Trends in Fontan surgery and risk factors for early adverse outcomes after Fontan surgery: The Australia and New Zealand Fontan Registry experience

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Objectives: This study examined changes in practice and analyzed risk factors for adverse early outcomes after Fontan surgery through use of a binational, population-based registry.

Methods: Demographic, preoperative, and perioperative data were collected from all participating institutions of the Australia and New Zealand Fontan Registry. Patient and operative characteristics were analyzed with multivariable logistic regression for impact on early mortality, early Fontan failure (death, takedown, or mechanical support), effusions (prolonging hospital stay >30 days or requiring surgical reintervention), and stay longer than 30 days.

Results: Overall mortality was 3.5% (37/1071) and declined throughout the study period, from 8% (1975-1990) to 4% (1991-2000) and 1% (2001-2010). There were no differences between the extracardiac and lateral tunnel modifications for any outcome. After 2006, the extracardiac conduit was performed exclusively, with 1.3% mortality. The proportion of patients with hypoplastic left heart syndrome rose to 17% in the current era, and this group had more effusions (odds ratio, 3.0; 95% confidence interval, 1.4-6.6) and stayed on average 2 days longer in the hospital. Hypoplastic left heart syndrome was also an independent risk factor for composite adverse early outcome (death, failure, prolonged effusions, or prolonged stay >30 days; odds ratio, 2.6; 95% confidence interval 1.4-4.8 respectively).

Conclusions: The extracardiac conduit is now the exclusive Fontan modification performed in Australia and New Zealand. Even with a higher proportion of high-risk cases, perioperative outcomes are excellent in the modern era. Hypoplastic left heart syndrome confers a higher risk of prolonged pleural effusion and early composite adverse outcome. (J Thorac Cardiovasc Surg 2014;148:566-75)

After Fontan and Baudet's initial description of the atriopulmonary connection,¹ subsequent modifications were introduced in 1988 by de Leval and colleagues² and in 1990 by Marcelletti and associates.³ The atriopulmonary connection has now been abandoned because of the survival attrition of these patients and the progressive decline in functional capacity.⁴⁻⁶ It has long been assumed that the lateral tunnel and the extracardiac conduit techniques would yield equivalent early outcomes, and that differences between these techniques would only become obvious in the

analysis of long-term outcomes after Fontan surgery. In a recent report from the Society of Thoracic Surgeons Congenital Heart Surgery Database, patients undergoing an extracardiac conduit were found to have a higher risk of early reintervention and failure and were likely to stay in the hospital longer than those undergoing the lateral tunnel.⁷ Along with the modification of techniques, the population offered Fontan surgery has evolved during the course of the last 2 decades. In particular, the improved survival after Norwood surgery has been responsible for an increase in the

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Abbreviations and Acronyms

CI	= confidence interval
HLHS	= hypoplastic left heart syndrome
IQR	= interquartile range
OR	= odds ratio

proportion of patients with hypoplastic left heart syndrome (HLHS) reaching Fontan surgery.⁸

In 2008, the Australia and New Zealand Fontan Registry was established to clarify long-term expectations of patients undergoing Fontan procedures and to enable recruitment of larger numbers of patients into prospective studies. During the creation and recruitment of patients into this registry, the preoperative and perioperative data of all patients undergoing Fontan procedures in Australia and New Zealand were collected. We thus sought to determine trends in indications and demographic characteristics of patients undergoing the Fontan procedure since its introduction in the region in 1975 and to analyze the impact of these trends on early outcomes, with a focus on the surgical techniques used. This analysis represents the entire experience of Fontan surgery in Australia and New Zealand.

MATERIALS AND METHODS

Institutional approval to collect data at all participating centers was obtained, and the need for consent was waived because of the retrospective nature of the study. All Fontan procedures performed in Australia and New Zealand were identified by consulting the cardiac surgical and cardiology databases at each institution (Appendix Table 1). Preoperative, perioperative, and early postoperative data collected are described in Appendix Table 2. Operative reports, echocardiographic reports, and discharge summaries were reviewed. Patients for whom insufficient data existed to satisfy the minimum data set (age at Fontan, Fontan type, and discharge status) were excluded. Fontan conversions were excluded from the data set, with the exception of 3 patients who had previously undergone a Björk procedure and subsequently had a Fontan completion.

Outcomes

The primary outcome was early mortality, defined as death within the first 30 postoperative days or before hospital discharge if the stay was longer than 30 days. Secondary outcomes were early failure (takedown, major reintervention not bleeding related, including Fontan revision, fenestration creation, enlargement or closure, mechanical circulatory support, or percutaneous reintervention), prolonged effusions (lasting >30 days or requiring reoperation for transcatheter intervention, pleurodesis, or Fontan revision), and a composite adverse early outcome (death, failure, prolonged effusions, or prolonged stay >30 days).

Statistical Analysis

Patient, operative and outcome data were described according to era and Fontan type (Tables 1 and 2), with normally distributed, nonnormally distributed, and proportional data described as mean $\pm$ SD, median with interquartile range (IQR), and number and percentage, respectively. Logistic regression analysis models were constructed for each outcome, and multivariable models were designed a priori to compare lateral tunnel versus extracardiac Fontan types and morphologically left versus right ventricles while adjusting for sex, age, and morphology as

categorical variables. Remaining covariates were analyzed in univariable models to identify potential confounders and entered into the multivariable models if they were associated with a large effect size (odds ratio (OR) ≥ 2.5 or ≤ 0.4) or there was evidence against the null hypothesis of no association (2-tailed $P \leq .05$). Because of collinearity between Fontan type, era, staging with bidirectional cavopulmonary shunt, and fenestration, we included only Fontan type in multivariable models. Additionally, southern hemisphere respiratory syncytial virus season (the months of May to September) was analyzed for its effect on pleural effusions. The variables selected for multivariable models and their regression parameters are reported in Table 3.

Exposure groups in which no failures or deaths occurred could not be entered into logistic regression models. Numeric covariates were analyzed as continuous variables unless a nonlinear relationship could be demonstrated between covariate and outcome. Linearity was examined by performing a likelihood ratio test comparing regression models with continuous covariates against models in which the numeric variable had been categorically transformed. Age at Fontan operation had nonlinear associations with mortality (Figure 1) and the other end points and was analyzed as a categorical variable.

All analyses were performed with the Stata 11.2 statistical software package (StataCorp, College Station, Tex).

RESULTS

Description of Cohort

In all, 1095 Fontan procedures were identified, of which 1071 had sufficient data to be included for analysis.

A total of 1989 previous surgical palliations were performed in 990 patients. Previous staging with bidirectional cavopulmonary shunt occurred in 636 patients (59%); 4% who underwent the atriopulmonary technique, 16% who underwent lateral tunnel, and 96% who underwent extracardiac conduit. Mean pre-Fontan pulmonary arterial pressure was lowest among patients with extracardiac conduits (11.1 ± 2.7 mm Hg for extracardiac, 12.5 ± 4.5 mm Hg for lateral tunnel, and 13.1 ± 4.3 mm Hg for atriopulmonary; $P < .001$; $R^2 = 0.05$). The proportion with detected aortopulmonary collaterals increased with each era (3 patients [3%] before 1991, 47 patients [16%] from 1991 to 2000, and 115 patients [30%] after 2000), and 46 of 165 patients (28%) had these embolized before the Fontan procedure by transcatheter coiling. At 1 center, internal thoracic to pulmonary artery collaterals were routinely divided at operation if visualized.

Moderate or severe atrioventricular valve regurgitation was present before the Fontan procedure in a total of 65 patients (7.5%). Of the whole cohort, 40 patients (4.6%) had previously undergone atrioventricular valve repair or replacement; 18 (45%) were left with recurrent regurgitation by the time of the Fontan procedure, but re-repair was only attempted in 9 patients. Atrioventricular valve repair was undertaken concomitantly with the Fontan procedure in 28 patients (3%, 9 re-repairs and 19 de novo repairs).

Extracardiac conduit was the only modification performed after July 2006. Fenestration was performed in 50% of lateral tunnel and 44% of extracardiac connections.

TABLE 1. Description of baseline data by Fontan type

Variable	AP (1975-1995)	LT (1988-2006)	ECC (1997-2010)	Total
No. of patients	239 (22%)	296 (28%)	536 (50%)	1071
Age (y, median and IQR)	5.6 (3.2-9.3)	3.8 (2.8-5.8)	4.8 (3.9-6.0)	4.7 (3.4-6.5)
Male (No.)	132 (55%)	166 (56%)	320 (60%)	618 (58%)
Ventricular morphology				
Left	185 (77%)	183 (62%)	289 (54%)	657 (61%)
Right	44 (18%)	93 (32%)	190 (36%)	327 (31%)
Biventricular/indeterminate	10 (4%)	19 (6%)	57 (11%)	86 (8%)
Morphologic group				
TA	79 (33%)	73 (25%)	101 (19%)	253 (24%)
HLHS	2 (1%)	9 (3%)	78 (15%)	89 (8%)
DORV	34 (14%)	45 (15%)	71 (13%)	150 (14%)
CAVC	13 (5%)	17 (6%)	34 (6%)	64 (6%)
TGA	6 (3%)	18 (6%)	27 (5%)	51 (5%)
ccTGA	10 (4%)	13 (4%)	28 (5%)	51 (5%)
DILV	52 (22%)	65 (22%)	78 (15%)	195 (18%)
PA-IVS	17 (7%)	20 (7%)	47 (9%)	84 (8%)
CAVC-DORV	6 (3%)	16 (5%)	26 (5%)	48 (4%)
Other	20 (8%)	20 (7%)	46 (9%)	86 (8%)
Anatomic comorbidities				
Isomerism or heterotaxy	11 (5%)	22 (7%)	39 (7%)	72 (7%)
Dextrocardia or mesocardia	22 (9%)	18 (6%)	39 (7%)	79 (7%)
Previous operations				
No. (mean $\pm$ SD)	1.2 $\pm$ 0.8	1.6 $\pm$ 0.9	2.3 $\pm$ 1.0	1.9 $\pm$ 1.0
PA banding (No. and %)	55 (23%)	86 (29%)	141 (26%)	282 (26%)
Norwood procedure (No. and %)	2 (1%)	10 (3%)	81 (15%)	93 (9%)
Aortic arch intervention (No. and %)	17 (7%)	48 (16%)	185 (35%)	250 (23%)
BCPS (No. and %)	9 (4%)	111 (38%)	516 (96%)	636 (59%)
PA reconstruction (No. and %)	5 (2%)	18 (6%)	113 (21%)	136 (13%)
Pre-Fontan hemodynamics				
Arterial oxygen saturation (per %, median and IQR; n = 839)	81 (77-85)	82 (78-85)	82 (78-86)	82 (78-86)
PA pressure (mm Hg, mean $\pm$ SD; n = 869)	13.1 $\pm$ 4.3	12.5 $\pm$ 4.5	11.1 $\pm$ 2.7	11.9 $\pm$ 3.7
$\geq$ Moderate AV valve regurgitation (No.; n = 871)	9 (8%)	12 (5%)	44 (9%)	65 (7%)
Arteriovenous malformations (No.; n = 809)	2 (2%)	6 (3%)	32 (7%)	40 (5%)
Collaterals (No.; n = 799)	2 (2%)	21 (10%)	142 (29%)	165 (21%)
Operative variables (No.)				
Concomitant procedure	31 (13%)	52 (18%)	73 (14%)	156 (15%)
Fenestration	0 (0%)	149 (50%)	236 (44%)	385 (36%)
RSV seasonality (May to September)	108 (45%)	130 (44%)	183 (34%)	421 (39%)

When data were not available for all patients, values are given for study set and study set size is specified. AP, Atriopulmonary; LT, lateral tunnel; ECC, extracardiac conduit; IQR, interquartile range; TA, tricuspid atresia; HLHS, hypoplastic left heart syndrome; DORV, double-outlet right ventricle; CAVC, complete atrioventricular canal; TGA, transposition of the great arteries; ccTGA, congenitally corrected transposition of the great arteries; DILV, double-inlet left ventricle; PA-IVS, pulmonary atresia with intact ventricular septum; PA, pulmonary artery; BCPS, bidirectional cavopulmonary shunt; AV, atrioventricular; RSV, respiratory syncytial virus.

Pulmonary artery rehabilitation (percutaneous or surgical) was undertaken in a total of 191 patients (18%) at some stage during life: 55 patients underwent pulmonary artery patch reconstruction at the time of the Fontan procedure, 126 had surgical reconstruction or stenting before Fontan completion, and an additional 10 had both previous and concomitant intervention to the pulmonary arteries.

Age at Fontan completion varied according to Fontan type. The extracardiac conduit was performed 1 year later than the lateral tunnel (median, 4.8 years; IQR, 3.9-6.0 years; vs median, 3.8 years; IQR, 2.8-5.8 years; $P < .001$).

The proportion of patients with HLHS rose during the regional experience, from 1% in the era to 1990, to 3% between 1991 and 2000 and 17% after 2000. The peak proportion of patients undergoing Fontan surgery with HLHS was 28% in 2007. HLHS was present in 15% of patients undergoing extracardiac Fontan procedures.

Early Mortality

The early outcomes of patients are represented graphically in Figure 2 and in tabular form in Tables 2 and 4. Results of logistic regression analysis for each outcome are presented in Table 3.

TABLE 2. Description of early outcomes according to era

Outcome	1975-1990	1991-2000	2001-2010	Total
No.	246 (23%)	371 (35%)	454 (42%)	1071
Early mortality	19 (8%)	13 (4%)	5 (1%)	37 (3.5%)
Early failure*	21 (9%)	27 (7%)	17 (4%)	65 (6%)
Prolonged effusions†	11 (4%)	28 (8%)	35 (8%)	74 (7%)
Composite adverse early outcome‡	48 (26%)	61 (20%)	56 (12%)	165 (17%)
Prolonged stay (>30 d)	29 (16%)	37 (12%)	44 (10%)	110 (12%)
Stay among survivors (d, median and IQR; n = 913)	15.5 (12-27)	12 (9-20)	13 (9-20)	13 (10-21)

Data are expressed as No. and % except as specified. *IQR*, Interquartile range. *Death, mechanical support, takedown, or major reoperation. †Pleural effusions persisting >30 days or requiring surgical intervention. ‡Prolonged effusions, failure, or prolonged stay (>30 days).

TABLE 3. Univariate and multivariate logistic regression results for each end point

Variable	Early mortality (n = 37)				Early failure (n = 65)				Prolonged effusions (n = 75)				Composite adverse early outcome (n = 165)			
	Univariate		Multivariate		Univariate		Multivariate		Univariate		Multivariate		Univariate		Multivariate	
	P value	OR	95% CI	P value	P value	OR	95% CI	P value	P value	OR	95% CI	P value	P value	OR	95% CI	P value
Fontan type																
Lateral tunnel	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Atriopulmonary	<.001	3.9	1.1-13.2	.03	.05	1.7	0.6-4.9	.4	.5	0.9	0.4-1.9	.7	.006	1.6	0.7-3.6	.3
Extracardiac conduit	.4	1.2	0.3-4.6	.8	.2	0.6	0.2-1.3	.2	.2	1.1	0.6-2.0	.7	.2	0.9	0.5-1.6	.7
Age (y)																
4-5	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
<4	.05	4.5	0.6-37	.2	.3	1.2	0.5-3.2	.9	.04	0.6	0.3-1.1	.08	.3	0.7	0.4-1.3	.2
5-8	.09	3.6	0.4-32	.2	.6	0.9	0.3-2.8	.9	.04	0.5	0.3-1.0	.05	.3	0.5	0.3-1.1	.07
>8	.01	6.5	0.8-55	.09	.2	1.5	0.5-4.7	.5	.05	0.5	0.2-1.2	.1	.6	0.7	0.3-1.5	.4
Male sex	.6	1.2	0.7-4.5	.2	.2	1.8	0.9-3.9	.1	.9	0.8	0.5-1.3	.4	.5	0.8	0.5-1.3	.3
Ventricular morphology																
Left	Ref				Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Right	.8				.9	0.8	0.3-1.7	.5	.01	1.2	0.7-2.2	.5	.4			
BiV or indeterminate	.3				.09	2.2	0.8-6.5	.1	.6	1.3	0.5-3.2	.6	.5			
Morphologic group																
TA	Ref				Ref				Ref	*			Ref	Ref	Ref	Ref
HLHS	.4				.6				<.001	3.1	1.4-6.6	.005	.02	2.7	1.2-6.0	.01
DORV	.9				.9				>.99				.4	1.0	0.4-2.3	>.99
CAVC	.9				.4				.6				.06	2.1	0.8-5.3	.1
TGA	—†				.2				.7				.8	1.2	0.3-4.6	.8
ccTGA	.4				.4				.4				.2	1.5	0.5-4.3	.4
DILV	.3				.3				.4				.4	1.1	0.5-2.3	.9
PA-IVS	.8				.9				.7				>.99	1.0	0.4-2.8	>.99
CAVC-DORV	.3				.3				.3				.3	2.0	0.6-6.6	.2
Other	.4				.2				.2				.7	0.9	0.3-2.4	.8
Anatomic comorbidities																
Isomerism or heterotaxy	.3				.07				.3				.07			
Dextrocardia or mesocardia	.2				.04	2.3	0.8-6.4	.1	.5				.04	1.4	0.6-3.3	.4
Previous operations																
No.	.003	1.0	0.6-1.6	.9	.06				.1				.01	0.9	0.7-1.2	.7
PA banding	.2				.8				.9				.7			
Aortic arch intervention	.2				.8				.001	—‡			.3			

(Continued)

TABLE 3. Continued

Variable	Early mortality (n = 37)			Early failure (n = 65)			Prolonged effusions (n = 75)			Composite adverse early outcome (n = 165)		
	Univariate		P value	Univariate		P value	Univariate		P value	Univariate		P value
	P value	OR		P value	OR		P value	OR		P value	OR	
BCPS	<.001	—§		.003	—§		.09			<.001	—§	
Previous or concomitant PA reconstruction	.8			.6			.2			.9		
Pre-Fontan hemodynamics												
Arterial oxygen saturation, (per %; n = 839)	.2			.1			.3			.1		
PA pressure (per 5 mm Hg; n = 869)	.01	1.5	1.0-2.4	.06	.003	1.4	1.0-2.1	.08	.4	.03	1.3	0.9-1.8
AV valve regurgitation (n = 871)	—†			.08	0.4	0.04-3.0	.3	.5		.6		
Arteriovenous malformations (n = 809)	.1			.08	2.1	0.6-7.2	.3	.2		.03	2.6	1.2-5.8
Collaterals (n = 799)	.6			.08			.09			.5		
Operative variables												
Concomitant procedure	.1	2.2	0.8-6.0	0.1	.2		.007	2.2	1.2-3.8	.008	.01	1.9
Fenestration	.007	—§		.2			.1			.04	—§	
Postoperative effusions (mortality and failure end points only)	.3			<.001	14.5	6.5-32.5	<.001	—		—		
RSV seasonality (May-Sept prolonged effusions end point only)	—			—			.8			—		

Regression parameters are presented for covariates entered into multivariate models. OR, Odds ratio; CI, confidence interval; Ref, reference; BiV, biventricular; TA, tricuspid atresia; HLHS, hypoplastic left heart syndrome; DORV, double-outlet right ventricle; CAVC, complete atrioventricular canal; TGA, transposition of the great arteries; ccTGA, congenitally corrected transposition of the great arteries; DILV, double-inlet left ventricle; PA-IVS, pulmonary atresia with intact ventricular septum; PA, pulmonary artery; BCPS, bidirectional cavopulmonary shunt; AV, atrioventricular; RSV, respiratory syncytial virus. *Odds ratio for HLHS versus all other morphologies as reference group. †Excluded from analysis because of no failures in exposed group. ‡Excluded from analysis because of collinearity with HLHS morphology (multivariate). §Excluded from analysis because of collinearity with Fontan type (multivariate). ||Data available for n patients.

There were a total of 37 early deaths: 2 intraoperative, 3 after reintervention, 5 after takedown, and 26 not associated with any major reintervention. Early mortalities after extracardiac conduit and lateral tunnel modifications were low (7/536 [1.3%] and 6/296 [2.0%], respectively; $P = .4$), with higher early mortality after atriopulmonary connection (24/239 [10%]). A 1% mortality was achieved in the current era (Table 2). Risk factors associated with early mortality after adjustment for age and sex were atrio-pulmonary connection technique (OR, 3.9; 95% CI, 1.1-13.2) and preoperative elevation of pulmonary arterial

pressure (OR, 1.5 per 5-mm Hg increase; 95% CI, 1.0-2.4). Mortalities after lateral tunnel and extracardiac conduit did not differ (OR, 1.2; 95% CI, 0.3-4.6) independent of era. Fontan completion at 4 to 5 years of age was weakly associated with markedly lower univariate odds of mortality when compared with those younger than 4 years (OR, 4.5; 95% CI, 0.6-37), 5 to 8 years old (OR, 3.6; 95% CI, 0.4-32), and older than 8 years (OR, 6.5; 95% CI, 0.8-55). Despite large effect sizes in univariate models, however, the age of completion no longer reached statistical significance in the multivariate model.

FIGURE 1. Probability of early mortality against age at Fontan, obtained by means of fractional polynomial regression. *Dashed lines* indicate upper and lower 95% confidence limits.

Early Failure (Death, Takedown, Major Reintervention, or Mechanical Circulatory Support)

Early failure occurred in 6% of patients (65/1071). Among the 20 patients undergoing early Fontan takedown, 15 (75%) survived to hospital discharge with an intermediate palliation (10 bidirectional cavopulmonary shunts, 2 central shunts, 2 hemi-Fontan procedures, and 1 Kawashima procedure; **Figure 2**). In total, 5 patients required mechanical circulatory support (extracorporeal

membrane oxygenation, n = 4; ventricular assist device, n = 1), 3 of whom survived to hospital discharge. Two of these patients were put on extracorporeal membrane oxygenation after early reintervention (1 each revision and takedown). Prolonged pleural effusion was the only independent predictor of increased risk of early failure (OR, 14.5; 95% CI, 6.5-32.5). There were no deaths or failures among the 40 patients who had undergone concomitant or previous atrioventricular valve repair or replacement.

Pleural Effusions, Prolonged Stay, and Composite Adverse Early Outcome

Prolonged effusions occurred in 74 patients (7%), and the mortality among these patients was 5% (4/74, univariate *P* = .8). In 37 of these patients, 61 reoperations were undertaken; these included 7 takedowns, 9 revisions, 1 conversion, 9 embolizations or division of collaterals, 20 pleurodeses, 3 percutaneous fenestration dilatations, and 1 thoracic duct ligation. In multivariable models, HLHS and concomitant procedure at the time of the Fontan operation were strongly associated with prolonged effusions (OR, 3.1; 95% CI, 1.4-6.6; and OR, 2.2; 95% CI, 1.2-3.8, respectively). There was no association between prolonged effusions and Fontan completion during the southern hemisphere respiratory syncytial virus season (May to September).

FIGURE 2. Surgical progression and early outcomes. AP, Atriopulmonary; LT, lateral tunnel; ECC, extracardiac; pts, patients; ECMO, extracorporeal membrane oxygenation; VAD, ventricular assist device; BCPS, bidirectional cavopulmonary shunt.

TABLE 4. Description of early outcomes according to Fontan type

Outcome	AP	LT	ECC	Total
No.	239 (22%)	296 (28%)	536 (50%)	1071
Early mortality	24 (10%)	6 (2.0%)	7 (1.3%)	37 (3.5%)
Early failure*	26 (11%)	18 (6%)	21 (4%)	65 (6%)
Prolonged effusions†	11 (5%)	18 (6%)	45 (8%)	74 (7%)
Composite adverse early outcome‡	55 (29%)	39 (17%)	71 (13%)	165 (17%)
Prolonged stay (>30 d)	31 (16%)	26 (12%)	53 (10%)	110 (12%)
Stay among survivors (d, median and IQR; n = 913)	16 (12-27)	12 (10-20)	13 (9-20)	13 (10-21)

Data are expressed as No. and % except as specified. AP, Atriopulmonary; LT, lateral tunnel; ECC, extracardiac conduit; IQR, interquartile range. *Death, mechanical support, takedown, or major reoperation. †Pleural effusions persisting >30 days or requiring surgical intervention. ‡Prolonged effusions, failure, or prolonged stay (>30 days).

Median hospital stay was 13 days (IQR, 10-21 days); patients with HLHS and atrioventricular septal defects, respectively, stayed 2 and 5 days longer than other groups ($P = .04$ and $P = .008$), and this was the principal driver for the identification of HLHS as the strongest independent predictor (OR, 2.7; 95% CI, 1.2-6.0) of the composite adverse early outcome end point (death, failure, prolonged effusions, or stay >30 days). The remaining independent risk factors are presented in Table 4.

Permanent pacemaker was required by discharge in 23 patients (2%; atriopulmonary, n = 8; lateral tunnel, n = 4; extracardiac conduit, n = 11).

DISCUSSION

Our study is based on a unique, binational population-based registry that captures all available patients undergoing a Fontan procedure. We believe this design provides the most accurate data by eliminating potential referral and selection bias, as well as exploring outcomes for patients undergoing similar procedures in different institutions.

Trends in Fontan Surgery

It is likely that our experience in Australia and New Zealand reflects changes in Fontan surgery evident elsewhere. The preoperative condition of patients has improved, as reflected by the decrease in the proportion of patients with elevated preoperative pulmonary arterial pressures. It is remarkable that today the Fontan procedure has become an operation with 1% to 2% early mortality and a rate of early failure of 4%. We have replaced the atriopulmonary technique, which was associated with worse outcomes,⁵ with the lateral tunnel and now extracardiac modifications.

The most striking change seen in our practice in the last decade has been the increasing proportion of patients with HLHS who are offered Fontan surgery, which is the direct result of the improved survival of these patients after their initial surgeries. This subset of patients represents the worst end of the spectrum of patients

offered Fontan surgery,^{9,10} and it is therefore remarkable that the mortality associated with Fontan surgery has decreased during the same period, remaining around 1% in Australia and New Zealand. It is likely that a better understanding of the Fontan physiology, and resultant better patient selection, has improved the preoperative and postoperative management of patients. In particular, the improved care of atrioventricular valve regurgitation,^{11,12} collaterals,¹³ and pulmonary arteriovenous malformations have probably contributed to these improved outcomes. This increasing population with HLHS have low mortality similar to that of the other patients but create increased demands on the health system. Disproportionate use of inpatient cardiac critical care services by single-ventricle patients, in particular those with HLHS, has already been observed.^{14,15} Our study highlights that they have more early adverse outcomes and stay longer in the hospital because of their tendency to have prolonged effusions. This association had already been demonstrated by Gaynor and colleagues¹⁶ and Rogers and associates¹⁷ and cannot be clearly linked only to adverse morphology. Patients with HLHS have undergone more extensive surgery during earlier operations. It is possible that previous damage to the network of chylous channels around the aorta during the initial surgery and repetitive extensive dissections predispose these patients toward chyle leaks. The recent report of Stewart and coworkers⁷ demonstrated that patients undergoing an extracardiac conduit were at risk for prolonged hospital stay, and we have hypothesized that this may be related to more extensive dissection with this technique.¹⁸ The prolonged effusions observed in patients with HLHS could also be related to adverse physiologic characteristics not apparent in Stewart and coworkers' earlier study,⁷ such as a trend toward more atrioventricular valve regurgitation, more aortopulmonary collaterals, or higher end-diastolic ventricular pressure. One wonders whether patients like these who have a higher rate of early complications will perhaps be prone to earlier failure of the Fontan circulation.

Fontan Type and Age at Fontan Completion

There has been little clinical evidence that either of the prevailing techniques, the lateral tunnel and the extracardiac cardiac conduit, is superior to the other. Nevertheless, theoretic advantages have led all teams in Australia and New Zealand independently to adopt the extracardiac conduit technique.

Importantly, in our experience, there were no differences in the odds of development of any adverse early outcome between the lateral tunnel and extracardiac conduit modifications. This is in contrast to the recently published findings of Stewart and coworkers,⁷ who demonstrated increased odds of Fontan takedown, revision, Fontan failure, and longer postoperative stay after the extracardiac modification than after the lateral tunnel. The key difference between our series is the age at elective Fontan completion. Stewart and coworkers⁷ explicitly excluded patients older than 6 years from the analysis; however, these patients represent 30% of our cohort (318/1071). The reported North American experience reflects a willingness to proceed with Fontan completion at a very early age, with half of the patients operated on younger than 3 years. In Australia and New Zealand, by contrast, Fontan completion is undertaken at a later age, at a median of 4.7 years in the current era, and fewer than 7% of contemporary patients in this series had their Fontan procedure completed before the age of 3 years. The use of the lateral tunnel may be advantageous at such an early age, because the use of the extracardiac conduit will result in a size discrepancy between the adult-sized conduit and small vascular structures. Conduit size and the ratio of inferior vena cava to conduit diameter may be an important determinant of early outcomes, as the use of a conduit that is too large in a small patient promotes stagnation of caval flow and may contribute to loss of the respiratory pump, essential for inspiratory augmentation of pulmonary blood flow, and promote thrombosis formation in the early postoperative period.^{19,20} We have previously suggested that construction of the extracardiac conduit may be more prone to subtle technical deficiencies, such as distortion of the pulmonary arteries and a suboptimal fenestration, which are difficult to analyze without imaging data.¹⁸ These factors may also play a role in early hemodynamics and thus in outcomes.

We were interested to find that in our practice the age of 4 to 5 years was associated with better outcome according to univariate analysis but not in the multivariate model. It can be easily understood that within a policy of completing the Fontan around 4 years, patients younger than 4 years would be a select group with worse symptoms, such as those with pulmonary arteriovenous malformations and severe cyanosis. It is notable that later age at surgery seems to be associated with worse late functional outcomes but also worse early outcomes.²¹

Atrioventricular Valve Regurgitation

Atrioventricular valve regurgitation in patients with a single ventricle is likely to become an increasing issue in our patient population, and it appears to evolve to significantly adversely affect the course of patients during staged palliation despite an absence of truly discouraging long-term survival data.^{5,22,23} One in 10 patients in this series either displayed moderate to severe regurgitation immediately preoperatively, had previously undergone valve repair or replacement, or underwent repair or replacement at the time of the Fontan procedure. This series validates that excellent outcomes for these patients can be expected in the short term,²⁴ despite a trend toward more effusions in those who undergo concomitant surgery.

Limitations

This study is limited by its retrospective nature. Direct comparisons between different surgical modifications are clearly confounded by the fact that these were undertaken during different eras during the binational experience. Because of the very close correlation between era and atriopulmonary Fontan type, correction for era was not possible. It is thus not possible to conclude whether the poorer outcomes after the atriopulmonary Fontan procedure were driven primarily by the early era during which these procedures were undertaken or by the procedure itself. In reality, we suspect a combination of these factors.

Similarly, staging could not be analyzed in multivariable models because it was so strongly associated with the development of the later Fontan modifications. We have previously demonstrated that the introduction of staging before Fontan completion entailed a selection process.²⁵ Finally, this registry does not encompass all patients with single-ventricle physiology. This means that the true selection bias is not quantifiable, and the size of the era effect on patient selection is not known.

CONCLUSIONS

In conclusion, in Australia and New Zealand, all centers have progressively adopted the extracardiac conduit technique and offer Fontan surgery to patients around 4 to 5 years old. In this setting, the extracardiac conduit can be performed with a mortality of 1% and achieve similar early outcomes to the lateral tunnel. Patients with HLHS have more early complications, in particular pleural effusions, and this makes them a greater burden on delivery of care.

References

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. *Thorax*. 1971;26:240-8.
2. de Leval MR, Kilner P, Gewillig M, Bull C. Total cavopulmonary connection: a logical alternative to atriopulmonary connection for complex Fontan operations.

- Experimental studies and early clinical experience. *J Thorac Cardiovasc Surg.* 1988;96:682-95.
3. Marcelletti C, Corno A, Giannico S, Marino B. Inferior vena cava–pulmonary artery extracardiac conduit. A new form of right heart bypass. *J Thorac Cardiovasc Surg.* 1990;100:228-32.
 4. Fontan F, Kirklin JW, Fernandez G, Costa F, Naftel DC, Tritto F, et al. Outcome after a “perfect” Fontan operation. *Circulation.* 1990;81:1520-36.
 5. 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(11 Suppl):I157-64.
 6. d’Udekem Y, Cheung MM, Setyapranata S, Iyengar AJ, Kelly P, Buckland N, et al. How good is a good Fontan? Quality of life and exercise capacity of Fontans without arrhythmias. *Ann Thorac Surg.* 2009;88:1961-9.
 7. Stewart RD, Pasquali SK, Jacobs JP, Benjamin DK, Jaggars J, Cheng J, et al. Contemporary Fontan operation: association between early outcome and type of cavopulmonary connection. *Ann Thorac Surg.* 2012;93:1254-60; discussion 1261.
 8. d’Udekem Y, Xu MY, Galati JC, Lu S, Iyengar AJ, Konstantinov IE, et al. Predictors of survival after single-ventricle palliation: the impact of right ventricular dominance. *J Am Coll Cardiol.* 2012;59:1178-85.
 9. Tweddell JS, Hoffman GM, Mussatto KA, Fedderly RT, Berger S, Jaquiss RD, et al. Improved survival of patients undergoing palliation of hypoplastic left heart syndrome: lessons learned from 115 consecutive patients. *Circulation.* 2002;106(12 Suppl 1):I82-9.
 10. Czossek RJ, Anderson JB, Heaton PC, Cassidy A, Schnell B, Cnota JF. Staged palliation of hypoplastic left heart syndrome: trends in mortality, cost, and length of stay using a national database from 2000 through 2009. *Am J Cardiol.* 2013;111:1792-9.
 11. Ohye RG, Gomez CA, Goldberg CS, Graves HL, Devaney EJ, Bove EL. Tricuspid valve repair in hypoplastic left heart syndrome. *J Thorac Cardiovasc Surg.* 2004;127:465-72.
 12. Nakata T, Fujimoto Y, Hirose K, Tosaka Y, Ide Y, Tachi M, et al. Atrioventricular valve repair in patients with functional single ventricle. *J Thorac Cardiovasc Surg.* 2010;140:514-21.
 13. Reinhardt Z, De Giovanni J, Stickley J, Bhole VK, Anderson B, Murtuza B, et al. Catheter interventions in the staged management of hypoplastic left heart syndrome. *Cardiol Young.* Epub 2013 Feb 8.
 14. Dean PN, Hillman DG, McHugh KE, Gutgesell HP. Inpatient costs and charges for surgical treatment of hypoplastic left heart syndrome. *Pediatrics.* 2011;128:e1181-6.
 15. Menon SC, McCandless RT, Mack GK, Lambert LM, McFadden M, Williams RV, et al. Clinical outcomes and resource use for infants with hypoplastic left heart syndrome during bidirectional Glenn: summary from the Joint Council for Congenital Heart Disease National Pediatric Cardiology Quality Improvement Collaborative Registry. *Pediatr Cardiol.* 2013;34:143-8.
 16. Gaynor JW, Bridges ND, Cohen MI, Mahle WT, Decamp WM, Steven JM, et al. Predictors of outcome after the Fontan operation: is hypoplastic left heart syndrome still a risk factor? *J Thorac Cardiovasc Surg.* 2002;123:237-45.
 17. Rogers LS, Glatz AC, Ravishankar C, Spray TL, Nicolson SC, Rychik J, et al. 18 years of the Fontan operation at a single institution: results from 771 consecutive patients. *J Am Coll Cardiol.* 2012;60:1018-25.
 18. Iyengar AJ, Konstantinov IE, Brizard CP, d’Udekem Y. Unreliable associations between type of Fontan and early outcome? *Ann Thorac Surg.* 2013;95:774-5.
 19. Alexi-Meskishvili V, Ovrouski S, Ewert P, Dähnert I, Berger F, Lange PE, et al. Optimal conduit size for extracardiac Fontan operation. *Eur J Cardiothorac Surg.* 2000;18:690-5.
 20. Itatani K, Miyaji K, Tomoyasu T, Nakahata Y, Ohara K, Takamoto S, et al. Optimal conduit size of the extracardiac Fontan operation based on energy loss and flow stagnation. *Ann Thorac Surg.* 2009;88:565-72; discussion 572-3.
 21. Shiraishi S, Yagihara T, Kagisaki K, Hagino I, Ohuchi H, Kobayashi J, et al. Impact of age at Fontan completion on postoperative hemodynamics and long-term aerobic exercise capacity in patients with dominant left ventricle. *Ann Thorac Surg.* 2009;87:555-60; discussion 560-1.
 22. Driscoll DJ, Offord KP, Feldt RH, Schaff HV, Puga FJ, Danielson GK. Five- to fifteen-year follow-up after Fontan operation. *Circulation.* 1992;85:469-96.
 23. Gentles TL, Mayer JE Jr, Gauvreau K, Newburger JW, Lock JE, Kupferschmid JP, et al. Fontan operation in five hundred consecutive patients: factors influencing early and late outcome. *J Thorac Cardiovasc Surg.* 1997;114:376-91.
 24. Kerendi F, Kramer ZB, Mahle WT, Kogon BE, Kanter KR, Kirshbom PM. Peri-operative risks and outcomes of atrioventricular valve surgery in conjunction with Fontan procedure. *Ann Thorac Surg.* 2009;87:1484-8; discussion 1488-9.
 25. Tan AM, Iyengar AJ, Donath S, Bullock AM, Wheaton G, Grigg L, et al. Fontan completion rate and outcomes after bidirectional cavo-pulmonary shunt. *Eur J Cardiothorac Surg.* 2010;38:59-65.

APPENDIX TABLE 1. Participating Institutions

Victoria	New South Wales	Queensland	South Australia	Western Australia	New Zealand
The Royal Melbourne Hospital	The Children’s Hospital, Westmead	Prince Charles Hospital	The Women’s and Children’s Hospital	Princess Margaret Hospital	Starship Children’s Hospital
The Royal Children’s Hospital	Sydney Children’s Hospital	Mater Children’s Hospital	Royal Adelaide Hospital	Royal Perth Hospital	
Monash Medical Centre	The Royal Prince Alfred Hospital				

APPENDIX TABLE 2. Variables collected

Patient characteristics

Demographic characteristics

Sex

Age (grouped <4, 4 to 5, 5 to 8, ≥8)

Year of Fontan (grouped: 1975-1990, 1991-2000, 2001-2010)

Diagnosis

Tricuspid atresia

Hypoplastic left heart syndrome

Double outlet right ventricle

Complete atrioventricular canal

Transposition of the great arteries

Congenitally corrected transposition

Double inlet left ventricle

Pulmonary atresia with intact ventricular septum

Complete atrioventricular canal with double outlet right ventricle

Other

Morphology

Dextrocardia or mesocardia

Presence of common atrioventricular valve

Ventricular morphology (grouped: left, right, indeterminate, biventricular)

Previous surgery

Pulmonary artery band

Aortic arch procedure (including Damus, Norwood, or arch reconstruction)

Pulmonary artery reconstruction before or at time of Fontan

Atrioventricular valve repair before or at time of Fontan

Bidirectional cavopulmonary shunt (grouped: unilateral, bilateral, Kawashima, hemi-Fontan)

Preoperative hemodynamics

Mean pulmonary arterial pressure

Arterial oxygen saturation

Atrioventricular valve regurgitation (graded moderate or greater)

Operative characteristics

Type of Fontan

Atriopulmonary

Lateral tunnel

Extracardiac conduit

Procedure related

Presence of fenestration

Concomitant procedures

Postoperative course

Mortality during initial hospital stay or within 30 d

Length of stay (prolonged if >30 d)

Mechanical circulatory support (ECMO or VAD)

Major reoperation (including takedown, revision, or permanent pacemaker)

Effusions requiring reoperation or prolonging hospital stay >30 d

ECMO, Extracorporeal membrane oxygenation; VAD, ventricular assist device.