



Original Article

Children Surviving Post-Univentricular Repair: Single Center Experience

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Abstract:

Background: The children population who underwent single ventricle repair is growing in number with longer follow up periods and increased frequency of complications.

Aim of work: To evaluate the outcome and complications post Glenn and Fontan single ventricle repair in children.

Material and Methods: A retrospective study of data within files of all surviving patients post univentricular surgical repair, who were following up at Post Cardiac Interventions Clinic in Cairo University Children Hospital from October 2007 until October 2020.

Results: The files of 113 patients were enrolled in the study, 93 (82.3%) of them were post Glenn operation. Their mean± SD age at the time of the operation was 1.4± 0.9years, and mean follow up duration of 8.3 ±3 years. The study included 20 (17.7%) patients post Fontan operation, with a mean age at the time of the operation of 7.82± 1.63years, and mean follow up duration of 4.75 ±0.08 years. They were 77 (68.15%) males, and 36(31.85%) females. Complications post Glenn operation were heart failure in 34(36.5%) patients, pericardial and pleural effusion in 4 (4.3%) and hypoalbuminemia in 2 (2.15%). Complications post Fontan were heart failure in 4 (20%) patients, arrhythmia in 2 (10%), and protein losing enteropathy in 2 (10%). Frequency of complications was not related to the age at the time of the Glenn and Fontan operation (p =0.793) and (p=0.079) respectively.

Conclusion: Performing Glenn and Fontan at older age was not related to the frequency of complications in our patients. Heart failure was the most common complication post Glenn and Fontan operations.

Level of Evidence of Study: IV (1).

Keywords: single ventricle; Glenn; Fontan; outcomes; children.

Abbreviations: DILV: double inlet left ventricle; DIRV double inlet right ventricle; PA pulmonary atresia; PS pulmonary stenosis; SV single ventricle; TA tricuspid atresia.

Introduction

Repair of single ventricle (SV) physiology depends on the fact that the pulmonary blood flow can be maintained by moderately elevated central venous pressure without the need to pumping ventricle (2). This concept has been expanded to include patients with physiological single ventricle and is achieved through multiple stages of repair (Glenn and Fontan operations). Ultimately the number of patients is growing and is expected to be doubled in the next 20 years (2, 3). Multiple advances in the surgical techniques and postoperative care resulted in augmented survival of patients with longer periods of follow up and increased occurrence of late complications (3, 4). Focused efforts to anticipate and prevent future complications is mandatory to improve outcome of those patients. In this study we aimed to evaluate the outcome and complications post Glenn and Fontan single ventricle repair in children.

Subjects and Methods

This is a retrospective study in which we included all surviving children post univentricular heart repair, following up at the Post Cardiac Interventions Clinic at Cairo University Children Hospital during the period from October 2007 until October 2020. The study conformed to the requirements of Revised Helsinki Declaration of Bioethics (2013) (5). All relevant data were



collected as type of intervention, age at the time of intervention, gender, duration of follow up, heart failure according to NYHA classification of chronic heart failure (6), presence of complications (e.g. arrhythmias, protein-losing enteropathy (PLE), and thromboembolism), laboratory, echocardiographic and cardiac catheterization data for the patency of the anastomosis, and pulmonary arterial pressures (PAP). Univentricular repair included Glenn palliation, followed by sequential Fontan. In our center post Glenn patients are considered suitable for sequential Fontan if hemodynamic study by cardiac catheter revealed mean pulmonary artery pressure <15 mmHg, with competent AV valve.

Statistical Analysis

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Data was summarized as mean, standard deviation, minimum and maximum in quantitative data and as frequency (count) and relative frequency (percentage) for categorical data. For comparison of serial measurements within each patient paired t-test was used). P-values less than 0.05 were considered as statistically significant.

Results

The study included files of 113 patients post univentricular repair, of them 93 (82.3%) underwent Glenn and 20 (17.7%) underwent sequential Fontan operation. Forty (43%) children post Glenn and 10 (50%) post sequential Fontan had long term complications.

The Post- Glenn Cohort

The post- Glenn patients age range at the time of the operation was 0.5-4years with a mean \pm SD of 1.4 ± 0.90 years, and at the latest follow up was 2.5-15years with a mean of 9.77 ± 3.95 years. Mean follow up duration for post Glenn patients was 8.3 ± 3 years. The most common diagnosis was SV with pulmonary atresia in 27 (29.03%). (Table 1). The O₂ saturation showed significant improvement after the operation ($p < 0.001$), where O₂ was initially 80.82 ± 0.03 before the operation and 86.63 ± 0.04 after the surgery. Twenty nine (31.2%) patients dropped out during the COVID 19 lockdown period starting from Mars 2020 to October 2020. At latest follow up, 65 (70%) were between 5th -95th percentiles for weight with a mean \pm SD of 20 ± 3.44 and for height 17 ± 1.23 percentile for age, and 35 (30%) patients were below 5th percentile for age for weight and height. Forty (43%) children post Glenn had long term complications.

Table 1. Characteristics of the post Glenn group.

		N	%
Gender	Male	66	71
	Female	27	29
Diagnosis	SV+PS	27	29.03
	SV+TA	26	28
	SV+PA	13	14
	SV+TA+PS	10	10.69
	DIRV	9	9.67
	DILV	8	8.6
Follow up	Regular	64	68.8
	irregular	29	31.2

DILV: double inlet left ventricle; DIRV: double inlet right ventricle; PA: pulmonary atresia; PS: pulmonary stenosis; SV: single ventricle; TA: tricuspid atresia.

Table 2. Frequency of complications in post Glenn patients.

Late Complications (more than 6 month post-operatively) (N=40)	Number	%
Heart Failure	34	36.5
Pericardial, pleural effusion	4	4.3
Hypoalbuminemia	2	2.15

Most common complications were heart failure NYHA class II and III in 34 (36.5%). (Table 2). Hypoalbuminemia occurred in patients with Kawashima variant of Glenn operation. All our patients were on daily low dose salicylates treatment to prevent obstruction of Glenn communication, 22 (23.65%) patients were on pulmonary vasodilator (Sildenafil), and 71 (76.34%) patients were on: diuretics, angiotensin converting enzyme (ACE) inhibitors, 42 (45.16%) patients were on triple drug therapy (2 diuretics+ ACEI). Cardiac catheterization was done for preparing the post Glenn patients for Fontan with priority for patients with reduced physical activity, increased cyanosis, and failure to thrive. (Figure 1).

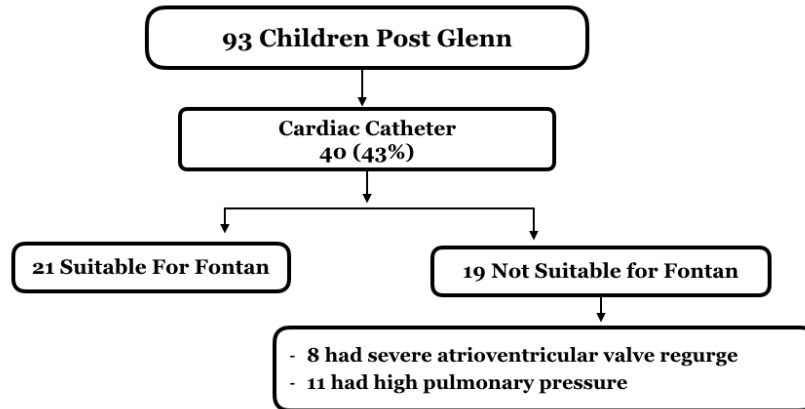


Figure 1. Flowchart of Post Glenn Patients Preparation for Fontan operation.

The Post- Sequential Fontan Cohort:

The mean ± SD inter-stage period between Glenn and Fontan completion was 6.19 ± 1.36 years (range 4-8 years). Their age range at the time of the operation was 4.9- 12years with a mean of 7.82± 1.63years, and at the latest follow up was 9-16years (mean 12.45 ±1.55years). Mean follow up duration for post Fontan patients was 4.75 ±0.08years. (Table 3). All patients showed significant improvement in post-operative O₂ saturation (84.78±4.71, 93.08±4.02) respectively (p<0.001). Nine (45%) dropped out during the COVID 19 lockdown from March 2020 to October 2020. At latest follow up, 13 (65%) were between 5th -95th percentiles for weight with a mean ±SD of 15± 2.55 percentile for age, and 12(55%) were between 5th -95th percentiles for height with a mean ±SD of 13± 0.33 percentile for age, while 7 (35%), and 8 (45%) patients were below 5th percentile for weight and height for age respectively.

Table 3. Characteristics of studied group post Fontan operation

		N = 20	%
gender	Male	11	55
	Female	9	45
Diagnosis	SV+PS	8	40
	SV+TA	5	25
	SV+PA	4	20
	SV+TA+PS	3	15
Follow up	Regular follow up	11	55
	dropout	9	45

PA: pulmonary atresia; PS: pulmonary stenosis; SV: single ventricle; TA: tricuspid atresia.

Table 4. Frequency of complications in post Fontan patients.

	Number=20	%
Heart Failure (NYHA II, III)	4	20
Late onset arrhythmia	2	10
Protein losing enteropathy	2	10
Stenotic Cavo pulmonary connection	1	5
Veno-venous Collaterals	1	5



Late complications of the sequential Fontan among our studied patients are enlisted in table 4. All Fontan patients (100%) were on diuretics, and ACEI, 4 (20%) patients were on sildenafil. All patients were on low dose salicylates except one (with PLE) was receiving warfarin as anticoagulants. Two patients (10%) with arrhythmia were receiving sotalol. Serum albumin level for all patients at the latest follow up visit ranged between 2.5-5.1 g/dl with mean 4.12 ± 0.71 . Two (10%) patients with PLE had hypoalbuminemia. Serum calcium level ranged between 6.8-9.7 mg/dl with mean 8.89 ± 0.88 . Our patients had normal level of liver enzymes in the last follow up visit; alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were less than 2 folds in the last follow up visit (15-49 IU/L, 20-40 IU/L respectively) (upper level of normal was 38 IU/L). Fourteen (70%) patients had undergone hemodynamic study to assess patency of Fontan conduit and measure PAP. All were having patent Fontan connection except 1 patient (5%) who had stenosis. One (5%) patient had veno-venous collaterals. All had normal PAP with mean 12 ± 3.12 mmHg. Complications rate was not related to age at time of operation among our studied patients post Glenn and post Fontan operation. (Table 5).

Table 5. Complications according to age at operation in post Glenn and post Fontan patients.

Mean age \pm SD	Complications		P value
	Yes	No	
Glenn	1.59 \pm 0.42	1.44 \pm 0.093	0.793
Fontan	7.33 \pm 1.19	8.27 \pm 1.74	0.079

Discussion

Our study included the surviving children post single ventricle repair. Revising their clinical picture and complications was particularly important to define the challenges we meet in their management. First challenge in our clinic was the older age at operation than that recommended due to failure of weight gain and crowded waiting list for Glenn operation (our mean age was 1.4 ± 0.9 years versus the recommended 3-6m) (4, 7). Or due to unavailability of Fontan conduit (our mean age was 7.82 ± 1.63 years versus the recommended 2-4 years) (2). However, we found that doing the operation at older age was not significantly associated with frequency of complications in our post Glenn and Fontan patients ($p=0.793$, $p=0.079$ respectively). Our results were comparable to others who recommended postponing Fontan to a feasible extent (8, 9). A previous study concluded that Glenn operation was enough as the outcome is reasonable with few late complications (7). Secondly, we face the problem of patients' incompletion as 29 (31.2%), and 9 (45%) patients post Glenn and Fontan respectively dropped out especially after COVID-19 lockdown period, mostly were around the age of 16 years. The need for adult congenital heart disease clinic is mandatory to provide follow up accomplished in coordination with adult cardiologists.

Generally, our patients were in good health as 59 (63.5%) post Glenn and 16 (80%) post Fontan patients were in NYHA class I, 65 (70%) post Glenn and 13 (65%) post Fontan were having adequate growth. All having significant improvement of oxygen saturation post operatively ($p < 0.001$). The most important complication in our patients post Glenn and Fontan was heart failure (grade II, III NYHA) found in 34 (36.5%), 4 (20%) patients respectively, for which they were controlled on diuretics and ACE inhibitors. Procedures as Fontan conversion or heart transplantation are possible solutions but unfortunately currently unavailable.

Other complications include atrial arrhythmia in 2 (10%) patients, it was supraventricular tachycardia, responded to sotalol. Arrhythmias are well known complication following Fontan with incidence of 16-50% (2, 10). PLE occurred in 2 (10%) patients, conforming with the acceptable worldwide incidence (5-12%) (2, 11). However, our incidence may be underestimated due to incompletion of post Fontan patients to regular follow up especially after getting older more than 16 years old. One (5%) patient had stenotic Fontan for which he had been referred to surgery. Our type and incidence of complications were closely similar to other studies (12-14). Some complications were not reported in our study e.g., infective endocarditis mainly due to strict subacute bacterial endocarditis prophylaxis, thromboembolic manifestations, and hepatic fibrosis perhaps due to relatively short period of follow up.



This study was limited by patients' incompliance to regular follow up and relatively short follow up duration for patients post Fontan which did not allow for studying the long-term complications as PLE and hepatic fibrosis.

Conclusion and recommendations

Performing Glenn and Fontan at older age was not related to the occurrence of complications in our patients. Heart failure was the most common complication post Glenn and Fontan operations. The longer survival post-single ventricle repair poses a lot of challenges compounded by incompliance of patients to regular follow up especially in older age. Multispecialty team and long term follow up are necessary to face late organ dysfunction.

Author Contributions:

LAI: collection, interpretation of data, manuscript preparation, drafting of the article and review of literature. FMG: concept, design of the study, analysis of data, and final approval of the version to be published. BMN: concept, design of the study, analysis of data, and final approval of the version to be published. NAA: Interpretation, analysis of data, and review the literature. All authors had full access to the data (including statistical results and tables), approved the final manuscript as submitted, and approved the final submitted work.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in connection with the reported study. Authors declare veracity of information.

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