

Original Research

Impact of Age at Fontan Completion on Functional Status at Mid-Term Follow Up

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Introduction: Although the Fontan palliation is now being applied to younger patients, the influence of patients' age at the time of surgery on mid- and long-term results remains unclear. It has been our policy to perform Fontan operations when patients are around 5 years old in order to fit a larger conduit and minimize the risk of later obstruction. We sought to investigate whether age at Fontan completion affects subsequent clinical status in patients followed up for more than 3 years.

Methods: We carried out a cross-sectional study of Fontan patients who underwent total cavopulmonary connection between 1997 and 2009 and were followed up for ≥ 3 years with detailed chart review, ECG, echocardiogram, and functional status questionnaire.

Results: Of the total of 58 patients there were 56 long-term survivors. Of these, 41 had undergone surgery ≥ 3 years prior to the time of the study. We were able to contact 37 patients, who comprised our study cohort (mean follow up 6.3, range 3.0-11.0 years). Mean age at operation was 7.4 years (median 5.5, range 3.0-29.5 years). At latest follow up, 97% were in NYHA class I or II. In terms of somatic development, 21% (8/37) for weight and 19% (7/37) for height were below the 25th percentile for age-matched controls. Excluding one patient with developmental delay due to an underlying syndrome, there were 5 patients (13.5%) with mild learning disabilities and one with moderate delays. No additional surgeries had been performed. Tissue Doppler imaging measurements of systolic and diastolic velocities of the lateral annulus of the dominant ventricle revealed abnormalities of both systolic function and diastolic compliance, although qualitatively the systolic function of the single ventricle was considered adequate in all patients.

Conclusions: Although earlier Fontan palliation is considered beneficial in the long term from the viewpoint of exercise capacity and hemodynamics, even late Fontan completion provides acceptable mid-term results in terms of the patients' functional status.

Patients with single ventricle physiology who have undergone the Fontan palliation are predisposed to various long-term complications. The optimal timing of surgery is now considered by many to be between 2 and 3 years of age, on the grounds that older age at Fontan completion has been associated with worse exercise capacity and hemodynamics,¹ as well as a greater degree of atrioventricular valve regurgitation and deteriorating diastolic function.² Howev-

er, the effect of age at completion on the clinical status of the patients has not been completely elucidated.

Since our surgical technique³ involves placement of an extracardiac conduit for Fontan completion, it has been our policy to delay performing the Fontan operation until the patient is about 5 years of age, provided oxygen saturation is satisfactory, in order to fit a larger conduit and minimize the risk of late conduit outgrowth. Other subjects in our series were first re-

ferred for Fontan completion at an even older age. Thus, our cohort consisted of subjects who had Fontan completion at an age significantly greater than 2-3 years. Our aim was to investigate the mid-term outcome of those patients and to compare their functional status with the results of published international series.

Methods

Study population

All Fontan patients with ≥ 3 years of follow up were invited to participate in this cross-sectional study, which involved a detailed medical history review, a functional status questionnaire, an electrocardiogram and an echocardiogram for assessment of systolic and diastolic ventricular function. The information gathered from the chart review included diagnosis, age at operation, previous palliative procedures, history of arrhythmia, and postoperative catheterizations. The questionnaire that was completed by the parents and/or older patients addressed exercise capacity, school performance, behavioral issues, medication use and somatic development (see Appendix).

Echocardiography

Qualitative echocardiographic assessment of ventricular systolic function was graded as normal, mildly depressed, moderately depressed, or severely depressed. Semi-quantitative assessment of the atrioventricular (AV) valve regurgitation, based on the diameter of the *vena contracta* and the relative area of the jet compared to the area of the atrium, was reported as none or trace, mild, moderate, and severe. Ventricular function was quantitatively assessed with measures derived from pulsed Doppler interrogation of the AV valve inflow (early and late diastolic inflow velocities, E and A) and the lateral annulus of the AV valve of the dominant ventricle from the apical 4-chamber view by Doppler tissue imaging: peak early diastolic velocity (E'), peak late diastolic velocity (A'), peak systolic velocity (S'); isovolumic relaxation time, E/E' ratio, E'/A' ratio. The angle between the myocardial wall and the ultrasound beam was kept at less than 30° and the frame rate ranged between 120-170 frames/s. All the above were measured off line and were averaged from 3-5 cardiac cycles by a single observer.

Statistical analysis

Descriptive statistics were used to characterize the cohort. Distributions were described using percentages. The central tendency of the distribution was estimated by calculating mean \pm standard deviation (SD), or median (range). 95% confidence intervals were also calculated where applicable. The subgroup of subjects that underwent echocardiographic evaluation was divided into two groups according to the age at operation (>5.5 years, ≤ 5.5 years) and their Doppler tissue imaging measurements were compared using the unpaired t-test.

Results

A total of 58 patients had the Fontan operation between 1992 and 2009, with 56 late survivors. Of these, 41 patients were eligible. We were unable to contact 4 patients; 63% (23/37) had an on-site visit, while the remaining 37% completed the questionnaire over the phone. The mean age at enrollment was 13.7 years; 48.6% were male (Table 1). The mean Fontan age was 7.4 years (median 5.5, range 3.0-29.5 years).

The most common diagnosis was tricuspid atresia (Table 2), and the majority (34/37) had an extracardiac Fontan, with a conduit size of 18-22 mm. A fenestration was performed in 19/37 (51.3%) and was subsequently closed, either spontaneously or by device, in 17/19. Remarkably, there were no cases of protein-losing enteropathy during a follow up of up to 11.0 years.

The mean stature and mean weight for age were both slightly below the reported mean for normal subjects (Table 1) with height more impaired than weight, in accordance with published results.⁴ However, 8/37 patients for weight and 7/37 patients for height were below the 25th percentile for age-matched controls. Of these, 6/37 (16.2%) patients for weight and 5/37 (13.5%) for height, were actually below the 5th percentile.

In terms of learning disability (Table 3), excluding one patient with developmental delay due to an underlying syndrome, there were another 5 patients with a mild and one patient with a moderate learning disability. Six patients had a history of cerebrovascular accident prior to the Fontan palliation. Coumadin treatment alone was used in 65% of patients, 24% were treated with aspirin, 8% were receiving both, and one patient (2.7%) was on no anticoagulation. Other medications, predominantly diuretics and an-

Table 1. Patient demographics.

Characteristics	n	Mean ± SD
Male/female	18/19	
Age at Fontan	37	7.4 ± 6.1
Prior cavopulmonary anastomosis	31	
Years of follow up	37	6.3 ± 2.2
Growth:		
Percentile weight-for-age	37	48.2 ± 32.4
Percentile height-for-age	36	46.4 ± 30.1
Fontan type:		
Lateral tunnel	3	
Extracardiac conduit	34	
Dominant ventricle:		
Left	24	
Right	6	
Mixed	7	
Predominant rhythm:		
Sinus	33	
Atrial escape	3	
Paced	1	

Table 2. Cardiac anatomic diagnosis.

Diagnosis	n	%
Tricuspid atresia	12	32.4
Heterotaxy	8	21.6
Double inlet left ventricle	6	16.2
D-and L-transposition	5	13.5
Unbalanced atrioventricular canal	4	10.8
Other	2	5.4

Table 3. Echocardiographic assessment.

Echocardiographic measures	n	Mean ± SD
IVRT, ms	21	73.4 ± 93.7
E', cm/s	23	11.65 ± 15.03
E/E' ratio	20	6.3 ± 9.4
E'/A' ratio	22	1.9 ± 2.55
S', cm/s	23	6.99 ± 8.79
Atrioventricular valve regurgitation:	19	
None / Trivial	12	
Mild	5	
Moderate	2	
Severe	0	

A – late diastolic inflow velocity; A' – peak late diastolic tissue velocity; E – early diastolic inflow velocity; E' – peak early diastolic tissue velocity; IVRT – isovolumic relaxation time; S' – peak systolic tissue velocity.

giotensin-converting enzyme inhibitors, were used in 67%. Based on the responses to the questionnaire regarding exercise capacity and symptomatology, 97% of the subjects were classified as NYHA class I or II (Table 3).

Qualitative assessment of the ventricular systolic function revealed adequate systolic function in all.

Shortening fraction by M-mode was obtained in 7 patients with dominant left ventricular morphology and good acoustic windows, and ranged between 30 and 43%. The results from the AV valve regurgitation assessment and the tissue Doppler imaging measurements are shown in Table 4. Notably, the mean values and 95% confidence intervals of the E wave of the AV valve inflow, as well as the E' and S' waves of the lateral annulus of the dominant ventricle were all below the published norms,⁵ indicating possible subclinical systolic and diastolic dysfunction. There was also significant prolongation of the isovolumic relaxation time, as has been described before.^{6,7} No age-specific comparisons were made in view of the small size of the cohort. The comparison of E, E', A', and S' of the subgroups based on age at operation (5.5 years was arbitrarily selected since it was the median age at operation) yielded non-significant results.

Discussion

The objective of this study was to evaluate the mid-term functional status of all patients who had the Fontan operation in Greece. Due to mostly late referral, our cohort had the Fontan completion later in life compared to the international experience. We have shown that the patients have an excellent perceived quality of life and we rarely encountered well-known complications of the Fontan circulation, such as protein-losing enteropathy, significant arrhythmias, and cerebrovascular accidents. The prevalence of learning disability was within the reported range,^{8,9} with most patients reporting normal school evaluations and attendance at regular classes. The same was true for somatic growth delay.⁴ The subgroup of patients with severe somatic underdevelopment reported significant emotional disturbances secondary to the growth delay, raising the issue of growth hormone therapy in this subgroup of patients.

Table 4. Functional status.

Learning disability:	
Mild	6
Moderate	1
Severe	0
NYHA Class:	
I	23
II	13
III	1
IV	0

In terms of ventricular function evaluation, despite the perceived adequacy of global systolic function as assessed by an experienced observer and the lack of significant atrioventricular valve regurgitation in the majority of the cases, we observed remarkable deviations from the normal range for all tissue Doppler parameters measured, in accordance with those reported in other series.^{2,6,10}

Limitations

The cohort size in this study was small, as was the number of subjects undergoing echocardiography, so we interpret these results with caution. However, we advocate frequent follow up and measurement of those indices in order to be able to diagnose the early stages of systolic and diastolic dysfunction and treat accordingly. Despite our good mid-term results we do not aim to propose Fontan completion at a later age. Our objective was to contribute to current knowledge by describing this cohort's functional status, since concern over late results of the single ventricle palliation and optimal age of operation still exists. In the majority of our patients the single ventricle was of

left or mixed ventricular morphology. This may have contributed to our good results although the effect of ventricular morphology on long-term survival and functional status has been controversial.^{11,12,13}

Conclusions

The mean age of Fontan completion in our cohort was higher but the rate of complications at mid-term follow up was comparable to large series of patients operated on at an earlier age.¹⁴ The long-term outcome of these older Fontan patients should also be studied before firm conclusions about the effect of age on Fontan completion can be drawn.

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Appendix

Patient evaluation questionnaire

Age: Age at Fontan:

Height: Weight: O2 saturation:

Which anticoagulant, aspirin or coumadin?

Other medication?

If yes, which ones? If no, any history of medication use?

Date of last echocardiogram?

Catheterization or other interventional procedure after the Fontan operation?

Is the child attending regular school? Participating in Gym class?

How does he/she perform compared to his/her classmates?

Is he/she reporting any symptoms? Tires easily?

NYHA Class:

Arrhythmia postoperatively or later that requires treatment

Pacemaker placement Y/N; if yes, when?

Fenestration Y/N

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