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CLINICAL STUDY

Factors influencing the intermediate outcome in patients with single-ventricle physiology after Fontan operation

Nosal M, Valentik P, Kantorova A, Nagi AS, Sagat M, Poruban R

Depatment of Cardiac Surgery, National Institute of Cardiovascular Disease – Children´s Heart Centre Slovakia, Bratislava, Slovakia. **nosal@dkc-sr.sk**

Abstract: *Objective:* This study was conducted to analyze the factors affecting the intermediate outcome following the Fontan procedure in the current era.
Methods: Between January 1992 and December 2008, 189 patients underwent Fontan procedure at a median age of 3.4 years (0.4-37 years). Single left ventricle was present in 77 (40 %) patients, right ventricle in 70 (37 %), in 7 (3.7 %) patients, the ventricular morphology was indetermined and in 35 (18.5 %) a dominant systemic ventricle with smaller second ventricle was present. The Fontan procedure was performed using an atriopulmonary connection (n=5, 5.6 %), lateral atrial tunnel (n=99, 52 %) or extracardiac conduit (n=85, 45 %). 97.4 % of patients recieved fenestration.
Results: The hospital survival was 95% and five patients required a takedown of Fontan circulation. The survival at 1.5 and 10 years was 94 %, 93 % and 92 %, respectively. Multivariate analysis identified that the outcome was influenced by the diagnosis of a complete common AV canal (p=0.015), duration of ventilation (p<0.0001) and duration of pleural effusions (p=0.003). Failure-free survival at 1.5 and 10 years was 95 %, 92 % and 89 %, respectively. The overall freedom from reoperation was 73 %. Risk factors for reoperation were preoperative pulmonary artery pressure and duration of ventilation.
Conclusions: The Fontan procedure is associated with excellent operative and intermediate survival. Common atrioventricular canal, duration of pleural effusions and ventilation have an adverse influence on the intermediate outcome. Reintervention is associated with pulmonary artery pressure and duration of ventilation *(Tab. 7, Fig. 3, Ref. 16)*. Full Text in free PDF *www.bmj.sk.*
Key words: heart defects, congenital, paediatrics, Fontan procedure, total cavopulmonary connection, risk factors.

The surgical treatment of complex single-ventricle patients requires a staged operative approach aimed at creating the final hemodynamic state of total cavopulmonary connection represented by Fontan operation (1–3). Owing to advances in the diagnosis and treatment, the number of patients who undergo the Fontan procedure and survive into the adulthood is substantially increasing (4, 5). However, there still remains a continuing risk of early and late failure of Fontan circulation (6, 7). We conducted this study in order to analyze the intermediate-term outcome and risk factors for Fontan failure in patients with single-ventricle physiology in the current era. We analyzed the impact of a variety of patients and operative factors on the outcome of the completion of Fontan. This study features a single institution experience in a timeframe of 1992–2008.

Methods

A retrospective chart analysis of all patients who underwent the Fontan operation at the Children´s Heart Center, Slovakia from January 1992 to December 2008 was undertaken. The data were collected from the medical records, surgical database as well as from operative and postoperative reports.

Operative technique: The Fontan completion included atriopulmonary anastomosis, lateral tunnel with fenestration or extracardiac tunnel with fenestration. Lateral tunnel and atriopulmonary anastomosis were performed on cardiopulmonary bypass in moderate hypothermia using aortic cross-clamping with cold cardioplegia. Extracardiac tunnel was performed on cardiopulmonary bypass on beating heart in normothermia with spontaneus temperature drift. For the lateral tunnel, a gore-tex ™ patch and for extracardiac tunnel, a gore-tex tube graft™ of 16–20 mm in diameter were used. In all but atriopulmonary anastomoses, fenestration of the tunnel with a diameter of 4–5 mm has been applied.

Outcome variables and statitical analysis: Continuous data are presented as mean ± standard deviation or median + range. Categorical variables are summarized with frequencies and percentages. Fontan failure was defined as death or takedown of the Fontan circuit to another palliative procedure. The estimated actuarial survival, failure-free survival and freedom from late events were determined by the Kaplan-Meier method. Univariate analysis (logistic regression and chi-square test) was used to assess the factors associated with Fontan failure and reoperation. Significant risk factors were entered into a multivariate analysis using

Depatment of Cardiac Surgery, National Institute of Cardiovascular Disease – Children´s Heart Centre Slovakia, Bratislava, Slovakia

Address for correspondence: M. Nosal, MD, National Institute of Cardiovascular Disease – Children´s Heart Centre Slovakia, Limbova 1, SK-833 51 Bratislava, Slovakia.
Phone: +421.2.59371327

Tab. 1. Diagnostic distribution.

Hypoplastic left heart syndrome	45
Tricuspid atresia	38
Double outlet right ventricle	27
Heterotaxia	20
Double inlet left ventricle	16
Single left ventricle	9
Pulmonary atresia/ IVS	8
Common A-V kanal	8
Single right ventricle	5
Corrected transposition of great arteries	5
Transposition of great arteries	3
Ebstein´s anomaly	2
Double inlet right ventricle	1
Pulmonary atresia /VSD	1
Single ventricle other	1
N	189

A-V – atrioventricular, VSD – ventricular septal defect, IVS – intact ventricular septum

Tab. 2. Preoperative patient characteristcis.

	Median (range)	Mean±SD
Age at Fontan , years	3,4 (0,4–37)	5,1±4,6
Age at I.st. stage, years	0,033 (0,003–3,3)	0,5±1,9
Age at II.-nd stage, years	0,8 (0,25–3)	1,7±3,7
Male/Female	113/76	
Hemoglobin, mmol/l	159 (101–224)	159±19
Oxygen saturation ,%	82 (51–99)	80±7
Pulmonray artery pressure/ mmHg	13 (6–22)	13±2,9
Pulmonary vascular resistance index, Wood units/m^2	1,7 (0,4–4)	1,6±0,7
SV end-diastolic pressure,mmHg	8 (3–17)	8±2,3
Qp/Qs, litre	0,6 (0,25–4)	0,7± 0,5
AV valve regurgitation		
0	126	
1	50	
2	13	

Qp/Qs – pulmonary/systemic flow ratio, AV – atrioventricular, SV – single ventricle, SD – standard deviation

a forward stepwise logistic regression model. Multivariate risk analysis was performed with Cox regression test. The data were analyzed using SAS statistical software JMP 5.0.1 (SAS Institute Inc, Cary, NC). A value of p <0.05 was considered to be statistically significant.

Results

Between January 1992 and December 2008, a total of 189 patients underwent the Fontan operation. 171 (90 %) patients have had a previous palliation before the final procedure. The diagnostic distribution is listed in Table 1 . Dominant left ventricle was present in 77 (40 %) patients, right ventricle in 70 (37 %) patients, in 7 (3.7 %) patients, the ventricular morphology was undetermined and in 35 (18.5 %) patients, the dominant systemic ventricle was associated with smaller second ventricle. The median age at operation was 3.4 years (0.4–37 years). Preoperative patient characteristics are shown in Table 2. The Fontan procedure was performed using an atriopulmonary connection (n=5, 5.6 %) or total cavopulmonary connection involving the lateral atrial tunnel (n=99, 52 %) or extracardiac conduit (n=85, 45 %). All, except the atriopulmonary patients received fenestration (97.4 %).

Tab. 3. Additional procedures.

Procedure	N	%
PA plasty	25	13,2
TV plasty	2	1
TAPVD correction	1	0,5
VSD enlargement	1	0,5
Damus operation	1	0,5
Atrial septum enlargement	1	0,5

PA – pulmonary artery, TV – tricuspid valve, TAPVD – total anomalous pulmonary venous connection, VSD – ventricular septal defect

Tab. 4. Perioperative data.

	Median (range)	Mean±SD
Cardiopulmonary bypass / min	100 (49–299)	108±41
Aortic cross clamp / min *	57 (21–134)	61±22
Transpulmonary gradient	8 (3–18)	7,6±1,9
Oxygen saturation ,%	89 (49–99)	87±6
Ventilation, hours	17 (0–2976)	63±264
Pleural effusions, days	7 (1,6–24)	8,4±6
Fontan Lateral tunnel	99	
Extracardiac	85	
Atriopulmonary	5	

*– intracardiac tunnel only, SD – standard deviation

The most commonly applied additional procedure was that of pulmonary artery plasty performed in 25 patients (13.2 %). Ad-

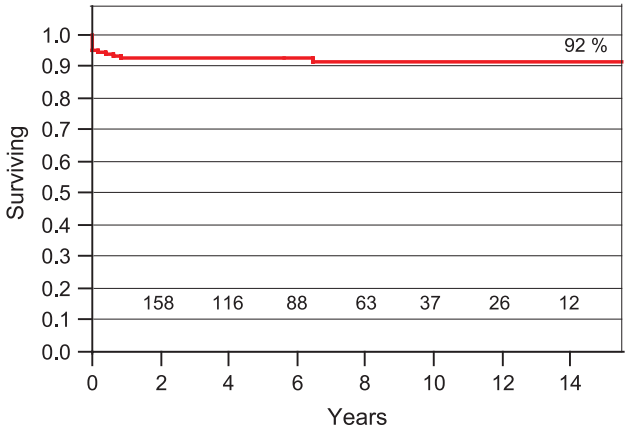

Fig. 1. Kaplan–Meier survival curve.

Tab. 5. Postoperative complications.

Complication	N	%
Respiratory infection	35	18,5
Chylothorax	25	13,2
Arrhytmia (tachycardia, AV blok)	10	5,2
Renal insufficiency	9	4,7
Thrombosis	9	4,7
Stroke	8	4,2
Sepsis	7	3,7
Mediastinitis	5	2,6
Phrenical palsy	5	2,6
Plastic bronchitis	3	1,6
Other	4	2,1

AV – atrioventricular

Tab. 6. Risk factor analysis – Fontan failure.

Variable	Univariate P value	Multivariate P value
Complete AV canal	0.004	0.01
MPAP preoperative	0.01	
Single ventricle end-diastolic pressure	0.007	
Postoperative oxygen saturation	0.0001	
MPAP postoperative	0.002	
Transpulmonray gradient	0.01	
Duration of ventilation	0.001	0.0001
Warfarin postoperative	0.006	
Pleural effusions	0.01	0.003

AV – atrioventricular, MPAP – pulmonary artery pressure

Tab. 7. Risk factors for reoperation.

Variable	Univariate	Multivariate
TAPVD	0.045	
Oxygen saturation postoperative	0.0005	
MPAP postoperative	0.0005	<0.0001
End-diastolic pressure postoperative	0.0003	
Duration of ventilation	0.049	0.0042
Warfarin	0.007	

TAPVD – total anomalous pulmonary venous connection , MPAP – pulmonary artery pressure

ditional procedures are summarized in Table 3. The details of perioperative and postoperative hemodynamic data are shown in Table 4. The mean duration of follow-up was 6.2 ± 4.3 years. There were 11 early and 3 late deaths. The causes of deaths included single-ventricle failure in 6 patients, elevated pulmonary vascular resistance in 3, cerebral bleeding in 1 patient and in 4 patients, the reason of death was unknown. Figure 1 shows Kaplan-Meier actuarial survival for the whole cohort. The actuarial survival at 1,5 and 10 years was 94 %, 93 % and 92 % respectively. Postoperative complications are listed in Table 5. Five patients were taken down to bidirectional cavopulmonary shunt. In addition to takedown procedures, there were 7 reoperations including 2 tunnel revisions, 1 right ventricle outflow tract occlusion, 1 right ventricle obliteration, 1 thrombectomy, 1 subaortic membrane resection and 1 fenestration creation. Overall freedom from reoperation is 73 % at 15 years (Fig. 2). There was no transplantation procedure performed in the whole cohort. Failure-free survival at 1,5 and 10 years was 95 %, 92 % and 89 % respectively (Fig. 3).

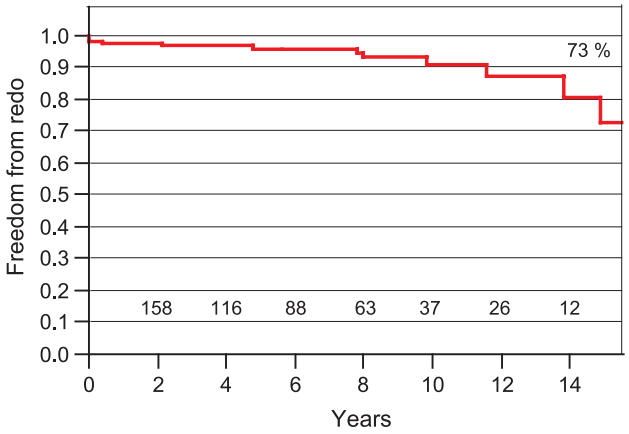

Fig. 2. Freedom form reoperation.

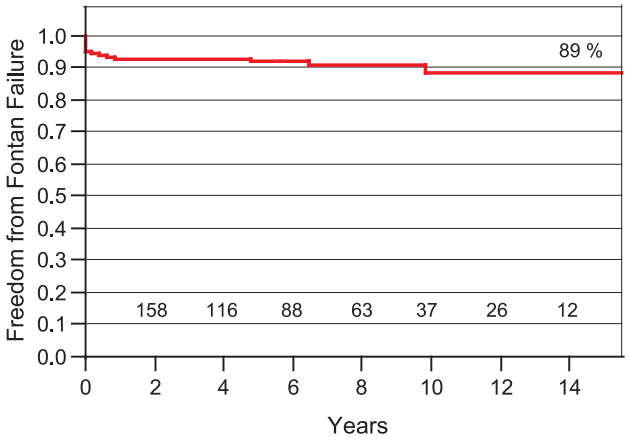

Fig. 3. Freedom from Fontan failure.

Factors affecting the outcome. Univariate and multivariate analyses demonstrated that the Fontan failure was associated with a number of perioperative variables. Risk factors for Fontan failure in univariate and multivariate analyses are shown in Table 6. The multivariate analysis demonstrated an association between the failure and preoperative diagnosis of complete common atrioventricular canal (CAVC) (p=0.015). Of postoperative factors, the duration of ventilation (p<0.0001) and duration of pleural effusions (p=0.003) came up as risk factors for Fontan failure. Risk factors for reoperation in univariate and multivariate analysis are listed in Table 7. In multivariate analysis, there was an association between reoperation and postoperative pulmonary artery pressure (p<0.0001), and duration of ventilation (p=0.04).

Discussion

Advances in the management of single-ventricle patients along with the application of staged operative approach have led to an increase in survival (5–8). This study describes a single institution experience with the Fontan procedure in patients who have been staged towards the Fontan procedure. We have analysed the intermediate-term survival and identified the risk factors predisposing to Fontan failure. Additionally, the risk factors for reoperation were analysed.

In our group of 189 patients, the hospital survival was 94 %. There was little mortality during the follow-up period, with a 10-year actuarial survival of 92 %. This result corresponds with the results of other recently published study groups (7, 8) and can be attributed to the stage approach policy (3), which was applied in the whole cohort from the very early stages. Since 1992, 90 % of all patients in our institution underwent a staged palliative procedure before the final operation. The predominant use of lateral and extracardiac tunnel techniques in our cohort and the small number of patients with atriopulmonary anastomosis might have positively contributed to the overall survival.

Among the factors analysed, we identified the complete common AV canal, duration of ventilation and duration of pleural effusions as factors associated with Fontan failure. In our study population, the diagnosis of CAVC proved to be a preoperative risk factor for Fontan failure. Being often associated with heterotaxy syndrome, CAVC could have a possible negative impact on Fontan outcome (9). Although heterotaxia alone has not been prooved as a risk factor in our cohort, out of 29 patients with CAVC, 20 had an associated heterotaxy syndrome. These patients have a complex of associated cardiac anomalies including anomalous systemic and pulmonary venous drainage and common AV valve, which might be prone to regurgitation. The reported overall long-term outcome of heterotaxy patients is poor (10, 11). We have found the duration of ventilatory support to be a postoperative risk factor for Fontan failure. The prolonged ventilation may be associated with poorer postoperative hemodynamics, desaturation, postoperative complications, and eventually facilitates the takedown procedure (12, 13). The median duration of postoperative ventilation in our cohort was 17 hours. However, there were patients who required long-term ventilation up to several months. Those were complex patients suffering mostly from prolonged sepsis, desaturation and multiorgan failure. Our current strategy is based on an early attempt of extubation before leaving the operating room, or shortly after the arrival to the intensive care unit. The development of pleural effusions after the Fontan procedure is a very common postoperative complication. The median duration of chest drainage in our cohort was 7 days. There were several patients in whom the effusions went on for several weeks. Postoperative infection was found to play a role in prolonged pleural effusions (14). In our cohort, the respiratory infection was one of the most common postoperative complications with an incidence of 18.5 % and might have contributed to the length of pleural drainage. In some studies, the fenestration policy was found to reduce the duration of pleural effusions (15). As opposed to the latter, other authors have not found a positive role of fenestration in the reduction of pleural effusions (16). Based on the fact that in our series, the tunnel fenestration was applied routinely (97 %), we were not able to analyse the impact of fenestration on pleural effusions in our cohort.

The overall freedom from reoperation in our group is 73 % at 15 years. All but 2 reoperations were performed in the early postoperative period. In multivariate analysis, the reoperation was associated with the postoperative elevated pulmonary artery pressure and duration of ventilation. The elevated pulmonary pressure can reflect the decreased ventricular function, presence of aorto-pulmonary collaterals or pulmonary artery distortion. All these factors may contribute to the necessity of reintervention in the early postoperative stage. Similarly to Fontan failure, the longer duration of ventilation as a risk factor can be a sign of poor postoperative Fontan hemodynamics and thus project into the need for reintervention.

Limitations: This analysis has all of the limitations of a retrospective study.

Conclusion

The Fontan procedure is associated with excellent operative and intermediate survival rates. The common atrioventricular canal, the duration of pleural effusions and ventilation have an adverse influence on the intermediate outcome**.** Reintervention is associated with elevated postoperative pulmonary artery pressure and duration of ventilation.

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