ORIGINAL RESEARCH

Reintervention and survival in 1428 patients in the Australian and New Zealand Fontan Registry

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ABSTRACT

Objective Patients undergoing single-ventricle palliation have experienced significant improvement in survival in the recent era. However, a substantial proportion of these patients undergo reoperations. We performed a review of the Australia and New Zealand (ANZ) Fontan Registry to determine the overall reintervention and reoperative burden in these patients.

Methods A retrospective longitudinal cohort study was performed using data from patients who underwent a Fontan operation between 1975 and 2016 from the ANZ Fontan Registry. The data obtained included Fontan operation, reinterventions and most recent follow-up status. We examined the type and timing of reinterventions and survival.

Results Of the 1428 patients identified, 435 (30%) underwent at least one reintervention after the Fontan operation: 110 patients underwent early reintervention and 413 underwent late reinterventions. Excluding Fontan conversion and transplantation, 220 patients underwent at least one interventional procedure and 209 patients underwent at least one reoperation. Fenestration closure and pacemaker-related procedures were the most common catheter and surgical interventions, respectively. The cumulative incidence of reintervention following Fontan was 23%, 37% and 55% at 10, 20 and 30 years, respectively. Survival and freedom from failure were worse in patients requiring later reintervention after Fontan surgery (51% vs 83% and 42% vs 69%, respectively at 30 years, p<0.001). This difference persisted after excluding pacemaker-related procedures (p<0.001). Operative mortality for non-pacemaker late reoperations after Fontan was 6%.

Conclusions A substantial proportion of Fontan patients require further intervention to maintain effective single-ventricle circulation. Patients undergoing reoperation after Fontan have higher rates of mortality and failure, despite intervention.

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INTRODUCTION

The Fontan procedure is often described as the last in a series of procedures performed for single ventricle palliation. As this growing population ages, it is increasingly being recognised that this population will require intensive follow-up and numerous interventional catheterisation procedures and repeated cardiac surgery procedures.[1–3] However, the incidence of these reinterventions, their nature and, more importantly, their consequences are still unclear. As our population of patients with a Fontan circulation increases, we are more frequently faced with the decisions to reintervene or abstain from further intervention. These decisions are especially challenging because we do not know the risks of these procedures and their potential benefits in patients who seem only mildly affected by the identified issues.

In an initial attempt to better circumscribe the indications of reinterventions in patients with a Fontan circulation, we decided to study the rate of interventions of patients in the Australia and New Zealand (ANZ) Fontan Registry and their relative outcomes.

METHODS

The ANZ Fontan Registry collects health data of all patients who have survived hospital discharge after a Fontan procedure and are living in the two countries. The design of the ANZ Fontan registry have been previously described.[4] Under this design, ongoing approval for study of the retrospective data contained in the registry is maintained with patient consent. Patient demographics, operative and reoperative details and follow-up data were collected from the registry, with a special focus on reintervention.

A total of 1524 patients were identified to have undergone a Fontan procedure between 3 June 1975 and 14 November 2016. Ninety-six patients were excluded because of lack of follow-up data or missing information. The remaining 1428 patients comprised 435 patients who underwent at least one cardiothoracic reintervention and 993 patients who did not undergo a reintervention during the follow-up period.

The atriopulmonary Fontan was performed in early era, then lateral tunnel until 1996, after which the extracardiac conduit (ECC) has been performed almost exclusively across the ANZ centres.

Definitions

Early mortality after reintervention included mortality prior to hospital discharge or within 30 days of the procedure.

Late mortality included mortality >30 days after the procedure and after hospital discharge.

Early reinterventions included surgical or interventional procedures that occurred within 30 days of the Fontan operation or prior to initial hospital discharge. Minor reinterventions involving clot

evacuation, sternal wound or drains were excluded from the analysis.

Late reinterventions were those occurring after the first 30 days or after hospital discharge.

Fontan failure was defined as death, transplantation, take-down or the recorded presence of protein losing enteropathy, plastic bronchitis or New York Heart Association class III/IV at latest follow-up. If multiple failure events occurred, the time of failure was noted as the first event to occur after the most recent reoperation.

Statistical analysis

Analyses were performed in Stata V.14 (StataCorp, College Station, Texas, USA) and R V.3.5.1 software (R Foundation, Vienna, Austria, http://www.r-project.org).

Values are given as median (range), unless otherwise stated. Statistical significance was defined as $p<0.05$.

After initial description, transplantation and Fontan conversion procedures (including associated Cox-Maze/cryoablation) were excluded from main analysis because their outcomes were perceived to be dependent on their underlying conditions or on the specific risks of these interventions, rather than having a reintervention to improve their circulation. Additionally, all procedures after transplantation were also excluded from analysis. Other concurrent procedures were maintained in the analysis.

Time zero was measured as time of the Fontan completion. Time-to-event end points were analysed using the Kaplan-Meier method or the cumulative incidence curve, with death treated as the competing risk with the R packages 'survival' and 'cmprsk'. The extended Kaplan-Meier method was used to illustrate the effect of a late reintervention and late surgical reintervention, which were treated as time-varying covariates.[5] The likelihood ratio test was used to test the association between time-to-event endpoints with late reintervention and late surgical reintervention.

RESULTS

Four hundred and thirty-five of the 1428 survivors of Fontan procedure underwent a cardiothoracic reintervention (30%). One hundred and ten patients underwent a total of 149 early reinterventions during hospital stay or within 30 days of Fontan (table 1). Four hundred and thirteen patients underwent 774 late reinterventions at a median of 4.2 years (range: 30 days–33 years) following the Fontan procedure. Thirty-one patients underwent transplantation during the follow-up period. Of these patients, 20 underwent at least one separate intervention prior to transplantation. Median time to transplantation was 8 years (range 3 months–33 years). Forty-nine patients underwent Fontan conversion to ECC at a median time of 18 years (range 5–29 years) after Fontan. Ten of these patients underwent at least one separate intervention prior to conversion and 42 underwent a concomitant procedure at the time of the conversion. Although the exact criteria for Fontan conversion varies between centres, there has been a trend towards early conversion given their improved outcomes.[6]

Late reinterventions excluding transplantation and conversion

Patient demographics are listed in table 2. Three hundred and ninety-four patients underwent a total of 645 procedures. Of the 394 patients, 144 underwent more than one procedure. Eighty patients had 2 procedures, 41 patients had 3, 12 patients had 4 and 11 patients had 5 or more procedures. The list of catheter

Table 1 Early interventions following Fontan operation

Catheter-based interventions	N
Coiling of aortopulmonary or venovenous collaterals	13
Fenestration enlargement	6
Fenestration occlusion	3
Balloon dilation and stenting of LPA	2
Surgical-based interventions	
PPM insertion/revision	38
Pleurodesis	25
Fontan circuit revision	15
Fenestration creation/enlargement	11
Pulmonary artery reconstruction	3
AV valve repair	2
AV valve re-closure following patch dehiscence	2
Ligation of anomalous vein	2
Diaphragm plication	2
Atrial septectomy	1
VSD enlargement	1
PDA ligation	1
Pericardial window	1
Fontan circuit clot evacuation	1
RMBT shunt takedown	1
Damus-Kaye-Stansel shunt	1
Other	18

AV, atrioventricular; LPA, left pulmonary artery; PDA, patent ductus arteriosus; PPM, permanent pacemaker; RMBT, right modified Blalock-Taussig; VSD, ventricular septal defect.

reinterventions and surgical reoperations and their respective early and late mortality is given in tables 3 and 4. The cumulative incidence of late reinterventions (other than transplantation and conversion) 10, 20 and 30 years after Fontan were respectively 23% (95% CI 20% to 25%), 37% (95% CI 33% to 40%) and 55% (95% CI 47% to 60%) (figure 1).

Survival and freedom from failure

Survival of patients undergoing any *late reintervention* (excluding transplantation and conversion) was lower than the survival of patients avoiding late reinterventions and were respectively at 10 and 30 years: 73% (95% CI 61% to 87%) vs 96% (95% CI 95% to 98%) and 51% (95% CI 40% to 64%) vs 83% (95% CI 76% to 90%) ($p<0.001$) (figure 2). The rate of Fontan failure was 64% (95% CI 53% to 77%) vs 94% (95% CI 92% to 95%) and 42% (95% CI 33% to 53%) vs 69% (95% CI 60% to 79%) at 10 and 30 years, respectively, and was worse in those having a reintervention ($p<0.001$) (figure 3).

Survival and freedom from Fontan failure of patients undergoing *late surgical reoperation* were also lower than for patients avoiding late surgical reintervention. Survival respectively at 10 and 30 years: 62% (95% CI 49% to 80%) vs 97% (95% CI 96% to 98%) and 41% (95% CI 30% to 56%) vs 82% (95% CI 76% to 89%) (figure 4). The rate of freedom from Fontan failure was respectively at 10 and 30 years: 52% (95% CI 40% to 68%) vs 93% (95% CI 92% to 95%) and 31% (95% CI 22% to 43%) vs 70% (95% CI 62% to 78%) ($p<0.001$) (figure 5). The difference in mortality was mainly related to a lower survival percentage in patients requiring reintervention soon after Fontan completion. Thirteen of the 39 patients who required reoperation within 1 year of the Fontan procedure died during follow-up. Three of these were operative mortalities, and the median time to death in

Table 2 Patient demographics

	Overall, n (%) or median (IQR) (n=1428)	Patients avoiding late reintervention, n (%) or median (IQR) (n=1034)	Patients undergoing late reintervention, n (%) or median (IQR) (n=394)	P value
Female sex	611 (43)	432 (42)	179 (45)	0.213
Age at Fontan, years	4.6 (1.1–27.5)	4.7 (1.5–26.5)	4.4 (1.3–21.3)	0.256
Heterotaxy/isomerism	102 (7)	73 (7)	29 (7)	0.984
Non-cardiac abnormalities/syndrome	174 (12)	127 (12)	47 (12)	0.579
Dominant LV	832 (58)	602 (58)	230 (58)	0.958
Preoperative AVVR ≥moderate (n=1090)	104 (7)	70 (7)	34 (9)	0.514
Preoperative mean PA pressure, mm Hg (n=1018)	11 (5–25)	11.4 (5–22)	12.2 (6–22)	**0.0238**
Fontan type				
Atriopulmonary	218 (15)	116 (11)	102 (26)	**<0.001**
Lateral tunnel	277 (19)	179 (17)	98 (25)	**0.001**
ECC	926 (65)	735 (71)	191 (48)	**<0.001**
Fenestration	523 (37)	340 (24)	183 (46)	**<0.001**
Cardiopulmonary bypass time, min (n=806)	105 (35–361)	101 (41–298)	113 (49–311)	**<0.001**
Aortic cross-clamp, min (n=680)	29 (0–168)	26 (0–136)	43 (0–168)	**<0.001**

Bold values represents statistically significant results.
AVVR, atrioventricular valve regurgitation; ECC, extracardiac conduit; LV, left ventricle; PA, pulmonary artery.

these patients was 1.4 years (range: 0.3– 27 years) from the time of the Fontan procedure.

Specific reoperations

Fontan takedown

Eleven patients underwent a Fontan takedown at median of 1.1 years (2 months–2.6 years) after Fontan completion. Two of these patients were converted to biventricular circulation 9 and 14 years post-Fontan. At latest follow-up, six of the nine patients converted to BCPS had died. Both patients converted to biventricular circulation are alive at latest follow-up.

Left outflow tract obstruction

Thirty patients suffered from intracardiac obstruction which necessitated a Damus-Kaye-Stansel (DKS) procedure (10 patients), a VSD enlargement (6 patients), a bulbo-ventricular enlargement (3 patients) and a subaortic stenosis resection (15 patients). With the exception of subaortic stenosis resection, most of these procedures were performed in the early era of the study with only one patient undergoing a DKS procedure with VSD augmentation since 2005. Survival in these patients was 96% (95% CI 78% to 100%) and 89% (95% CI 70% to 96%) at 10 and 20 years post-Fontan, respectively. Freedom from failure was 93% (95% CI 76% to 98%) and 86% (95% CI 67% to 95%) at 10 and 20 years post-Fontan, respectively.

Valve repair/replacement

Twenty-nine patients underwent a total of 33 valve operations post-Fontan with a survival of 85% (95% CI 65% to 94%) and 75% (95% CI 51% to 88%) at 10 and 20 years post-Fontan, respectively. Freedom from failure was 82% (95% CI 62% to 92%) and 63% (95% CI 40% to 79%) at 10 and 20 years post-Fontan respectively.

Pacemaker-related reoperation

Forty-six patients underwent a single pacemaker-related reoperation, and 17 patients underwent multiple pacemaker-related reoperations, in the absence of other procedures. Patients who underwent pacemaker-related surgery had similar survival but higher freedom from failure than the remaining patients

Table 3 Catheter-based late reinterventions (total: 220 patients)

Catheter-based reintervention	Number of procedures	Median time to intervention (range)	Early mortality, n (%)	Late mortality	Failure at latest follow-up
Fenestration closure	132	1.7 y (1 m–23 y)	0 (0)	5	12
Catheter-based ablation of arrhythmia	54	20 y (3 y–31 y)	1 (2)	2	5
Balloon dilation and stenting of PAs	41	2.7 y (3 m–19 y)	0 (0)	1	3
Coiling of collaterals	32	2.8 y(1 m–18 y)	0 (0)	3	5
Other					
Device occlusion of left or right SVC	4	2.6, 3.8 13.2 and 14.3 y	0	0	0
Distal aortic arch stent	3	3.3, 8.2 and 9.1 y	0	0	0
Stenting of Fontan conduit	2	3.8 and 10.5 y	0	0	0
Device occlusion of MPA	1	0.2 y	0	0	0
Stenting of LAD	1	12.9 y	0	0	0
Device occlusion of ASD	1	4.3 y	0	0	0
Balloon dilation of Damus-Kaye-Stansel anastamosis	1	2.0 y	0	0	0

ASD, atrial septal defect; LAD, left anterior descending; m, month; MPA, main pulmonary artery; PA, pulmonary artery; SVC, superior vena cava; y, year.

Table 4 Late reoperations (209 patients)

Late reoperation	Number of procedures	Median time to intervention (range)	Early mortality, N (%)	Late mortality, n	Failure at latest follow-up	Survival after Fontan (95% CI)		
						10 years	20 years	30 years
Pacemaker-related procedure	176	8.2 y (3.5 y–18 y)	4 (2)	22	41	94% (88% to 97%)	84% (76% to 90%)	70% (57% to 80%)
AV valve repair	18	4.1 y (2.2 y–14 y)	0 (0)	6	8	81% (52% to 94%)	63% (30% to 83%)	N/A
SAS resection	16	12 y (3.6 y–16 y)	1 (6)	1	3	93% (59% to 99%)	86% (54% to 96%)	N/A
PA reconstruction	15	5.2 y (1.6 y–14 y)	1 (7)	1	6	91% (51% to 99%)	99% (51% to 99%)	N/A
Fontan circuit revision	15	3.2 y (1.6 y–11 y)	1 (7)	5	8	75% (41% to 91%)	75% (41% to 91%)	N/A
Pleurodesis	13	2 m (1 m–1.6 y)	0 (0)	1	3	81% (43% to 95%)	N/A	N/A
Fontan takedown	11	1.2 y (5 m–2.6 y)	4 (36)	2	N/A	50% (19% to 76%)	N/A	N/A
AV valve replacement	10	1.2 y (8 m–18 y)	1 (10)	2	6	90% (47% to 99%)	77% (34% to 94%)	N/A
Damus-Kaye-Stansel procedure	10	5.5 y (3.3y–6.8 y)	0 (0)	1	1	100%	89% (43% to 98%)	N/A
Fenestration creation/enlargement	8	1.4 y (5 m–7 y)	1 (13)	0	4	87% (36% to 98%)	87% (36% to 98%)	N/A
Other procedures								
Aortic repair (root, ascending, arch)	12	6.7 y (4.6 y–9.3 y)	0 (0)	0	0			
Venous ligation (left SVC, proximal coronary sinus, HV-LA fistula, anomalous hemiazygous, unspecified)	9	3.2y (2.8 y–13.3 y)	0 (0)	1	3			
AV valve closure/re-closure	7	2.2 y (9 m–3.1 y)	0 (0)	1	2			
VSD enlargement	6	2.9 y (3 m–5.9 y)	0 (0)	1	1			
RA reduction/exclusion	4	12.0 y, 14.1 y, 16.0 y, 19.6 y	0 (0)	1	1			
Bulboventricular foramen enlargement	3	2.9 y, 3.5 y and 12 y	0 (0)	0	0			
Semilunar valve replacement	3	3.3 y, 3.6 y and 5.9 y	0 (0)	0	1			
Semilunar valve repair	2	2.8 y and 6.6 y	0 (0)	0	0			
Diaphragm plication	2	1.0 y and 2.2 y	0 (0)	1	0			
Thoracic duct ligation	2	0.5 y, 1.1 y	1 (50)	0	2			
Conversion to lateral tunnel Fontan	2	2.0 y and 4.0 y	0 (0)	0	0			
Other	29	5.2y (1 m–14.7y)	1 (4)	6	12			

AV, atrioventricular; HV-LA, hepatic vein-left atrium; m, month; N/A, not available; RA, right atrium; SAS, subaortic stenosis; SVC, superior vena cava; VSD, ventricular septal defect; y, year.

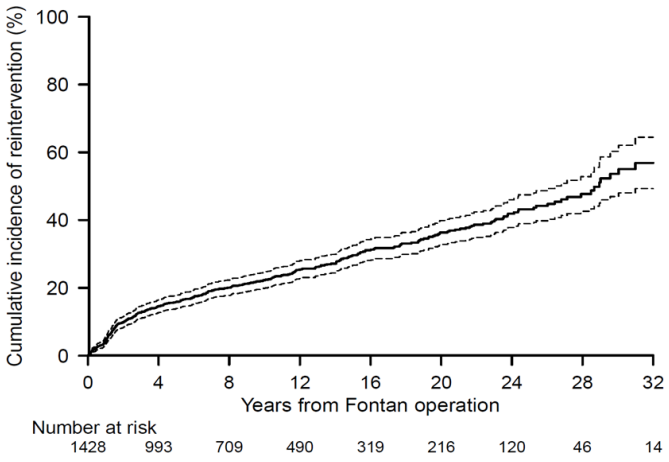

Figure 1 Reinterventions among Fontan patients. Cumulative incidence curve of all cardiothoracic reinterventions (catheter-based and surgical) in Fontan patients (dotted line: 95% CI).

who underwent repeated cardiothoracic surgery (p=0.10 and p=0.002, respectively).

Ninety-two patients undergoing surgical reoperation (106 procedures) *did not require* pacemaker-related procedures. Twenty of these patients died during the follow-up period, of which 7 (7%) were operative mortalities following reoperation.

Of the patients *that did require* pacemaker intervention during follow-up, 60 non-pacemaker-related surgical procedures were performed. Twenty of these patients died during the follow-up period, of which three were operative mortalities.

Overall, operative mortality in patients undergoing reoperation, excluding *isolated* pacemaker procedures, was 6% (10/166).

DISCUSSION

The Fontan procedure is thought to be the last major physiological change brought by surgery to the univentricular heart circulation but it may not be the last cardiac intervention performed in these patients. In the follow-up of the patients enrolled in the ANZ Fontan Registry, half the of patients required an additional intervention by 30 years. There are only scarce data on rate of

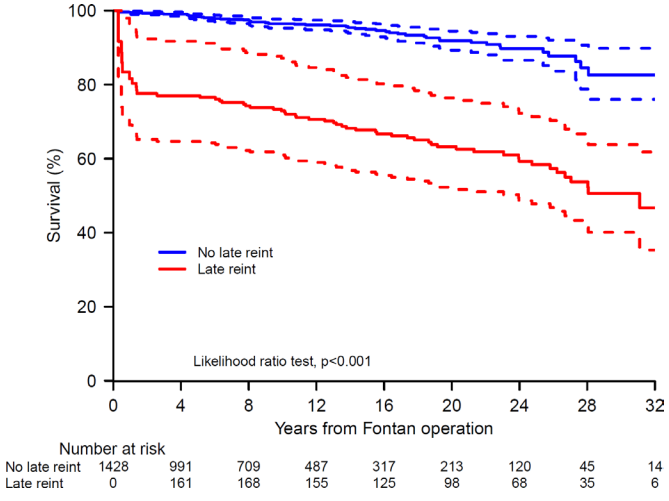

Figure 2 Survival of patients requiring late reinterventions (surgical and interventional) vs no reintervention. Time varying-covariate Kaplan-Meier curve for estimated survival in patients requiring late reintervention (red, dotted line: 95% CI) and patients avoiding late reintervention (blue, dotted line: 95% CI) (p<0.001).

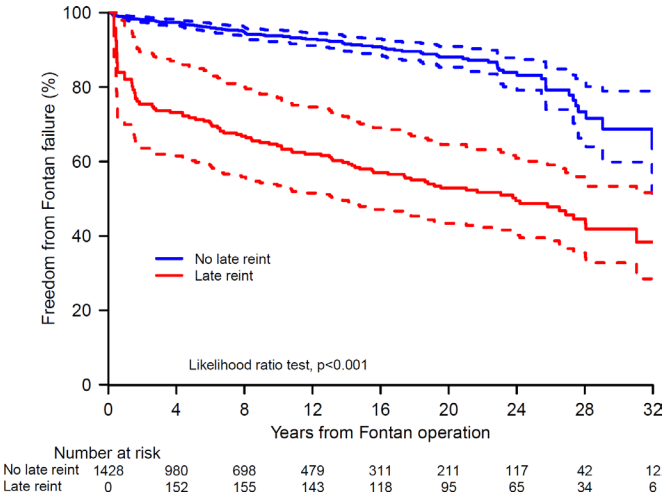

Figure 3 Overall failure comparison of late reintervention (surgical and intervention) vs no reintervention. Time varying-covariate Kaplan-Meier curve for estimated freedom from Fontan failure in patients requiring late reintervention (red, dotted line: 95% CI) and patients avoiding late reintervention (blue, dotted line: 95% CI) (p<0.001).

reintervention after Fontan in contemporary cohorts. Our data are comparable to the rate of 31% surgical and 47% catheter-based reinterventions observed in the series of Philadelphia at 15 years, and 28% surgical and 57% catheter reinterventions occurring over a 15-year study period in the repeated cross-sectional study of the Paediatric Heart Network study.[3 7] Fifteen per cent (214/1428) of our patients required a catheter-based intervention. Fenestration closure constituted the largest proportion of these catheter-based interventions. Delayed fenestration closure has become an integral part of Fontan surgery in many centres.[8 9] The arrhythmic load of this population increases as they age and it is no surprise that a total of 122 patients needed a pacemaker implantation and 47 an ablation procedure.[10 11] Ablation procedures have been shown to be successful in this population, but often requires multiple reinterventions.[11 12] There is little doubt that the need for these anti-arrhythmic procedures will no doubt increase in the future.

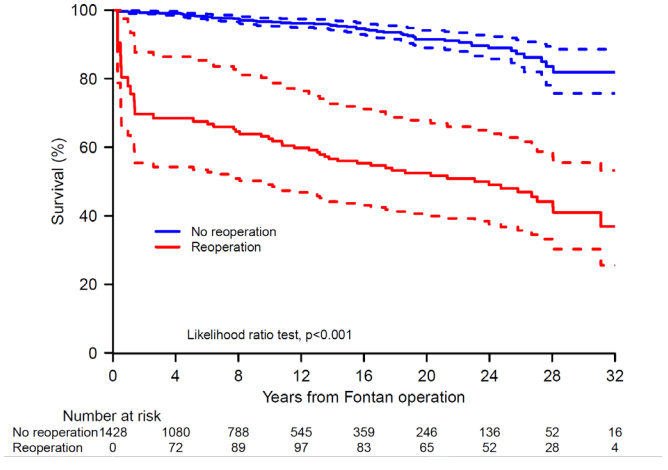

Figure 4 Overall survival comparison of late reoperations vs no reoperations. Time varying-covariate Kaplan-Meier curve for estimated survival failure in patients requiring late reoperation (red, dotted line: 95% CI) and patients avoiding late reoperation (blue, dotted line: 95% CI) (p<0.001).

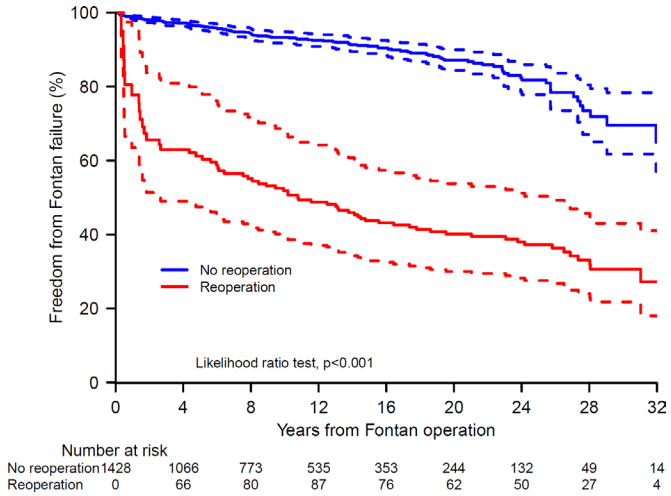

Figure 5 Overall failure comparison of late reoperations vs no reoperations. Time varying-covariate Kaplan-Meier curve for estimated freedom from Fontan failure in patients requiring late reoperation (red, dotted line: 95% CI) and patients avoiding late reoperation (blue, dotted line: 95% CI) (p<0.001).

By 20 years, 37% of our patients required repeated cardiothoracic intervention, which compares well with 31% of the patients requiring surgery by 15 years in the Philadelphia series.[3] As this population grows, and our understanding of their physiology increases, we are prone to perform more in-depth regular investigations during their follow-up.[2 13] It is likely that in the future, we will depict a higher proportion of anatomical issues and that the rate of reoperation will subsequently increase.

Apart from Fontan takedown, the early mortality of these redo surgeries was reassuring low for such complex surgeries. Our patients who necessitated repeated surgery had worse late survival and higher rate of Fontan failure than those who did not, but the difference observed was related to a higher mortality rate following interventions soon after Fontan completion. Most of the deaths and failure events marking the difference between these two groups occurred within the first 2 years following the Fontan operation. This probably eludes to problems that were present before the Fontan operation or technical issues at the time of Fontan operation. Interestingly, the slope of survival and Fontan failure seemed quite similar beyond this period. Patients requiring a reoperation were without doubt sicker than those who had no reoperation, especially those operated early after Fontan. The fact that only a relatively small difference in survival and failure rate was observed for those operated late is likely sign that elective repeated surgery can be achieved with relative safety and provide lasting results.

The closer examination of the reasons for reoperations and their relative outcomes provide us with some insights. Our analyses suggest that outcomes of patients who undergo pacemaker procedures are not very different than outcomes of those undergoing more extensive procedures. The poor prognosis of patients with single ventricle requiring long-term pacing has been recently highlighted.[14–16] Some operations, considered as historical as they are only rarely performed nowadays such as DKS procedures, VSD and bulbo-foramen enlargement and resection of subaortic stenosis, are operations that provide long-lasting results with acceptable risks.[17 18] The benefit of reoperation should be weighed against the risk of reoperation which varies between individual centres and is patient-specific. Our data seem to point to the fact that benefits may be achieved in reoperation if we are able to decrease the risk of mortality. Earlier reintervention to decrease mortality should be explored.

A surprisingly low number of reinterventions were performed to optimise the Fontan circuit: only 17 patients had an intervention on the Fontan conduit (15 surgeries) and 40 patients on the pulmonary arteries (15 surgeries) counting for <2% and 3%, respectively of our entire population of Fontan. In the Philadelphia cohort (773 patients), there were 31 Fontan conduit revisions (19 surgeries) and 84 pulmonary artery interventions (5 surgeries), a considerably higher proportion of patients than in our cohort.[3] The presence of unrestricted laminar flow in the Fontan circuit has been accepted as one of the predominant factors determining outcome after Fontan surgery and one could suspect that optimisation of this circuit by surgery and stenting may benefit patients.[19 20]

The requirement for aortic arch repair and valve repair/replacement is likely to increase in these patients, in particular atrio-ventricular valve surgery. We have previously demonstrated that there seems to be a constant rate of failure of common atrioventricular valves in the decades following Fontan, but that these patients are rarely offered surgery.[21 22] The poor late survival of these patients shows that much progress is needed in this specific field. Gathering outcome data on larger datasets will allow us to better specify the ideal timing for intervention in these patients.

Limitations

Our study limitations include those inherent to retrospective longitudinal cohort studies. The Fontan procedure is performed on an array of single-ventricle pathologies, as well as some complex biventricular pathologies, with varying prognoses. Specific indications, as well as outcomes, for reinterventions after Fontan could sometimes be considered a reflection of the underlying pathology, rendering a generalised comparison difficult to interpret.

Key questions

What is already known on this subject?

- As this population ages, it is now realised that a growing proportion of these patients may require reintervention.
- Clinicians do not currently have the information of outcomes allowing them to take these difficult decisions.

What might this study add?

- Our study found that over a third of patients (37%) require a reintervention by 20 years post-Fontan.
- Only a small portion of patients in the Australian and New Zealand Fontan cohort underwent reintervention on the Fontan circuit (1.2%) or pulmonary arteries (2.8%), which is substantially less than other published cohort data.
- Patients undergoing reintervention had worse survival and freedom from failure.

How might this impact on clinical practice?

- Our manuscript highlights that the outcomes of these patients who need reoperation is favourable provided that these reoperations do not occur early after Fontan.
- It also shows that only a fraction of them have reinterventions on their pulmonary arteries and their Fontan circuit and this finding opens new avenues to potentially improve these patients.

Although the cohort includes patients across many institutions and two countries, only patients who are discharged from hospital with a Fontan circulation are included in the registry.

The ANZ Fontan Registry includes a combination of Fontan types (atriopulmonary, lateral tunnel and ECC), which are known to be prognostically different.[23 24] This is the basis of our decision to remove Fontan conversion procedures from the main analysis. Additionally, there is a strong link between era and Fontan type. Since 1996, the ECC type has been performed exclusively throughout the ANZ centres, making era and Fontan-type analyses problematic due to their inevitable association and varying follow-up.

CONCLUSION

In conclusion, the Fontan procedure can no longer be considered the last procedure in single ventricle palliation, as half of our patients needed reintervention by 30 years. As this growing population ages, a larger number of reinterventions will likely be necessary. Patients undergoing reoperation after Fontan have higher rates of mortality and failure, despite intervention. Indications for reinterventions need to be better circumscribed to improve these outcomes.

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REFERENCES

1 Atz AM, Zak V, Mahony L, *et al*. Longitudinal Outcomes of Patients With Single Ventricle After the Fontan Procedure. *J Am Coll Cardiol* 2017;69:2735–44.
2 Schilling C, Dalziel K, Nunn R, *et al*. The Fontan epidemic: population projections from the Australia and New Zealand Fontan registry. *Int J Cardiol* 2016;219:14–19.
3 Downing TE, Allen KY, Goldberg DJ, *et al*. Surgical and Catheter-based reinterventions are common in long-term survivors of the Fontan operation. *Circ Cardiovasc Interv* 2017;10:e004924.
4 Iyengar AJ, Winlaw DS, Galati JC, *et al*. The Australia and New Zealand Fontan registry: description and initial results from the first population-based Fontan registry. *Intern Med J* 2014;44:148–55.
5 Snapinn SM, Jiang Q, Iglewicz B. Illustrating the impact of a time-varying covariate with an extended Kaplan-Meier estimator. *Am Stat* 2005;59:301–7.
6 Poh CL, Cochrane A, Galati JC, *et al*. Ten-Year outcomes of Fontan conversion in Australia and New Zealand demonstrate the superiority of a strategy of early conversion. *Eur J Cardiothorac Surg* 2016;49:530–5. discussion 35.
7 Atz AM, Zak V, Mahony L, *et al*. Survival data and predictors of functional outcome an average of 15 years after the Fontan procedure: the pediatric heart network Fontan cohort. *Congenit Heart Dis* 2015;10:E30–42.
8 Goff DA, Blume ED, Gauvreau K, *et al*. Clinical outcome of fenestrated Fontan patients after closure: the first 10 years. *Circulation* 2000;102:2094–9.
9 Atz AM, Travison TG, McCrindle BW, *et al*. Late status of Fontan patients with persistent surgical fenestration. *J Am Coll Cardiol* 2011;57:2437–43.
10 Carins TA, Shi WY, Iyengar AJ, *et al*. Long-Term outcomes after first-onset arrhythmia in Fontan physiology. *J Thorac Cardiovasc Surg* 2016;152:1355–63.
11 Moore BM, Anderson R, Nisbet AM, *et al*. Ablation of atrial arrhythmias after the Atriopulmonary Fontan procedure: mechanisms of arrhythmia and outcomes. *JACC Clin Electrophysiol* 2018;4:1338–46.
12 Moore JP, Shannon KM, Fish FA, *et al*. Catheter ablation of supraventricular tachyarrhythmia after extracardiac Fontan surgery. *Heart Rhythm* 2016;13:1891–7.
13 Rychik J, Atz AM, Celermajer DS, *et al*. Evaluation and management of the child and adult with Fontan circulation: a scientific statement from the American heart association. *Circulation* 2019:CIR0000000000000696.
14 Williams RV, Travison T, Kaltman JR, *et al*. Comparison of Fontan survivors with and without pacemakers: a report from the pediatric heart network Fontan cross-sectional study. *Congenit Heart Dis* 2013;8:32–9.
15 Bulic A, Zimmerman FJ, Ceresnak SR, *et al*. Ventricular pacing in single ventricles-a bad combination. *Heart Rhythm* 2017;14:853–7.
16 Poh CL, Celermajer DS, Grigg LE, *et al*. Pacemakers are associated with a higher risk of late death and transplantation in the Fontan population. *Int J Cardiol* 2019;282:33–7.
17 Lee MGY, Brizard CP, Galati JC, *et al*. Outcomes of patients born with single-ventricle physiology and aortic arch obstruction: the 26-year Melbourne experience. *J Thorac Cardiovasc Surg* 2014;148:194–201.
18 Shimada M, Hoashi T, Kagisaki K, *et al*. Clinical outcomes of prophylactic Damus-Kaye-Stansel anastomosis concomitant with bidirectional Glenn procedure. *J Thorac Cardiovasc Surg* 2012;143:e1:137–43.
19 Lardo AC, Webber SA, Friehs I, *et al*. Fluid dynamic comparison of intra-atrial and extracardiac total cavopulmonary connections. *J Thorac Cardiovasc Surg* 1999;117:697–704.
20 Whitehead KK, Pekkan K, Kitajima HD, *et al*. Nonlinear power loss during exercise in single-ventricle patients after the Fontan: insights from computational fluid dynamics. *Circulation* 2007;116(11 Suppl):I165–71.
21 King G, Gentles TL, Winlaw DS, *et al*. Common atrioventricular valve failure during single ventricle palliation†. *Eur J Cardiothorac Surg* 2017;51:1037–43.
22 King G, Ayer J, Celermajer D, *et al*. Atrioventricular Valve Failure in Fontan Palliation. *J Am Coll Cardiol* 2019;73:810–22.
23 d'Udekem Y, Iyengar AJ, Galati JC, *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:S32–8.
24 Pundi KN, Johnson JN, Dearani JA, *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.