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ORIGINAL ARTICLE

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Surgical and interventional rescue strategies for Fontan failure

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Key question

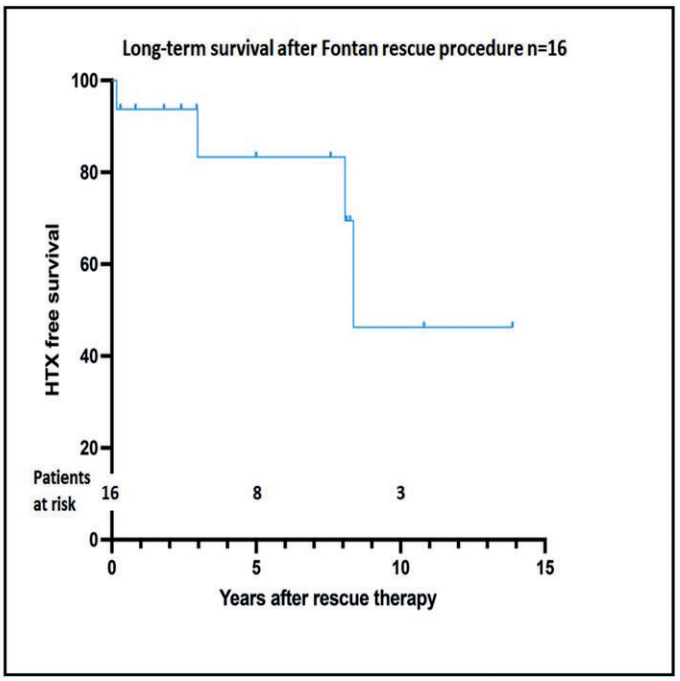
Can rescue procedures in Fontan patients with PLE/PB and a failing Fontan circulation postpone or avoid HTX?

Key finding(s)

HTX free survival after a rescue therapy is 75% at a median follow up time of 4.0 years (range: 3.5 month - 13.9 years).

Take-home message

Rescue strategies for Fontan failure can postpone HTX for a sustained period of time-more than 13.9 years in one of our FU patients.



Abstract

OBJECTIVES: Fontan patients are at lifelong risk for developing complications, which may result in Fontan failure. Survival rates after heart transplantation (HTX) are still unsatisfying in these patients. Long-term survival of extracardiac Fontan patients in the modern era was investigated. The objective of this study was to investigate if surgical and interventional procedures in patients with protein-losing enteropathy (PLE) and/or plastic bronchitis (PB) and a failing Fontan circulation can postpone or avoid HTX.

METHODS: Retrospective data collection of all children who underwent a Fontan procedure between January 1999 and July 2021 at our centre was performed. Patients were surveyed regarding the occurrence of PLE or PB and their outcome was reported descriptively. HTX-free survival of patients who underwent a rescue procedure due to PLE/PB was evaluated.

RESULTS: Three hundred and seventy [94.1% (95% confidence interval, 91.4–96.3)] Fontan patients were free of HTX or death at last follow-up after a median follow-up time of 6.7 years. PB/PLE was diagnosed in 34 patients during the observation period. A rescue

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procedure was undertaken in 16 pts. at a median time of 6.5 months (range: 1 day to 9.4 years) since the initial diagnosis of PLE/PB. In these patients, HTX-free survival was 75% (95% confidence interval, 47.6–92.7) at a median follow-up time of 4.0 years after the procedure. Range: 3.5 months to 13.9 years.

CONCLUSIONS: Extracardiac Fontan patients in the modern era expect reasonable HTX-free survival rates. Surgical and/or interventional rescue strategies for Fontan failure can postpone HTX for a sustained period of time.

Keywords: Fontan operation • Single ventricle palliation • Fontan failure • Plastic bronchitis • Protein-losing enteropathy

ABBREVIATIONS

CI	Confidence interval
HTX	Heart transplantation
PB	Plastic bronchitis
PLE	Protein-losing enteropathy

INTRODUCTION

In children with functional single ventricle heart defects a stepwise palliation therapy with the establishment of a Fontan circulation, first performed by Fontan and colleagues, is pursued [1]. As this circulation is driven by only 1 ventricle with passive, in series perfusion of the lungs, Fontan patients are at lifelong risk for developing Fontan-associated complications, which may result in Fontan failure. Early postoperative Fontan failure is rarely seen, but can lead to Fontan takedown, listing for heart transplantation (HTX) or death before hospital discharge or within 30 postoperative days [2]. The experience in long-term treatment of Fontan patients rises and confronts us with possible serious complications late after Fontan surgery [3, 4]. Protein-losing enteropathy (PLE), plastic bronchitis (PB) and functional single ventricle failure are, among others, common reasons for a late failing Fontan circulation [5, 6]. The management spectrum of a failing Fontan circulation ranges from Fontan take down, Fontan conversion procedures in atriopulmonary Fontan patients [6, 7], to lymphatic interventions [8–10], fenestration reopening or decompression of the thoracic duct [11] in PLE- and PB-associated Fontan failure.

The ultimate therapy option for the treatment of Fontan failure is an orthotopic HTX. Fontan patients have a high risk for perioperative complications at HTX and survival rates after 5 and 10 years (=66–73% and 45–57%) are still unsatisfying [12, 13]. Furthermore, a growing population of patients with Fontan circulation, as well as patients with contraindications for HTX have to be considered for future therapeutic algorithms. Therefore, new surgical and catheter interventional therapy strategies have to be established and evaluated.

The objective of this study was to investigate if surgical and interventional procedures in patients with PLE and/or PB can postpone or avoid HTX. Long-term survival of extracardiac Fontan patients in the modern era—after the advances of staged superior cavopulmonary shunt, extracardiac Fontan baffle creation and the use of a fenestration, was investigated.

PATIENTS AND METHODS

Ethics statement

This retrospective study was approved by the ethics committee of the Medical Faculty at Johannes Kepler University Linz on 13 October 2021 (EK Nr: 1270/2021); written patient informed consent was waived.

All children receiving a Fontan procedure at our centre between January 1999 and July 2021 were included in this study (=total study cohort). HTX-free survival was evaluated; therefore, patient records were followed retrospectively until their last clinical follow-up visit, date of HTX or death.

Patients were surveyed regarding the occurrence of PLE and/or PB during the observation period. PB/PLE patients were treated by enforced medication and, if applicable, with catheter interventions regarding residual anatomic problems. If the disease progressed to a late Fontan failure, a surgical or interventional rescue procedure was undertaken.

Clinical outcome and HTX-free survival after the rescue therapy were evaluated as main objective of this study. Subgroup analysis between patients with PLE and PB was performed.

Late Fontan failure was defined for patients with chronic ventricular failure leading to HTX or death or patients acquiring severe PLE and/or PB and refractory ascites, pleural effusions, hypoxaemia, which led to HTX, a rescue procedure or death.

Fontan procedure

All but one of our patients received an extracardiac Fontan operation [99.7%]. A 20 mm in diameter polytetrafluoroethylene prosthesis [Gore-Tex® (W. L. Gore & Associates, Inc., Flagstaff, Arizona, USA)] was used whenever suitable and a fenestration was created in patients without excessive pulmonary arterio-venous malformations [89% (95% confidence interval (CI), 85.8–92.2)] based on the visual impression at preoperative angiography scans and haematocrit level in combination with the degree of preoperative cyanosis. Standard closure of the fenestration was usually performed 6 months after Fontan completion. Fontan patients receive Warfarin until 3-month post-fenestration closure at our centre, which is then switched to acetylsalicylic acid. Those with poor ventricular function, coagulation disorder, atrioventricular valve insufficiency or history of thrombosis receive Warfarin or Edoxaban lifelong.

Diagnostic and therapeutic algorithm

PB/PLE patients underwent early cardiac catheterization with morphologic and functional assessment. Detected residual anatomic problems were treated either in the catheterization laboratory or surgically to achieve an anatomically optimal Fontan pathway.

Oral medication with angiotensin-converting enzyme inhibitors, pulmonary vasodilator therapy, diuretics and Budesonid was initiated or escalated. Bronchoscopy with bronchial lavage was performed in PB patients for cast evacuation. If this conservative therapy failed to relieve their PB/PLE symptoms, the

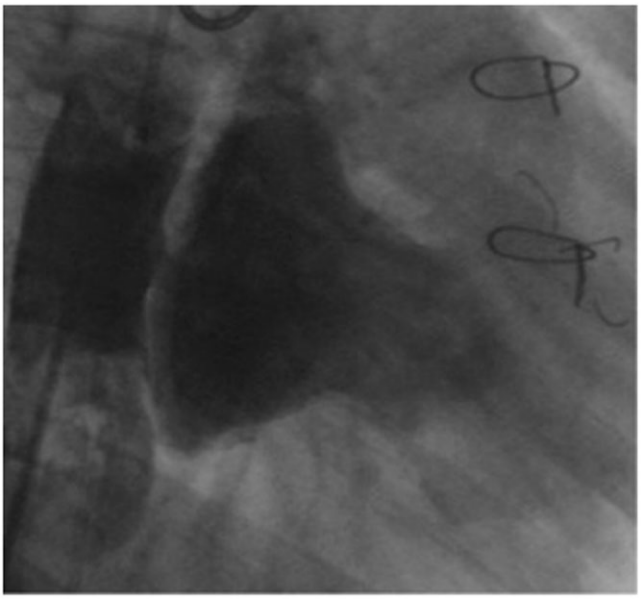

Figure 1: Open fenestration after Fontan procedure.

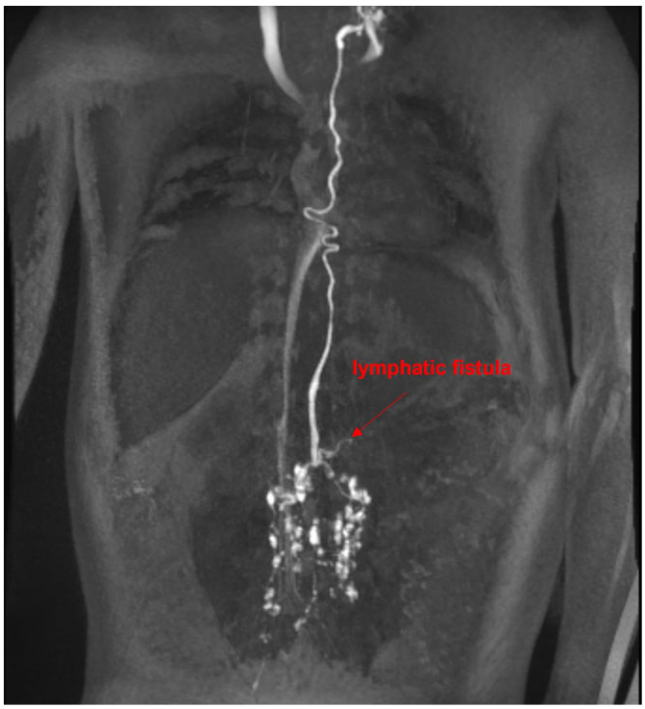

Figure 2: Lymphatic fistula draining into the intestine.

indication for either a Fontan rescue procedure or primary HTX was evaluated.

The following measures were alternatively undertaken as a rescue procedure: A surgical or interventional refenestration procedure was performed during the whole study period to lower the Fontan pressure, maintain cardiac preload and reduce lymphatic congestion (Fig. 1). Lymphatic intervention was performed since March 2016 to close lymphatic fistulas to extralymphatic compartments (Fig. 2). Since March 2019, direct decompression of the thoracic duct via an anastomosis draining the innominate vein into the common atrium as described by Dr Hraska [11] was

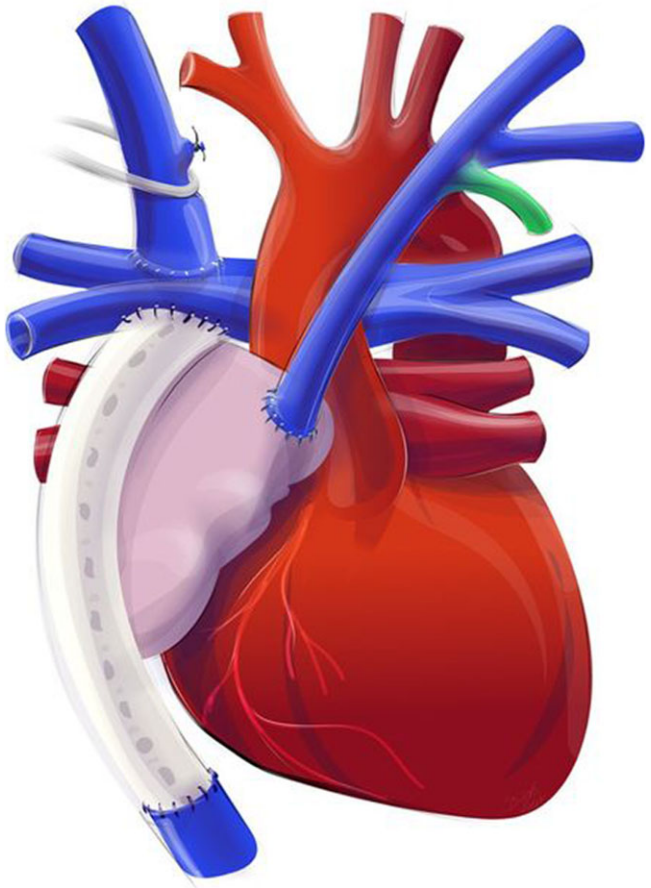

Figure 3: Thoracic duct decompression procedure, reprinted from Bauer *et al.* [14] by permission of the European Society of Cardiology.

established in patients with PB/PLE at our centre (Fig. 3). In one of these cases, a left internal jugular vein banding was necessary to decrease the amount of venous shunt into the common atrium.

Cardiac catheter details were collected and compared prior to the Fontan operation, at the time of fenestration closure and after onset of PLE/PB. Catheterization data were evaluated to calculate the cardiac index and the pulmonary vascular resistance index using the Fick principle with assumed oxygen consumption (VO2) [15, 16] as described in other studies [17–19].

Patients were surveyed regarding physical activity (good exercise tolerance, moderate exercise tolerance, poor exercise tolerance), failing Fontan-related symptoms (oedema, ascites, cough, casts, diarrhoea and dyspnoea) and laboratory abnormalities (e.g. total protein levels).

The study design was retrospective and all Fontan procedures were undertaken at a single centre.

Statistical analysis

Categorical variables are expressed using absolute numbers (*n*) and relative numbers (%).

All data of continuous variables were checked for normal distribution (test of normality: Kolmogorov–Smirnov with Lilliefors significance correction, type I error = 10%) and in the case of normal distribution also for variance heteroscedasticity (Levene test, type I error = 5%). In the case of normality and variance homogeneity, the independent 2-sample *t*-test was used for group

Table 1: Patient details: total study cohort

Variable	Patients ($n = 393$)		
Median age, years	3.6		
Male sex, *n*	258	(66%)	
Type stage I operation, *n*			
Norwood	250	(64%)	
Shunt/PDA stent	66	(17%)	
PAB	30	(8%)	
No stage I	47	(12%)	
Extracardiac conduit, *n*	392	(99%)	
Fenestration, *n*	351	(89%)	
20-mm baffle prosthesis, *n*	346	(88%)	
Median time to fenestration closure, months	6.3		(range: 0d–4.7y)
Long-term complications, *n*			
PLE	21	(5.3%)	[3.3–8.1, 95% CI]
PB	11	(2.8%)	[1.4–5.0, 95% CI]
PB + PLE	1	(0.3%)	[0.0–1.4, 95% CI]
Ventricular failure	8	(2.0%)	[0.9–4.0, 95% CI]
Ventricular failure + PLE	1	(0.3%)	[0.0–1.4, 95% CI]
Cause of death, *n*	16		
Early postoperative Fontan failure	2	(12.5%)	
Chronic ventricular failure	4	(25%)	
Fontan failure/PLE	5	(31%)	
Sepsis	3	(19%)	
Sudden death	2	(12.5%)	

CI: confidence interval; PAB: pulmonary artery banding; PB: plastic bronchitis; PDA: patent ductus arteriosus; PLE: protein-losing enteropathy.

comparisons. For variables without normally distributed data and for variables measured on ordinal scales the exact Mann–Whitney *U*-test was used. For the comparison of the occurrence of exitus/HTX, depicted by Kaplan–Meier plots, the log-rank test was used. A competing risk analysis regarding the occurrence of PB/PLE was performed.

Missing data were not replaced. The type I error was not adjusted for multiple testing. Therefore, the results of inferential statistics are descriptive only. Statistical analyses were performed using the open-source R statistical software package, version 4.0.5 (The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

In total, 370/393 [94.1% (95% CI, 91.4–96.3)] Fontan patients were free of HTX or death at last follow-up after a median follow-up time of 6.7 years. Patient details are listed in Table 1. Total observation time was 2797 patient-years (range: 2 days to 21.9 years). Early mortality (in hospital or 30 days) occurred in 4 (=1.0%) patients whereas late death after Fontan completion was observed in 12 (=3.1%) patients. Seven (=1.8%) patients had to undergo HTX. Thirty-four patients acquired either PB or PLE during follow-up. A competing risk analysis of the total Fontan cohort regarding the occurrence of PB/PLE adjusted for death or HTX showed a risk of 13% (95% CI: 7.49%; 20.60%) at 10 years after the Fontan procedure.

Outcome of patients diagnosed with protein-losing enteropathy/plastic bronchitis ($n = 34$)

Median time from Fontan operation to diagnosis of PLE or PB was 2.5 years (95% CI, 1.6–4.7; Table 2: PLE/PB patients). Long-term survival is shown in Fig. 4A. The majority of these patients had hypoplastic left heart syndrome ($n = 26$ [76.5%]) and 14 [41.2%] had needed at least one additional operation or cardiac intervention other than the staged procedures before their Fontan operation. In 3 patients (=8.8%), an episode of CPR was documented at a previous palliation stage.

Retrospective cardiac catheterization haemodynamic evaluation has shown a steady decrease of the cardiac index in patients with PLE/PB from prior Fontan procedure [mean 5.1 l/min/m^2 (95% CI, 4.5–5.7)], prior fenestration closure [mean 4.3 l/min/m^2 (95% CI, 3.7–4.8)], after fenestration closure [mean 3.6 l/min/m^2 (95% CI, 2.7–4.4)] until the time of PLE/PB onset [mean 2.9 l/min/m^2 (95% CI, 2.5–3.4)]. Inversely, an increase in pulmonary vascular resistance index from mean 1.9 wood units*m^2 (95% CI, 1.5–2.4) to mean 2.4 wood units*m^2 (95% CI, 1.9–2.9) occurred.

Table 2: Protein-losing enteropathy/plastic bronchitis patients

Variable	Patients ($n = 34$)		
Male sex, *n*	21	(62%)	[43.6–77.8, 95% CI]
Mean age at diagnosis, years	7.3		(range: 3.0–17.3)
Median time Fontan to PB/PLE	2.5		[1.6–4.7, 95% CI]
Mean time PB/PLE to follow-up, years	5.6		[4.2–6.9, 95% CI]
Fenestration closed at diagnosis	27	(79%)	[62.1–91.3, 95% CI]
Underlying anatomy, *n*			
HLHS	26	(76%)	
Single ventricle	3	(8.8%)	
TA	1	(2.9%)	
DORV (MS/MA)	2	(5.9%)	
DILV, TGA	1	(2.9%)	
Unbalanced CAVC	1	(2.9%)	
Type of systemic ventricle, *n*			
Right	29	(85%)	
Left	2	(5.8%)	
Single ventricle/undefined	3	(8.8%)	
Type stage I operation, *n*			
Norwood	30	(88%)	
BT shunt	1	(2.9%)	
PAB	2	(5.9%)	
No stage I	1	(2.9%)	
Cardiac catheterization details			
Pre Fontan			
Mean cardiac index, L min^{-1} m^{-2}	5.1		[4.5–5.7, 95% CI]
Mean PVRI, WU*m^2	1.9		[1.5–2.4, 95% CI]
Fenestration closure			
Mean cardiac index pre-closure, L min^{-1} m^{-2}	4.3		[3.7–4.8, 95% CI]
Mean cardiac index post-closure, L min^{-1} m^{-2}	3.6		[2.7–4.4, 95% CI]
At diagnosis of PLE/PB			
Mean Fontan pressure, mmHg	13		(range: 6–20)
Mean cardiac index, L min^{-1} m^{-2}	2.9		[2.3–3.4, 95% CI]
Mean PVRI, WU*m^2	2.4		[1.9–2.9, 95% CI]

BT: Blalock-Taussig; CAVC: complete atrioventricular canal defect; CI: confidence interval; DILV: double inlet left ventricle; DORV: double outlet right ventricle; HLHS: hypoplastic left heart syndrome; MA: mitral atresia; MS: mitral stenosis; PAB: pulmonary artery banding; PB: plastic bronchitis; PLE: protein-losing enteropathy; PVRI: pulmonary vascular resistance index; TA: tricuspid atresia; TGA: transposition of the great arteries; WU: wood units.

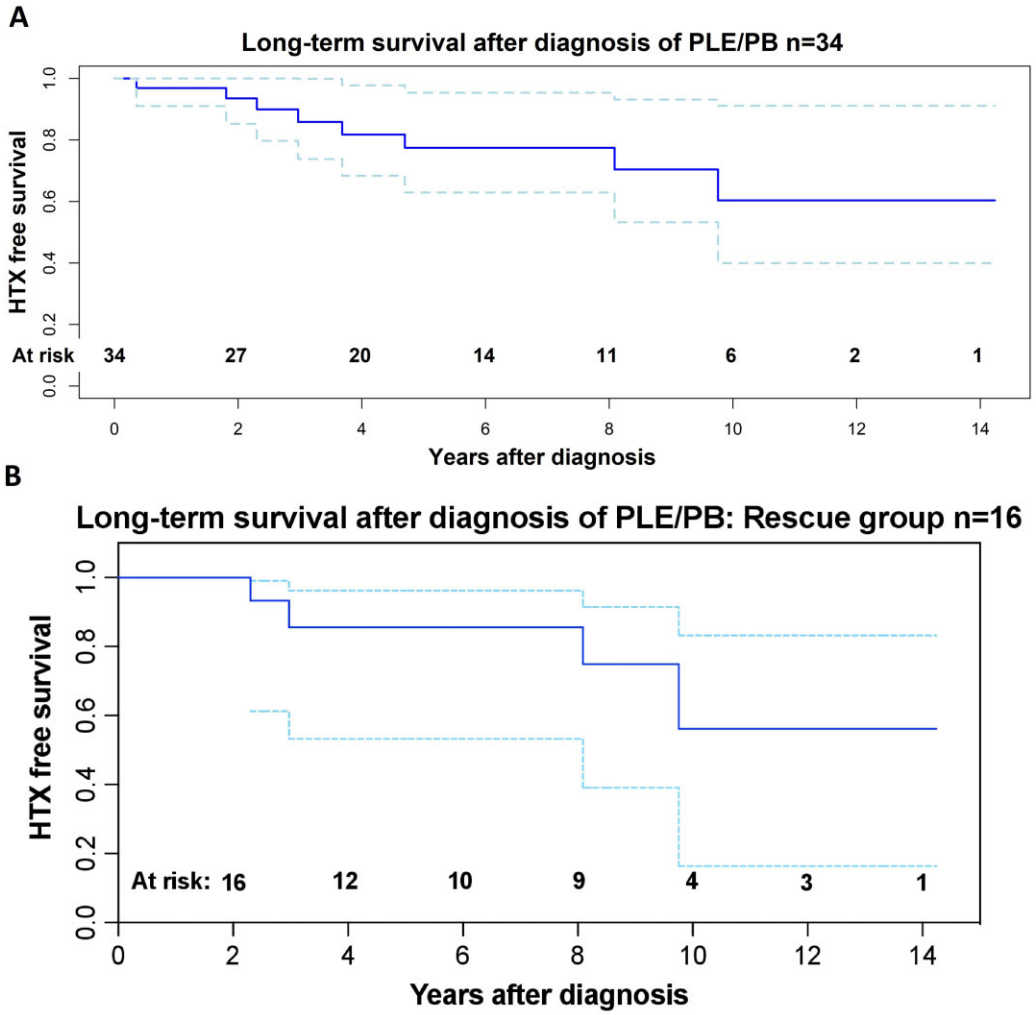

Figure 4: (**A**, **B**) Long-term survival after diagnosis of PLE/PB. HTX: heart transplantation; PB: plastic bronchitis; PLE: protein-losing enteropathy.

In 14 PB/PLE patients enhancement of medical therapy and interventional treatment of residual anatomic problems was sufficient to improve their clinical status significantly. The following anatomic interventions were undertaken in order to optimize Fontan physiology: 11 patients underwent left pulmonary artery stenting ($n = 7$), isthmus stenting ($n = 2$), combined right and left pulmonary artery stenting ($n = 1$) and pacemaker implantation ($n = 1$). A combination diuretic therapy (spironolactone/furosemide) was prescribed to all but one of these patients after the initial diagnosis. Angiotensin-converting enzyme inhibitors were used in 12 patients and at least 1 pulmonary vasodilator was used in 6 patients. In 13 of these patients, symptoms of PLE/PB disappeared and total protein levels returned to normal in 11 patients. PLE/PB is still under remission after a median follow-up time since beginning of treatment of 4.9 years (range 2.8 months to 11.3 years). Thirteen patients or their parents stated a good exercise tolerance at the last follow-up visit and the remaining female patient with additional Fanconi anaemia had a moderate exercise tolerance.

Two PB/PLE patients with preserved ventricular function and an open fenestration were primarily transplanted 1.8 and 3.7 years after initial diagnosis of PB/PLE without rescue procedure. Another 2 PB/PLE patients died 4 months and 4.7 years after diagnosis without further surgery.

Sixteen of 34 PB/PLE patients underwent a rescue procedure at a median time of 6.5 month (range: 1 day to 9.4 years) since the initial diagnosis of PLE ($n = 9$) or PB ($n = 7$) Fig. 4B. Median time from Fontan operation was 4.7 years (range 22 days to 15.2 years). All of these patients had had a Norwood procedure as stage I palliation with a systemic right ventricle in the majority ($n = 15$, 93.8%).

Rescue therapy patients diagnosed with PB showed a significant ($P < 0.05$) larger decrease in cardiac index between prior Fontan and time of PB/PLE onset compared to patients with PLE.

A total of 19 rescue procedures (see Table 3) were undertaken in these 16 patients implying that one patient received an additional lymphatic intervention after a refenestration procedure and one patient had to undergo a thoracic duct decompression and lymphatic intervention after a refenestration procedure due to a persisting chylothorax. Additional surgical/interventional procedures treating residual anatomic problems were necessary in 11 [68.8%] patients either combined during the rescue procedure or as an independent procedure.

HTX-free survival in recue therapy patients is 75% (95% CI, 47.6–92.7) at a median follow-up time of 4.0 years after the

Table 3: Rescue procedures

Results patients ($n = 16$)			
Male sex, *n*	11	(=69%)	
Rescue procedures, *n*	19		
Refenestration	11		
Lymphatic intervention	5		
Thoracic duct decompression	3		
Additional procedures, *n*			
Recurrent aortic arch repair	1		
Tricuspid valve repair	1		
Right pulmonary artery or Left pulmonary artery reconstruction	2		
Atrioseptectomy	1		
Epicardial pacemaker	3		
Isthmus stenting	3		
Left pulmonary artery stenting	4		
Fenestration closure	1		
Medication, *n*			
Spironolactone + furosemide	11		
Furosemide	4		
ACE inhibitor	16		
Pulmonary vasodilator	8		
HTX-free survival, *n*	12	(=75%)	[47.6–92.7, 95% CI]
Median follow-up time, years	4.0		[2.2–8.2, 95% CI]
Follow-up			
Exercise tolerance			
Good, *n*	8	(=67%)	
Moderate, *n*	2	(17%)	
Poor	2	(17%)	
PB/PLE symptoms			
Present, *n*	2	(=17%)	
Absent, *n*	10	(=83%)	

ACE inhibitor: angiotensin-converting enzyme inhibitor; CI: confidence interval; HTX: heart transplantation; PB: plastic bronchitis; PLE: protein-losing enteropathy.

procedure. Range: 3.5 months to 13.9 years, 64 cumulative patient-years (Fig. 5).

All patients who received a lymphatic intervention due to PB ($n = 2$) or PLE ($n = 1$) as well as our patient with PB who received a refenestration procedure with subsequent lymphatic intervention are alive with their Fontan circulation at a median time of 4 years (range: 1.8–7.6 years) after the rescue procedure. Symptoms regarding PLE/PB resolved, total protein levels are normal and 3 patients stated good and 1 moderate exercise tolerance.

Thoracic duct decompression procedures were undertaken in 2 patients with PLE and 1 patient with PB. Follow-up times are 2.4 years, 10 and 4 months. Symptoms resolved in the first 2 patients, but total protein levels are below the normal range. One of them is clinically stable at home, but currently listed for HTX. The patient with PB received an additional thoracic duct decompression after a refenestration procedure with postoperatively persisting chylothorax. Unfortunately, thrombosis of the innominate vein occurred during selective thoracic duct embolization which was nevertheless clinically successful.

Nine solitary refenestration procedures were performed in patients with PLE ($n = 5$), PB ($n = 3$) and PLE with ventricular failure ($n = 1$). Five patients were alive with their Fontan circulation at last follow-up (median time since rescue procedure 8.2 years; range: 2.4–13.9) and have a complete remission of their symptoms regarding PLE/PB. Exercise tolerance is good in 4 and moderate in 1 at last follow-up. One patient received successful HTX 8.1 years after the refenestration procedure due to a recurrent fulminant episode of PB. Three patients died 2 months, 3 and 8.4 years after a refenestration procedure due to progressive PLE resulting in Fontan failure.

DISCUSSION

Fontan patients are at lifelong risk for serious cardiopulmonary and other organ complications. Therefore, cardiac institutions worldwide are challenged with an increasing population of failing Fontan patients [20, 21]. Among our patients, the leading cause for a failing Fontan circulation was PLE, PB or chronic ventricular failure of the single ventricle. Arrhythmias, which were described as the most prevalent indication (=43.6%) for a failing Fontan surgery in 1 European multicentre study [6] was not as frequently seen in our extracardiac Fontan cohort. However, they might be responsible for 2 unexpected late sudden deaths in our Fontan cohort.

Fontan patients frequently suffer not only from cardiopulmonary complications but also from other organ malfunctions due to increased central venous pressure and chronic low cardiac output. They are therefore at high risk when undergoing HTX. Moreover, the staged single ventricle palliation therapy plus eventual unplanned reoperations [22] lead to multiple sternotomies making HTX a much more difficult procedure compared to other patients. The immunologic situation after several blood transfusions might be a possible contraindication for HTX. Even after successful transplantation lifelong immunosuppressive therapy can lead to infectious, malignant and organ failure complications. Therefore, there is need for successful treatment of Fontan-related complications to postpone or avoid HTX.

Ventricular failure ($n = 8$) was a main reason for late mortality and listing for HTX in our cohort. Timely surgical treatment of residual anatomic problems as well as reducing additional workload by coiling of aorto-pulmonary collateral arteries is crucial in Fontan patients to preserve ventricular function. Advances in the use of mechanical assist devices for failing Fontan patients can help in bridging more patients to HTX and will have to be inserted in future strategy algorithms [23, 24]. Two patients of our entire Fontan cohort received a mechanical assist device due to chronic ventricular failure as bridge to transplant therapy.

The survival of patients diagnosed with PLE has improved in the current era but the risk of PLE causing a failing Fontan within 5 years at the Children's Hospital of Philadelphia was still described as high as 40% [25]. Similarly, John *et al.* [26] have shown that the mortality in patients diagnosed with PLE was 12% at 5 years.

Low cardiac index (<2.5 l min^{-1} $m^{-2)}$ and high pulmonary vascular resistance index (>2 wood units*m^2) have been described as independent risk factors for Fontan failure [19]. Maintaining sufficient cardiac output and lowering the central venous pressure are therefore 2 important approaches to postpone or avoid an otherwise necessary HTX for Fontan failure. This has to be considered especially at the time of fenestration closure and standardized catheterization protocols should be established to avoid a preventable low cardiac output state.

Since 1999, 16 of our failing Fontan patients were eligible for a rescue procedure. The refenestration procedure was performed at our centre throughout the observation period in cases of PLE/PB causing Fontan failure as ultimate therapy option before listing for HTX. Clinical improvement could be achieved in 5 out of 9 patients resulting in satisfying follow-up conditions.

The introduction of new therapeutic possibilities as lymphatic imaging and interventions during the observation period has led to a more targeted therapy option for PLE/PB. When identifying

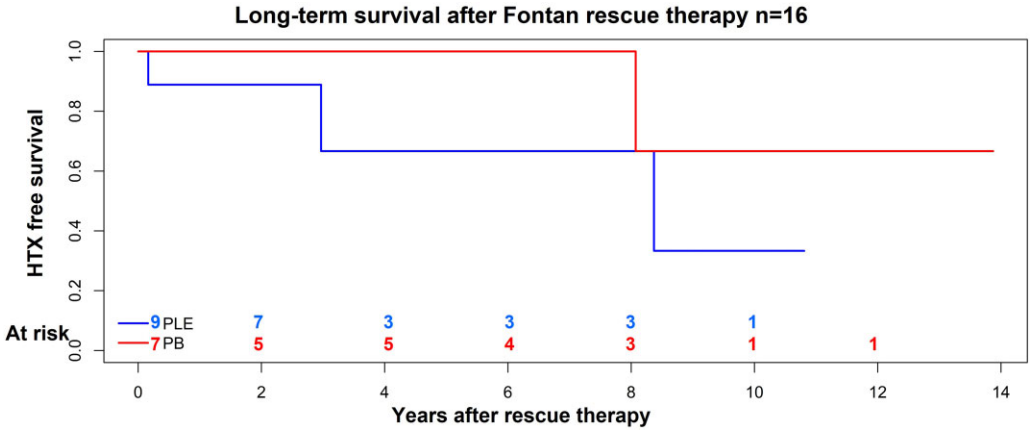

Figure 5: Long-term survival after Fontan rescue therapy. HTX: heart transplantation.

abnormal fistulas, lymphatic interventions have shown resolution of PLE/PB symptoms and therefore are promising treatment options [8–10]. In our cohort, all 4 patients receiving lymphatic interventions due to a Fontan failure had a relief of symptoms and therefore HTX could be avoided.

The decompression of the thoracic duct technique by redirecting the innominate vein to the common atrium as first described by Dr Hraska [11] has shown to be a sufficient therapeutic option and therefore should be considered for lymphatic complications of persistent chylothorax, PB and PLE [27]. We introduced this procedure at our centre in March 2019 and demonstrate our first experience with this technique in this study. Although symptoms regarding PLE could be averted in 2 patients, one of these patients remained on the transplantation list. In the patient with PB receiving a thoracic duct decompression, PB and chylothorax have ceased after thoracic duct embolization, which unfortunately led to innominate vein thrombosis.

Regarding our experience, in 76.5% of PLE/PB patients, Fontan failure could be prevented by medication, surgical and interventional procedures treating residual anatomic problems and Fontan rescue procedures. Twenty-one (61.8%) patients had good exercise tolerance and the vast majority was free of their Fontan complications at last follow-up.

For this reason, our effort in patients with Fontan long-term complications as PLE/PB is to follow an algorithm in terms of sufficient clarification of the underlying reason by cardiac catheterization, haemodynamic evaluation, exclusion of anatomic issues and escalation of medical treatment. If there is no sufficient relief of the patients' symptoms deliberately applied rescue procedures may postpone HTX for a sustained period of time, frequently with satisfactory clinical outcome.

Limitations

The small cohort group of patients with rescue procedures and the short follow-up period makes conclusions difficult and therefore this study is predominantly descriptive. The development of new therapeutic possibilities as lymphatic imaging and interventions as well as new surgical techniques (e.g. thoracic duct decompression) during the observation period are further limitations to this study.

Data collection, based on the studies design, was retrospective and cardiac catheterization calculation was achieved using assumed oxygen consumption (VO2) as direct measurement was not possible at our centre.

CONCLUSION

Extracardiac Fontan patients in the modern era expect reasonable HTX-free survival rates (94.1%). A significant proportion of these patients develop long-term complications after the Fontan procedure as PLE and/or PB [10 years risk of 13% (95% CI: 7.49%; 20.60%)]. Surgical and/or interventional rescue strategies for Fontan failure can postpone HTX for a sustained period of time. Long-lasting effects on exercise tolerance and against Fontan-associated complications could be achieved after a rescue procedure at our centre.

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Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Conflict of interest: none declared.

Author contributions

Gregor Gierlinger: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Writing—original draft. **Eva Sames-Dolzer:** Conceptualization; Methodology; Supervision; Validation; Writing—review & editing. **Michaela Kreuzer:** Supervision; Writing—review & editing. **Roland Mair:** Data curation; Writing—review & editing. **Mohammad-Paimann Nawrozi:** Data curation; Writing—review & editing. **Andreas Tulzer:** Data curation; Formal analysis; Writing—review & editing. **Christoph Bauer:** Formal analysis; Resources; Visualization. **Gerald Tulzer:** Formal analysis; Resources; Supervision; Validation. **Rudolf Mair:** Resources; Supervision; Validation; Writing—review & editing.

Reviewer information

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REFERENCES

[1] Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971;26: 240–8.
[2] Rochelson E, Richmond ME, LaPar DJ, Torres A, Anderson BR. Identification of risk factors for early Fontan failure. Semin Thorac Cardiovasc Surg 2020;32:522–8.
[3] Pundi KN, Johnson JN, Dearani JA, Pundi KN, Li Z, Hinck CA *et al.* 40-Year follow-up after the Fontan operation: long-term outcomes of 1,052 patients. J Am Coll Cardiol 2015;66:1700–10.
[4] 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(11 Suppl 1):S32–8.
[5] Deal BJ, Jacobs ML. Management of the failing Fontan circulation. Heart 2012;98:1098–104.
[6] van Melle JP, Wolff D, Hörer J, Belli E, Meyns B, Padalino M *et al.* Surgical options after Fontan failure. Heart 2016;102:1127–33.
[7] Backer CL, Mavroudis C. 149 Fontan conversions. Methodist Debakey Cardiovasc J 2019;15:105–10.
[8] Dori Y, Keller MS, Rome JJ, Gillespie MJ, Glatz AC, Dodds K *et al.* Percutaneous lymphatic embolization of abnormal pulmonary lymphatic flow as treatment of plastic bronchitis in patients with congenital heart disease. Circulation 2016;133:1160–70.
[9] Maleux G, Storme E, Cools B, Heying R, Boshoff D, Louw JJ *et al.* Percutaneous embolization of lymphatic fistulae as treatment for protein-losing enteropathy and plastic bronchitis in patients with failing Fontan circulation. Catheter Cardiovasc Interv 2019;94:996–1002.
[10] Itkin M, Pizarro C, Radtke W, Spurrier E, Rabinowitz DA. Lymphatic management in single-ventricle patients. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2020;23:41–7.
[11] Hraska V. Decompression of thoracic duct: new approach for the treatment of failing Fontan. Ann Thorac Surg 2013;96:709–11.
[12] Michielon G, van Melle JP, Wolff D, Di Carlo D, Jacobs JP, Mattila IP *et al.* Favourable mid-term outcome after heart transplantation for late Fontan failure. Eur J Cardiothorac Surg 2015;47:665–71.
[13] Backer CL, Russell HM, Pahl E, Mongé MC, Gambetta K, Kindel SJ *et al.* Heart transplantation for the failing Fontan. Ann Thorac Surg 2013;96: 1413–9.
[14] Bauer C, Mair R, Mair R, Tulzer G. Thoracic duct decompression and jugular vein banding-an effective treatment option for protein-losing enteropathy and plastic bronchitis in severe failing Fontan circulation: a case report. Eur Heart J Case Rep 2020;4:1–4.
[15] LaFarge CG, Miettinen OS. The estimation of oxygen consumption. Cardiovasc Res 1970;4:23–30.
[16] Kappagoda CT, Greenwood P, Macartney FJ, Linden RJ. Oxygen consumption in children with congenital diseases of the heart. Clin Sci 1973; 45:107–14.
[17] Salim MA, Case CL, Sade RM, Watson DC, Alpert BS, DiSessa TG. Pulmonary/systemic flow ratio in children after cavopulmonary anastomosis. J Am Coll Cardiol 1995;25:735–8.
[18] Kwan WC, Shavelle DM, Laughrun DR. Pulmonary vascular resistance index: getting the units right and why it matters. Clin Cardiol 2019;42: 334–8.
[19] Egbe AC, Connolly HM, Miranda WR, Ammash NM, Hagler DJ, Gr V *et al.* Hemodynamics of Fontan failure: the role of pulmonary vascular disease. Circ Heart Fail 2017;10:e004515.
[20] Rychik J, Atz AM, Celermajer DS, Deal BJ, Gatzoulis MA, Gewillig MH *et al.*; On behalf of the American Heart Association Council on Cardiovascular Disease in the Young and Council on Cardiovascular and Stroke Nursing. Evaluation and management of the child and adult with Fontan circulation: a scientific statement from the American Heart Association. Circulation 2019;140:CIR0000000000000696.
[21] Ephrem G, Hebson C, John A, Moore E, Jokhadar M, Ford R *et al.* Frontiers in Fontan failure: innovation and improving outcomes: a conference summary. Congenit Heart Dis 2019;14:128–37.
[22] Sames-Dolzer E, Gierlinger G, Kreuzer M, Schrempf J, Gitter R, Prandstetter C *et al.* Unplanned cardiac reoperations and interventions during long-term follow-up after the Norwood procedure. Eur J Cardiothorac Surg 2017;51:1044–50.
[23] Giridharan GA, Ising M, Sobieski MA, Koenig SC, Chen J, Frankel S *et al.* Cavopulmonary assist for the failing Fontan circulation: impact of ventricular function on mechanical support strategy. ASAIO J 2014;60: 707–15.
[24] Broda CR, Taylor DA, Adachi I. Progress in experimental and clinical subpulmonary assistance for Fontan circulation. J Thorac Cardiovasc Surg 2018;156:1949–56.
[25] Allen KY, Downing TE, Glatz AC, Rogers LS, Ravishankar C, Rychik J *et al.* Effect of Fontan-associated morbidities on survival with intact Fontan circulation. Am J Cardiol 2017;119:1866–71.
[26] John AS, Johnson JA, Khan M, Driscoll DJ, Warnes CA, Cetta F. Clinical outcomes and improved survival in patients with protein-losing enteropathy after the Fontan operation. J Am Coll Cardiol 2014;64:54–62.
[27] Hraska V, Mitchell ME, Woods RK, Hoffman GM, Kindel SJ, Ginde S. Innominate vein turn-down procedure for failing Fontan circulation. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2020;23:34–40.