgent reoperation. Intraoperative invasive measurements were reassessed from both the proximal and distal parts of all anastomosis lines. In patients with elevated Fontan pressure (≥20 mmHg) throughout the system without focal anastomotic stenosis, the fenestration between the conduit and the right atrium was expanded using an ePTFE ringed tube graft (1 cm in diameter).

Statistical Analysis

Statistical analyses were conducted using the Statistical Package for Social Sciences for Windows, version 27.0 software (SPSS, IBM Corp., Armonk, NY, USA). Frequency tables and descriptive statistics were employed to interpret the findings. Parametric methods were applied for measurement values that followed a normal distribution. Specifically, the "Independent Sample t-test" was used to compare the measurement values of two independent groups.

For measurement values not following a normal distribution, non-parametric methods were utilized. The "Mann-Whitney U test" was employed to compare the measurement values of two independent groups under these non-parametric methods. The relationships between two qualitative variables were examined using "Pearson's χ^2" cross-tabulation. Additionally, backward LR logistic regression analysis was applied, including all parameters that were significant in the univariate analyses of the study.

Results

A total of 21 Fontan patients were included in the study. EFF occurred in ten patients (47.6%) after the operation, and three patients (14.2%) died in the early postoperative period. Comparative demographic data of patients with and without EFF, including cardiac morphology, operations and interventions before Glenn and Fontan surgery, as well as data related to the Fontan surgery, are presented in Table 1.

It was noted that sixteen patients (76.2%) did not undergo any surgical interventions between Glenn and Fontan surgeries. Furthermore, eighteen patients (85.7%) had antegrade pulmonary blood flow before the Fontan procedure. Preoperative catheter measurements revealed a mean pulmonary artery pressure of 12±2.26 mmHg and a McGoon ratio of 2.29±0.2. No statistically significant relationships were found in the comparative analysis of preoperative variables between patients developing EFF and those who did not.

The comparative analysis of operative variables between the two groups is summarized in Table 2.

There was no statistically significant relationship between the groups with and without EFF regarding additional surgical procedure other than ECF (p=0.269), the type of conduit used in ECF (p=0.234), failure to perform antegrade pulmonary closure during operation (p=0.130), absence of fenestration (p=0.696), presence of cross-clamp (p=0.916), duration of cross-clamp (p=0.501) and duration of CPB

Table 1. Preoperative variables related to EFF

Preoperative Variable	EFF n (%) or [mean±SD]or [median, IQR]			Statistical Analysis*
	Total n = 21	No n=11	Yes n=10	
Demographic Features				
Age (y) [median, IQR]	4.5 [4.0]	5.5 [3.0]	5.3 [5.0]	Z=-0.142 p=0.887
Weight (kg) [mean±SD]	21.95±9.53	19.59±4.67	24.55±12.78	t=-1.204 p=0.243
Gender				
Male	11 (52.4)	5 (45.5)	6 (60.0)	χ2=0.444 p=0.505
Female	10 (47.6)	6 (54.5)	4 (40.0)	
Primary Cardiac Pathology				
Tricuspid atresia Type 1c	6 (28.5)	4 (36.3)	2 (20.0)	χ2=4.295 p=0.745
Tricuspid atresia, other subtypes	4 (19.0)	2 (18.2)	2 (20.0)	
RV Hypoplasia, IVS, PA	3 (14.3)	2 (18.2)	1 (10.0)	
Unbalanced AVSD, RV/LV	1 (4.3)	-	1 (10.0)	
DORV, dominant RV/LV	3 (14.3)	1 (9.1)	2 (20.0)	
DILV	2 (9.5)	1 (9.1)	1 (10.0)	
Ebstein Anomaly, PS	1 (4.8)	1 (9.1)	-	
Other complex anomalies	1 (4.8)	-	1 (10.0)	
Ventricular Morphology				
Left	16 (76.2)	9 (81.8)	7 (70.0)	χ2=0.403 p=0.525
Right	5 (23.8)	2 (18.2)	3 (30.0)	
Pulmonary banding before Glenn or congenital severe PS				
Yes	6 (28.6)	3 (27.3)	3 (30.0)	χ2=0.019 p=0.890
No	15 (71.4)	8 (72.7)	7 (70.0)	
Intervention before Glenn (pulmonary banding excluded)				
No intervention	8 (57.2)	4 (57.1)	4 (57.1)	χ2=3.333 p=0.504
BT shunt	3 (21.7)	2 (28.6)	1 (14.3)	
Coarctation repair	1 (7.1)	-	1 (14.3)	
Central shunt	1 (7.1)	-	1 (14.3)	
PDA stenting	1 (7.1)	1 (14.3)	-	
Antegrade pulmonary flow before Fontan				
No	3 (14.3)	2 (18.2)	1 (10.0)	χ2=0.286 p=0.593
Yes	18 (85.7)	9 (81.8)	9 (90.0)	
Intervention before Fontan				
No intervention	16 (76.2)	8 (72.7)	8 (80.0)	χ2=4.964 p=0.291
Balloon dilation/stenting of the right Glenn anastomosis	2 (9.5)	1 (9.1)	1 (10.0)	
Occlusion of PLSVC	1 (4.8)	-	1 (10.0)	
Embolisation of venovenous collateral	2 (9.5)	2 (18.2)	-	
Preoperative catheterization				
Mean pulmonary artery pressure (mPAB) (mm Hg) [mean±SD]	12±2.26	11.81±2.56	12.20±1.98	t=-0.143 p=0.887
McGoon ratio [mean±SD]	2.29±0.2	2.36±0.16	2.21±0.23	t=-1.539 p=0.124

IQR: Interquartile ratio, TA: Tricuspid atresia, RV: Right ventricle, IVS: Intact ventricular septum, PA: Pulmonary atresia, AVSD: Atrioventricular septal defect, LV: Left ventricle, DORV: Double outlet right ventricle, DILV: Double inlet left ventricle, EFF: Early Fontan failure, PS: Pulmonary stenosis, BT: Blalock-taussig, PDA. Patent ductus arteriosus, PLSVC: Persistent left superior vena cava, PAB: Pulmonary artery pressure, SVC: Superior vena cava, SD: Standard deviation

Table 2. Relationship of operative variables with early Fontan failure

EFF n (%) or [mean±SD]				
Operative Variables	Total n = 22	No n=11	Yes n=10	Statistical Analysis*
Additional surgical procedure besides ECF				
No	15 (71.4)	9 (81.8)	6 (60.0)	χ2=1.222 p=0.269
Yes	6 (28.6)	2 (18.2)	4 (40.0)	
Conduit Type				
ePTFE	2 (9.5)	1 (9.1)	1 (10.0)	χ2=2.902 p=0.234
Handmade Bovine Pericardium	14 (66.6)	9 (81.8)	5 (50.0)	
Dacron	5 (23.8)	1 (9.1)	4 (40.0)	
Antegrade pulmonary flow closure during ECF				
Unable	12 (57.1)	8 (72.7)	4 (40.0)	χ2=2.291 p=0.130
Closed	9 (42.9)	3 (27.3)	6 (60.0)	
Fenestration				
No	5 (23.8)	3 (27.3)	2 (20.0)	χ2=0.153 p=0.696
Yes	16 (76.2)	8 (72.7)	8 (80.0)	
Cross Clamping				
No	17 (80.9)	9 (81.8)	8 (80.0)	χ2=0.011 p=0.916
Yes	4 (19.1)	2 (18.2)	2 (20.0)	
CCD (min) [mean±SD]	66.25±44.5	47.00±52.32	85.50±41.71	t=-0.814 p=0.501
CPB duration (min) [mean±SD]	96.04±40.6	84.90±33.74	108.30±45.7	t=-1.342 p=0.196

CCD: Cross clamp duration, CPB: Cardiopulmonary bypass ECF: Extracardiac Fontan, EFF: Early Fontan failure, ePTFE: Expanded polytetrafloroethilene, SD: Standard deviation

(p=0.196). The groups were found to be independent and homogeneous concerning the specified characteristics.

Table 3 presents a comparison of the variables observed during the ICU and hospital stay between patients developing EFF and those who did not.

In patients developing EFF, the maximum vasoactive-inotropic score (maxVIS) during the first 24 hours after the ICU admission was significantly higher (Z=-2,269; p=0.023). This score, which is considered as elevated at a value of ≥20 in the literature (12), also demonstrated a significant association with the development of EFF when analyzed separately (χ^2=5.743; p=0.017). Similarly, patients developing EFF showed an increasing VIS trend during the first 24 hours in the ICU compared to those who did not (χ^2=7.219; p=0.007).

The lactate levels in the initial arterial blood gas analyses taken in the ICU were found to be significantly different between patients developing EFF and those who did not (2,83±0,72 vs 5,89±3,36; t=-2,811; p=0.019).

Similarly, the need for RPT and extracorporeal membrane oxygenation (ECMO) treatment during the ICU duration was significantly higher in patients developing EFF compared to the other group (χ^2=5.435; p = 0.020 for both). Notably, none of the eleven patients (100.0%) not developing EFF required RPT or ECMO.

A significant relationship was found between the development of EFF and total intubation duration (χ^2=5.435; p=0.020). All patients not developing EFF were successfully extubated within the first 24 hours. In contrast, EFF was observed in all four patients with an extubation duration of ≥24 hours, while it was predominantly absent in those with an extubation duration of <24 hours.

Significant differences were also observed between patients developing EFF and those who did not in terms of the need for repeated angiography (χ2=5,435; p=0,020) and endovascular intervention (χ2=5,435; p=0,020). Similar differences were also noted for prolonged ICU stay (Z=-3,411; p<0,001), extended

Table 3. Relationship of postoperative variables with early Fontan failure

Postoperative Variables	EFF n (%) or [mean±SD] or [median, IQR]		Statistical Analysis*
	No n=11	Yes n=10	
MaxVIS value within 24 hours after ICU admission [median, IQR]	10.0 [12.0]	24.5 [17.8]	Z=-2.269 p=0.023
MaxVIS value within 24 hours after ICU admission			
≥20	2 (18.2)	7 (70.0)	χ2=5.743 p=0.017
<20	9 (81.8)	3 (30.0)	
Increasing trend in VIS during the first 12 hours in ICU			
Yes	-	5 (50.0)	χ2=7.219 p=0.007
No	11 (100.0)	5 (50.0)	
Lactate value in arterial blood gas upon initial admission to ICU (mmol/L) [mean±SD]	2.83±0.72	5.89±3.36	t=-2.811 **p=0.019**
Renal replacement requirement			
Yes	-	4 (40.0)	χ2=5.435 p=0.020
No	11 (100.0)	6 (60.0)	
ECMO requirement			
Yes	-	4 (40.0)	χ2=5.435 p=0.020
No	11 (100.0)	6 (60.0)	
Total duration of intubation (h) [median, IQR]	4.0 [1.0]	15.0 [273.8]	Z=-3.436 p<0.001
Total duration of intubation			
≥24 h	-	4 (%40.0)	χ2=5.435 p=0.020
<24 h	11 (%100.0)	6 (%60.0)	
Duration of ICU stay (h) [median, IQR]	2.0 [0.0]	8.5 [17.5]	Z=-3.411 **p<0.001**
Prolonged/repeated need for intensive care			
Yes	-	9 (90.0)	χ2=17.325 p<0.001
No	11 (100.0)	1 (10.0)	
Need for postoperative angiography.			
Yes	-	4 (40.0)	χ2=5.435 p=0.020
No	11 (100.0)	6 (60.0)	
Duration of pleural effusion (d) [mean±SD]	3.73±1.84	15.40±12.40	t=-2.947 **p=0.016**
Duration of pleural effusion			
≥7 d	-	8 (80.0)	χ2=14.215 p<0.001
<7 d	11 (100.0)	2 (20.0)	
Total duration of hospital stay(d) [median, IQR]	8.09±2.16	27.70±23.52	t=-2.759 **p=0.013**
Total duration of hospital stay(d)			
≥14 d	-	7 (70.0)	χ2=11.550 p<0.001
<14 d	11 (100.0)	3 (30.0)	

MaxVIS: Maximum vasoactive inotrophic score, ECMO: Extracorporeal membrane oxygenation,

EFF: Early Fontan failure, ICU: Intensive care unit, SD: Standard deviation

pleural effusion duration (t=-2,947; p=0,016), and total hospital length of stay(t=-2,759; p=0,013).

In the study, a Backward LR logistic regression analysis was performed using all parameters found to be significant in the multivariate analysis; the optimal model is presented in Table 4. In the current model, the duration of intubation (in hours) was identified as an important parameter influencing the risk of EFF. For every 1-hour increase in intubation duration, the risk of developing EFF increased by 84.4% [Odds ratio (OR)=1.844].

Table 4. Logistic Regression model based on EFF status

Variable	B	S.H.	Wald	SD	p	OR	95% CI (OR)	
							Min	Max
Duration of Entubation (hours)	0.612	0.293	4.368	1	0.037	1.844	1.039	3.275
Constant	-4.635	1.982	5.469	1	**0.019**	0.010		
CCR=76,9%	$\chi^2_{(2)}$=2,206; p=0,820							

CI: Confidence interval, EFF: Early Fontan failure, OR: Odds ratio, SD: Standard deviation

Discussion

Today, thanks to improved patient follow-up and treatment options, a better understanding of Fontan physiology, advanced endovascular treatment technologies, and refined operative techniques, remarkable successes have been achieved in Fontan surgery. Early mortality and EFF rates, which were 4 and 7% in the early 2000s, have decreased to 1 and 4%, respectively, over the last decade. Moreover, this success has been accomplished despite an increase in the number of Fontan palliations for complex pathologies such as hypoplastic left heart syndrome and heterotaxy in recent years (14). Unlike previous studies, the high early mortality rate (three patients, 14.2%) and EFF rate (10 patients, 47.6%) observed in our study have made it necessary to investigate possible perioperative causes and early postoperative factors that may predict EFF development.

In the literature, numerous preoperative factors have been identified in association with EFF. These include the presence of heterotaxy, Down syndrome co-existence, inadequate pulmonary artery development, distortion in pulmonary arterial bed, the use of ECC technique during surgery, non-fenestrated Fontan surgery, high preoperative ventricular end-diastolic pressure, high preoperative mPAB, pulmonary vascular resistance and transpulmonary gradient, the presence of a common AV valve morphology, moderate or greater AV valve regurgitation, the presence of ventricular systolic and diastolic dysfunction and right ventricle dominant ventricular morphology (15,16). In recent years, large series have shown that the presence of right ventricular dominance and heterotaxy no longer has a significant impact on early mortality (17). Furthermore, despite all these identified risk factors, it has been suggested that three main criteria are considered sufficient for a Fontan candidate: well-developed pulmonary arterial bed, absence of more than moderate AV valve regurgitation, and adequate systolic and diastolic function of the systemic ventricle. In our study, Fontan candidates were meticulously selected considering the risk factors identified in the literature. Our analyses revealed that demographic data, primary cardiac morphology, ventricular dominance, interstage interventions, and presence of antegrade pulmonary flow did not play a significant impact in the development of EFF.

Among the operative variables, studies conducted to date have shown that prolonged cardiopulmonary bypass (CPB) and cross-clamp times are associated with extended stays in ICU, longer pleural drainage, and increased hospitalization (18,19). Although cross-clamping is not frequently required in extracardiac Fontan modifications today, it may still be necessary in surgical interventions for atrioventricular valve insufficiencies (10). It is believed that the increased inflammatory response due to prolonged CPB and cross-clamp times contributes to higher postoperative morbidity (20). This condition can lead to severe diastolic dysfunction in the postoperative period, particularly in patients with high preoperative ventricular end-diastolic pressure (21). In our study, no significant difference was observed between these two variables regarding EFF development.

There are studies showing that fenestration in patients with elevated mPAB after Fontan operations reduces pleural drainage time, but does not impact the length of stay in the ICU or hospital (22). Fenestration is primarily used in the early postoperative period to prevent elevated pulmonary artery pressure from compromising adequate cardiac output. However, it has disadvantages, such as lower postoperative oxygen saturation, the risk of paradoxical embolism, and the need for angiographic procedures for re-closure. Large series have also been published demonstrating that, with proper patient selection, the operation can be completed without the need for fenestration (23). In our clinic, fenestration was performed in 16 patients (76.2%) and EFF was observed in eight of these patients (50%). No statistically significant difference was observed in terms of EFF development compared to patients not undergoing

fenestration.

In Fontan operations, it is recommended to close antegrade pulmonary blood flow and address any existing AV collaterals either endovascularly or surgically (1). However, in some patients, these procedures cannot be performed due to dense adhesions or intraoperative complications. There are limited studies investigating the postoperative effects of residual antegrade pulmonary blood flow. However, published case reports have shown that antegrade pulmonary blood flow can lead to increased pulmonary artery pressure, resulting in hospital readmissions due to Fontan insufficiency (24, 25). For these patients, endovascular closure of the outlet in the preoperative period is an option, if feasible (26). If closure cannot be achieved intraoperatively, it can be attempted postoperatively. In this study, antegrade pulmonary blood flow could not be closed in 12 patients (57.1%) and EFF was observed in four of these patients (33.3%). Although this result is not statistically significant, it is noteworthy.

VIS is a scoring system used to assess the hemodynamic status of critically ill patients and quantitatively express the total cardiovascular impact of vasoactive and inotropic agents. This score plays a crucial role in correlating the doses of vasoactive agents with clinical outcomes, particularly in pediatric and adult ICU patients, post-cardiac surgery patients, and conditions such as septic shock. Although numerous studies have attempted to determine cutoff values for defining "high" and "low" VIS, a universally accepted threshold has yet to be established (27, 28). Moreover, it has been suggested that VIS values measured at different time intervals may be more closely associated with patient outcomes depending on the specific clinical scenario.

Studies on congenital heart surgery have indicated that a VIS value exceeding 20 within the first 24 hours and a value over 15 between 24 and 48 hours are strongly associated with ICU-related morbidity and mortality (12). Additionally, some studies have highlighted that hemodynamically unstable patients frequently experience a critical cardiac event within the first 12 hours. Therefore, the trend of VIS increase in the first 12 hours has been strongly linked to mortality, cardiac arrest, and the need for ECMO support (29). Similarly, our experience showed that patients requiring high inotropic support upon ICU admission, particularly after Fontan surgery, demonstrated a significant increase in this requirement within the first 12 hours. Despite aggressive fluid resuscitation, these patients either experienced a major cardiovascular event within the first 24 hours, required ECMO support, or succumbed to their condition. Therefore, in our clinical practice, we prioritize the maxVIS value in 24 hours and upward trend in the first 12 hours considering them to have superior early predictive utility and life-saving potential.

In our study, the maximum VIS value within postoperative 24 hours and the upward trend within the first 12 hours were found to be significantly higher in patients developing EFF compared to those who did not. To the best of our knowledge, there is no study in the literature that directly investigates the relationship between VIS and EFF. However, VIS is associated with various morbidity factors following Fontan surgery. In a study by Algaze et al. (30) investigating risk factors for acute kidney injury after extracardiac Fontan, they found that high VIS scores on postoperative day 0 were associated with stage 2/3 acute kidney injury. The authors emphasized that high VIS values are a secondary marker for patients to develop heart failure and low cardiac output after surgery, and to require prolonged inotropic support. Pollak et al. (16), in their study investigating the effects of ventricular morphology on Fontan surgery outcomes, reported that patients with right ventricular morphology had higher postoperative VIS values compared to those with left ventricular morphology. Salvin et al. (31) found that patients in the standard recovery group after Fontan surgery had significantly lower inotropic scores compared to those in the prolonged recovery group. The study also revealed that patients with high volume requirements had significantly higher inotropic scores on the first postoperative night. Although a clear explanation for this finding was not provided, it was speculated that the increased volume requirement could be related to preoperative hemodynamic factors and the systemic inflammatory response induced by CPB. This was due to the right ventricle being less efficient in supporting systemic circulation.

High lactate levels observed during the ICU follow-up after congenital heart surgery have been associated with early morbidity and mortality (32). In Fontan patients, the major physiological changes in circulation following surgery alter the lactate production and elimination cycle. In addition to the altered circulatory physiology, the systemic inflammatory response induced by cardiopulmonary bypass (CPB) and potential cross-clamp-related myocardial dysfunction

may lead to impaired tissue perfusion and further lactate elevation. To address this condition, interventions aimed at increasing preload, reducing afterload, and decreasing pulmonary vascular resistance (PVR) are implemented. In a study conducted by Salvin et al. (31), post-bypass high lactate levels were found to be associated with prolonged ICU stays. Hamamoto et al. (33) conducted a study on 30 pediatric patients undergoing Fontan surgery and reported that serum lactate levels began to rise with the initiation of Fontan circulation. The lactate levels in the initial blood gas analyses taken in the ICU were found to be 3.2±2.4 mmol/L, peaked at the value of 4.8±2.3 mmol/L at an average of 7.4±2.1 hours following the completion of the operation, and returned to normal levels within 48 hours. Further analysis revealed a significant correlation between the higher initial serum lactate levels in the ICU and a transpulmonary gradient above 10 mmHg, the presence of base deficit in blood gas analysis, prolonged duration of intubation, prolonged drainage from the inserted peritoneal catheter, and elevated alanine transaminase levels. The authors stated that, given the inherent association of Fontan circulation with low cardiac output, they expected a close relationship between lactate levels and mixed venous saturation, one of the best indicators of low cardiac output. However, they did not find such a correlation. Therefore, they suggested that directly linking lactate levels to cardiac output status may not be appropriate, as significant fluctuations in lactate metabolism could occur within the first 6 to 8 hours due to increased hepatic and renal congestion. In conclusion, the authors recommend delaying extubation in patients with high initial lactate levels in the ICU until lactate levels stabilize, while advocating for early extubation protocols in other patients. In our study, we aimed to determine the relationship between the initial lactate levels in blood gas analyses taken in the ICU and the development of EFF. We observed that the initial lactate levels were significantly higher in patients developing EFF, compared to those who did not (2.83±0.72 vs. 5.89±3.36 mmol/L, t=-2.811; p=0.019). As suggested in the literature, we evaluated this finding alongside other indicators of cardiac output and used it to guide the postoperative ICU management of our patients.

In our study, 40% of the patients developing EFF required ECMO and renal replacement therapy. All of these patients underwent early postoperative catheterization, and anastomotic stenosis was ruled out. This finding suggests that, despite careful preoperative evaluation and meticulous surgical execution, some patients may experience elevated Fontan pressures in the absence of an anatomical cause, leading to low cardiac output and, consequently, severe acute kidney injury due to secondary low renal perfusion pressure.

Not surprisingly, patients developing EFF had longer durations of intubation, ICU stay, total hospital stay and pleural effusion, compared to those not developing EFF. These findings are consistent with the current literature (21, 23). In our clinic, it is routine practice for Fontan patients to proceed with extubation as early as possible once hemodynamic stabilization is achieved. However, in patients developing signs of low cardiac output and show an inadequate response to volume replacement, extubation is postponed. Kintrup et al. (34) investigated the effectiveness of an early extubation strategy in patients undergoing Fontan surgery. They reported that patients extubated in the operating room had lower central venous pressure, higher arterial pressure, and lower heart rates, compared to those extubated in ICU. Additionally, these patients exhibited less pleural effusion within the first 48 postoperative hours. Furthermore, those extubated in the operating room required less intravenous volume and had significantly shorter durations of inotropic support. The authors stated that even with only a 3-hour difference between the two groups, early extubation allowed for significant improvements in the entire Fontan circulation and an increase in cardiac output, likely due to the reduction in central venous pressure. In our study, we also identified a significant relationship between extubation duration and the development of EFF. Indeed, in the logistic regression analysis we conducted to assess significance of preoperative, operative and postoperative variables, intubation time was identified as the only significant factor affecting the development of EFF.

Conclusion

Fontan operation can now be performed worldwide with low mortality and morbidity rates. However, EFF is still considered a significant cause of mortality and morbidity. In the postoperative period, delayed extubation time, high inotropic support requirement and elevated initial lactate levels have been observed to be associated with EFF. This relationship needs to be further explored in new studies with larger, prospectively designed samples.

Conflict of interest:

The authors disclosed no conflicts of interest.

Financial support:

The authors stated that no funding was obtained for this investigation.

References

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971; 26: 240- 8.

2. d'Udekem Y, Iyengar AJ, Cochrane AD, Grigg LE, Ramsay JM, Wheaton GR, et al. The Fontan procedure: Contemporary techniques have improved long-term outcomes. Circulation 2007; 116: I-157-I-64.

3. Gewillig M, Brown SC. The Fontan circulation after 45 years: update in physiology. Heart 2016; 102: 1081-6.

4. Mazza GA, Gribaudo E, Agnoletti G. The pathophysiology and complications of Fontan circulation. Acta Bio Medica: Atenei Parmensis 2021; 92.

5. Mery CM, De León LE, Trujillo-Diaz D, Ocampo EC, Dickerson HA, Zhu H, et al. Contemporary outcomes of the Fontan operation: a large single-institution cohort. Ann Thorac Surg 2019; 108: 1439-46.

6. d'Udekem Y, Iyengar AJ, Galati JC, Forsdick V, Weintraub RG, Wheaton GR, et al. Redefining expectations of long-term survival after the Fontan procedure: twenty-five years of follow-up from the entire population of Australia and New Zealand. Circulation 2014; 130: S32-S8.

7. Venna A, Cetta F, d'Udekem Y. Fontan candidacy, optimizing Fontan circulation, and beyond. JTCVS open 2022; 9: 227-32.

8. Kotani Y, Chetan D, Zhu J, Saedi A, Zhao L, Mertens L, et al. Fontan failure and death in contemporary Fontan circulation: analysis from the last two decades. Ann Thorac Surg 2018; 105: 1240-7.

9. Marathe SP, Cao JY, Celermajer D, Ayer J, Sholler GF, d'Udekem Y, et al. Outcomes of the Fontan operation for patients with heterotaxy: a meta-analysis of 848 patients. Ann Thorac Surg 2020; 110: 307-15.

10. Podzolkov VP, Chiaureli MR, Yurlov IA, Zelenikin MM, Kovalev DV, Dontsova VI, et al. Results of Fontan operation in patients with atrioventricular valve regurgitation. Eur J Cardiothorac Surg 2015; 48: 308-15.

11. Alsaied T, Bokma JP, Engel ME, Kuijpers JM, Hanke SP, Zuhlke L, et al. Predicting longterm mortality after Fontan procedures: a risk score based on 6707 patients from 28 studies. Congenit Heart Dis 2017; 12: 393-8.

12. Gaies MG, Jeffries HE, Niebler RA, Pasquali SK, Donohue JE, Yu S, et al. Vasoactive-inotropic score is associated with outcome after infant cardiac surgery: an analysis from the Pediatric Cardiac Critical Care Consortium and Virtual PICU System Registries. Pediatr Crit Care Med 2014; 15: 529-37.

13. Şahutoğlu C, Yaşar A, Kocabaş S, Aşkar FZ, Ayık MF, Atay Y. Correlation between serum lactate levels and outcome in pediatric patients undergoing congenital heart surgery. Turk Gogus Kalp Damar Cerrahisi Derg 2018; 26: 375.

14. Iyengar AJ, Winlaw DS, Galati JC, Celermajer DS, Wheaton GR, Gentles TL, et al. Trends in Fontan surgery and risk factors for early adverse outcomes after Fontan surgery: the Australia and New Zealand Fontan Registry experience. J Thorac Cardiovasc Surg 2014; 148: 566-75.

15. Nordmeyer S, Rohder M, Nordmeyer J, Miera O, Peters B, Cho MY, et al. Systemic right ventricular morphology in the early postoperative course after extracardiac Fontan operation: Is there still a need for special care? Eur J Cardiothorac Surg 2017; 51: 483-9.

16. Pollak U, Abarbanel I, Salem Y, Serraf AE, Mishaly D. Dominant ventricular morphology and early postoperative course after the Fontan procedure. World J Pediatr Congenit Heart Surg 2022; 13: 346-52.

17. Rochelson E, Richmond ME, LaPar DJ, Torres A, Anderson BR, editors. Identification of risk factors for early Fontan failure. Semin Thorac Cardiovasc Surg 2020: Elsevier.

18. Sasaki J, Dykes JC, Sosa LJ, Salvaggio JL, Tablante MD, Ojito J, et al. Risk Factors for Longer Hospital Stay Following the Fontan Operation. Pediatr Crit Care Med 2016; 17: 411-9.

19. Tsubura M, Osaki M, Motono K, Hamamoto N. Risk factors for prolonged ventilation after the modified Fontan procedure. Cardiol Young 2022; 32: 969-74.

20. Gupta A, Daggett C, Behera S, Ferraro M, Wells W, Starnes V. Risk factors for persistent pleural effusions after the extracardiac Fontan procedure. J Thorac Cardiovasc Surg 2004; 127: 1664-9.

21. Murphy MO, Glatz AC, Goldberg DJ, Rogers LS, Ravishankar C, Nicolson SC, et al. Management of early Fontan failure: a single-institution experience. Eur J Cardiothorac Surg 2014; 46: 458-64; discussion 64.

22. Bouhout I, Ben-Ali W, Khalaf D, Raboisson MJ, Poirier N. Effect of fenestration on Fontan procedure outcomes: a meta-analysis and review. The Ann Thorac Surg 2020; 109: 1467-74.

23. Hosein RB, Clarke AJ, McGuirk SP, Griselli M, Stumper O, De Giovanni JV, et al. Factors influencing early and late outcomes following the Fontan procedure in the current era. The 'Two Commandments'? Eur J Cardiothorac Surg 2007; 31: 344-53.

24. Karagöz T, Gülgün M, Demircin M, Aykan HH, Akin A. Transcatheter closure of antegrade pulmonary blood flow with Amplatzer muscular VSD occluder after Fontan operation. Anatol J Cardiol 2014; 14: 565.

25. Li D, Li M, An Q, Feng Y. Successful transcatheter closure of residual ventriculopulmonary blood flow with muscular VSD occluder after ligation of pulmonary trunk in Fontan procedure. Int J Cardiol 2015; 191: 277-8.

26. Şahin GT, Tanıdır İC, Gökalp S, Güzeltaş A. Transcatheter occlusion of antegrade pulmonary blood flow in children with univentricular heart. Turk Gogus Kalp Damar Cerrahisi Derg 2019; 27: 274.

27. Belletti A, Lerose CC, Zangrillo A, Landoni G. Vasoactive-inotropic score: evolution, clinical utility, and pitfalls. J Cardiothorac Vasc Anesth 2021; 35: 3067-77.

28. Sun Y-t, Wu W, Yao Y-t. The association of vasoactive-inotropic score and surgical patients' outcomes: A systematic review and meta-analysis. Syst Rev 2024; 13: 20.

29. McIntosh AM, Tong S, Deakyne SJ, Davidson JA, Scott HF. Validation of the vasoactive-inotropic score in pediatric sepsis. Pediatr Crit Care Med 2017; 18: 750-7.

30. Algaze CA, Koth AM, Faberowski LW, Hanley FL, Krawczeski CD, Axelrod DM. Acute kidney injury in patients undergoing the extracardiac Fontan operation with and without the use of cardiopulmonary bypass. Pediatr Crit Care Med 2017; 18: 34-43.

31. Salvin JW, Scheurer MA, Laussen PC, Mayer JE, Jr., Del Nido PJ, Pigula FA, et al. Factors associated with prolonged recovery after the Fontan operation. Circulation 2008; 118: 171-6.

32. Basaran M, Sever K, Kafali E, Ugurlucan M, Sayin OA, Tansel T, et al. Serum lactate level has prognostic significance after pediatric cardiac surgery. J Cardiothorac Vasc Anesth 2006; 20: 43-7.

33. Hamamoto M, Uemura H, Imanaka H, Yagihara T. Relevance of the measurement of the concentration of lactate in the serum after the Fontan procedure in small children. Cardiol Young 2006; 16: 275-80.

34. Kintrup S, Malec E, Kiski D, Schmidt C, Brünen A, Kleinerüschkamp F, et al. Extubation, In the operating room after Fontan procedure: does it make a difference? Pediatr Cardiol 2019; 40: 468-76.