Results of orthotopic heart transplantation for failed palliation of hypoplastic left heart

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Abstract

OBJECTIVES: Previous studies have indicated that results for orthotopic heart transplantation (OHT) in patients with surgically palliated hypoplastic left heart (HLHS) are worse compared with patients with other forms of congenital heart disease (CHD) or acquired cardio-myopathy (CM) as well as those undergoing primary OHT for HLHS. In light of the decreasing donor pool for transplantation and increasing numbers of palliated HLHS patients with improving survival, we sought to review our results for OHT in surgically palliated HLHS patients and failing Glenn or Fontan circulations.

METHODS: We conducted a single centre, retrospective study of patients undergoing OHT from 2000 to 2011. Patients who were transplanted following any of the three stages of palliation were included. Indications for OHT were severe impairment of systemic right ventricular (RV) function with/without significant atrioventricular (AV) valve regurgitation or failure of Fontan physiology. The primary outcome of interest was survival; the secondary outcomes examined were the incidence of post-transplant RV failure and the need for extracorporeal membrane oxygenation (ECMO) support.

RESULTS: A total of 209 patients were transplanted during the study period. Of these, 16 were surgically palliated HLHS patients, 1 following Norwood I, 4 post-Fontan and 11 post-Glenn. Thirty-one patients had non-HLHS CHD and 154 patients had forms of acquired CM. Preoperative patient characteristics including age, weight and donor/recipient weight ratio were similar across groups, though the incidence of pulmonary hypertension (PHT) was higher in the CM group. Thirty-day survival was 100% in the palliated HLHS patients (vs 98.1% for the CM group), with 1- and 5-year Kaplan–Meier survivals of 100 and 87.5% (P = 0.393 vs CM; log-rank test). Intensive care unit stay was comparable with transplanted CM patients as was the incidence of RV failure and ECMO post-OHT.

CONCLUSIONS: Our results suggest that good early and mid-term outcomes following OHT in surgically palliated HLHS are achievable. These findings have implications for the optimal strategy and timing for managing palliated patients with HLHS as well as for counseling parents and affected children.

Keywords: Heart transplant • Hypoplastic left heart • Survival • Surgical palliation

INTRODUCTION

Hypoplastic left heart syndrome (HLHS) remains a complex and challenging condition that accounts for 7–9% of congenital heart disease (CHD) [1]. Recent studies suggest that there is a changing trend in the surgical management of these patients, with decreasing numbers of patients being offered primary transplantation and increasing numbers of patients following the Fontan pathway [2]. Although the results for staged surgical palliation have improved greatly in recent years, a number of patients come forward for rescue transplantation for interstage failure or Fontan failure [3–5]. Although some studies have reported acceptable results for orthotopic heart transplantation (OHT) for failed surgical palliation of HLHS, these have included small numbers of patients across more than one decade or have been multi-institutional [6–9] and suggest that the results for secondary OHT are worse compared with primary transplantation and further, less favourable than OHT for other complex CHD [9]. Potential reasons for this are the higher incidence of pre-operative sensitization, more complex surgical procedures often involving reconstruction of the central pulmonary arteries or the aortic arch, with longer graft ischaemic times and perhaps a higher subsequent incidence of primary graft failure.

In addition, patients with Fontan circulations (both HLHS and non-HLHS) have been found to have a poorer survival rate post-OHT, partly related to being in poorer condition prior to surgery with protein-losing enteropathy (PLE) and an increased
related occurrence of postoperative bleeding and infection [5, 6]. It is also possible that some HLHS patients transplanted with prior Fontan or Glenn circulations as reported in other series have had apparently worse outcomes due to unidentified elevated pulmonary vascular resistance (PVR). Haemodynamic catheter measurements can be particularly difficult to accurately interpret in these patients in the presence of low-cardiac output, non-pulsatile flow or collaterals [6]. It is also not clear whether patients with HLHS have better outcomes if they are transplanted following a failing Glenn or failing Fontan. We sought to examine our results for OHT following failed surgical palliation of HLHS and to examine the incidence of right ventricular (RV) failure and need for post-OHT extracorporal membrane oxygenation (ECMO) circulatory assistance.

MATERIALS AND METHODS

Patients

All patients who had received prior surgical palliation for HLHS and undergone OHT between January 2000 and February 2011 were included in the study. Follow-up for all patients was complete. Norwood I palliation had been performed using either a classical modified Blalock-Taussig shunt or the Sano modification using a right ventricle-pulmonary artery (RV-PA) conduit. Subsequent stage II palliation involved the construction of either a right-sided or bilateral bidirectional Glenn anastomosis; stage III Fontan completion was by a total cavopulmonary connection using a lateral tunnel (LT) or extracardiac conduit (EC). Patients transplanted for failing Glenn circulations were those with a poor systemic RV function and cardiac failure. Failing Fontans brought forward for OHT were those with poor RV function or a combination of poor cardiac output with preserved RV systolic function (the latter defined failed Fontan physiology) with PLE/chronic persistent effusions [5].

This study was an extension of our previously registered study [10] which had been registered and approved by the Research & Development Office at the Institute of Child Health, London with ethical approval for the use of retrospective, anonymized data. Follow-up data were obtained from patient records or by interrogation of the patient database (Cardiovascular Information Management System, CVIS, Philips Healthcare UK, Guildford, Surrey, UK). All patients were followed-up at Great Ormond Street Hospital or their local institution within the UK. Additional data concerning donors were obtained from the UK National Health Service Organ Donation & Transplantation Directorate, Bristol, UK. The following preoperative patient data were collected: recipient age, donor/recipient weight ratio, diagnosis, ABO mismatch status, the presence of preoperative pulmonary hypertension (PHT), need for pre-transplant ECMO or ventricular assist device (VAD) support. The policy of our unit is to support patients using ECMO or VAD as a bridge to transplantation where indicated. Intra-operative data collected included: cardiopulmonary bypass (CPB) and total donor ischaemic times. The post-operative need for ECMO or VAD support was also recorded.

In CM patients with biventricular circulations, preoperative PHT was defined as pulmonary vascular resistance index (PVRRI) >6 WU/m² with pulmonary vascular reactivity on haemodynamic testing using 100% fractional inspired oxygen and inhaled nitric oxide. Where catheter data were not available, echocardiographic criteria for elevated PVR were defined according to an estimated RV systolic pressure (RVSP) ≥2/3 systemic pressure as previously reported [10]. The inherent difficulties in accurately identifying PHT in patients with univentricular circulations have been described above. In these patients, we defined PHT by a transpulmonary gradient >15 mmHg. Criteria for post-transplantation RV failure have been defined by our group according to clinical and echocardiography (ECHO) criteria [10]: elevated central venous pressure and RVSP >2/3 systemic on intra-operative invasive pressure monitoring after weaning from CPB; clinical low-cardiac output state; poor RV systolic function on ECHO with significant tricuspid regurgitation and elevated estimated RVSP.

Surgical technique, immunosuppression and graft surveillance

Donor cardiectomy was performed by harvesting extended segments of systemic veins where possible as well as pulmonary arteries and the aorta to facilitate surgical reconstruction during OHT. Bicaval anastomosis was performed for all patients. In cases with a recipient left superior vena cava (SVC), this was anastomosed to the donor innominate vein. All patients with Glenn or Fontan circulations required reconstruction of the central pulmonary arteries before the onset of warm ischaemia. While an abnormal cardiac position may make OHT more technically challenging, none of the HLHS patients in our series had meso- or dextrocardia. Further, 2/4 of our patients with heterotaxy had bilateral SVCs and the two patients with right atrial isomerism (RAI) (Table 1) both had previous repair for total anomalous pulmonary venous connection (TAPVC), meaning that the cuffed of the atrium to be anastomosed to the donor left atrial (LA) cuff had been carefully trimmed to incorporate the site of the previous TAPVC repair.

Despite the use of the previous homograft tissue in all patients for aortic arch reconstruction during the Norwood I procedure, we did not encounter particular technical difficulties at the time of transplantation. Only mild calcification of the homograft patch was noted in some cases. In cases with a high degree of collateral flow and pulmonary venous (PV) return, transient low-flow CPB with moderate hypothermia was used to facilitate implantation. All patients had an LA vent sited and LA monitoring line at the conclusion of implantation prior to separation from CPB. Where patients had been on preoperative mechanical circulatory support (MCS) up until the time of transplant, this was discontinued at the initiation of CPB. Where post-transplant ECMO was instituted in the operating room, this was established via either central or peripheral cannulation using a neck approach with an additional LA vent. Pre-OHT VAD support utilized the Berlin Heart EXCOR device (Berlin Heart GmbH Inc., Berlin, Germany) in all cases as either isolated LV support (LVAD) or as biventricular (BiVAD) support.

Our current immunosuppression protocol comprises preoperative induction with Basiliximab which targets the T lymphocyte interleukin-2 receptor. For initial and maintenance immunosuppression, steroids and mycophenolate mofetil (MMF) are administered immediately post-transplant, as well as a repeat dose of Basiliximab on day 4. The calcineurin inhibitor tacrolimus is commenced when the patient tolerates feeds. Anti-rejection surveillance comprises serial ECHO and electrocardiograms for all patients.

Statistical analysis

All continuous data are reported as means ± SD or as medians with the stated range. Comparison of means between multiple
groups was performed using the unpaired t-test; comparison of medians was achieved using the Mann–Whitney test. Binomial or ordinal data are expressed as percentages, and comparative univariable analyses performed using the two-sided Fisher’s exact test or χ² test. Kaplan–Meier analysis was used for survival with the log-rank test used to determine significant differences. Univariate Cox proportional hazards regression analysis was performed for candidate risk factors influencing survival. Risk factors were also entered into a multivariable Cox model. In performing the multivariate analysis, all 201 patients were included (i.e. excluding only those 8 patients with either heterotopic transplants or re-transplants). A probability value of <0.05 was taken to represent a statistically significant difference between groups. Analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) version 19 (SPSS Inc., Chicago, IL, USA).

**RESULTS**

**Patient characteristics and intraoperative data**

Over the study period, 209 patients underwent OHT. Of these, 16 had received prior surgical palliation for HLHS (11 bidirectional Glenn or Kawashima; 4 Fontan completion; 1 patient following stage I Norwood palliation). Over the same period, 31 patients with non–HLHS CHD and 154 patients with acquired cardiomyopathy (CM) were transplanted. Two patients undergoing heterotopic transplantation and six patients who were re-transplants were excluded from subsequent analysis; thus all further analysis was performed using the cohort of 201 patients. Of the 16 HLHS patients, 8 were male. Two of sixteen had concomitant double outlet right ventricle (DORV) underlying morphology; 1 patient had corrected partial anomalous pulmonary venous connection (PAPVC); 2 patients had underlying heterotaxy with RAI and TAPVC; 2 patients had LA isomerism (LAI). Three of sixteen patients had an unbalanced complete atrioventricular septal defect (cAVSD) morphologic variant of HLHS; Table 1. One patient with a Glenn circulation had Turner’s syndrome. Fifteen of sixteen HLHS patients undergoing OHT had pre-transplant moderate-severe systemic RV dysfunction with moderate-severe AV valve regurgitation. One patient with prior Fontan completion had preserved systolic RV function though failing Fontan physiology with PLE (Table 1; patient no. 7). Importantly, the PLE in this patient resolved following transplantation.

The median age of patients in the HLHS group was 4.1 years (range: 0.5–17.6 years) and was lower compared with the CM group (Table 2). Median recipient weight for HLHS patients was 13.3 kg (range: 6.7–68.3 kg). Median body surface area (BSA) in HLHS patients was 0.6 m² (range: 0.3–1.9 m²). Median donor/recipient

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at Tx (years)</th>
<th>Sex</th>
<th>BSA (m²)</th>
<th>dwt/rwt ratio</th>
<th>Underlying morphology</th>
<th>Previous operations</th>
<th>Reason for failure</th>
<th>Interval to OHT from last op (months)</th>
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<tr>
<td>1</td>
<td>17.63</td>
<td>M</td>
<td>1.8</td>
<td>1.02</td>
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<td>Fontan</td>
<td>Severe RV dysfunction; moderate TR</td>
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<td>2</td>
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<td>F</td>
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<td>1.83</td>
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<td>Glenn</td>
<td>Severe RV dysfunction; moderate TR</td>
<td>39.7</td>
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<td>1.61</td>
<td>HLHS, LAI, DORV, bilat SVC, azygos continuation IVC</td>
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<tr>
<td>4</td>
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<td>M</td>
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<td>HLHS</td>
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<tr>
<td>5</td>
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<td>M</td>
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<td>Glenn</td>
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<td>34.8</td>
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<td>Glenn</td>
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<td>1.81</td>
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<td>Severe RV dysfunction; moderate TR</td>
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<td>Moderat RV dysfunction; moderate to severe TR</td>
<td>73.2</td>
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<tr>
<td>10</td>
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<td>M</td>
<td>0.49</td>
<td>3.03</td>
<td>HLHS (Turner’s syndrome)</td>
<td>Glenn</td>
<td>Severe RV dysfunction; mild TR</td>
<td>13.2</td>
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<td>1.93</td>
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<td>Glenn</td>
<td>Severe RV dysfunction; mild-moderate TR</td>
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<tr>
<td>12</td>
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<td>Glenn</td>
<td>Severe RV dysfunction; moderate TR</td>
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<td>Glenn</td>
<td>Severe RV dysfunction; severe TR</td>
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<tr>
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<td>3.21</td>
<td>HLHS, unbalanced cAVSD</td>
<td>Fontan; EC; non-fenestrated</td>
<td>RV dysfunction; severe TR</td>
<td>10.3</td>
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<td>Glenn</td>
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<td>16</td>
<td>1.99</td>
<td>M</td>
<td>0.51</td>
<td>1.27</td>
<td>HLHS</td>
<td>Glenn</td>
<td>Severe RV dysfunction; severe TR</td>
<td>18.6</td>
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</tbody>
</table>

HLHS: hypoplastic left heart syndrome; L/R-AI: left/right atrial isomerism; DORV: double outlet right ventricle; TR: tricuspid regurgitation; cAVSD: complete atrioventricular septal defect; P/T-APVC: partial/total anomalous pulmonary venous connection; LT: lateral tunnel; EC: extracardiac; PLE: protein-losing enteropathy; RV: right ventricle; S/I-VC: superior/inferior vena cava; dwt/rwt: donor weight/recipient weight ratio.
weight ratio was 1.85 (r: 1.02–3.21). In this regard, our institution-
al policy is the same for all transplant recipients, irrespective of
underlying pathology, and we apply a positive weight mismatch

Only one patient in the HLHS cohort had an ABO mismatch,
though none of the five HLHS patients who had undergone
cardiac catheterization prior to transplant had preoperative PHT.
No patient with HLHS had received preoperative ECMO or VAD
support. One patient transplanted with a failing Glenn circula-
tion, however, had received 3 days of ECMO support following
the initial Glenn procedure (patient no.16). The median interval
from Glenn to OHT was 32.2 months (r: 9.4–73.2 months) in 11
patients; the median interval from Fontan completion to OHT
was 46.8 months (r: 10.3–95.0 months) in 4 patients (Table 1).

Intra-operatively, almost all HLHS patients required patching
of right and/or left PAs at the site of previous cavopulmonary
connections. In addition, two patients had hypoplastic central
PAs that required more extensive reconstruction using donor PA
tissue. Mean CPB time for HLHS patients was 213.1 ± 76.4 min;
mean total donor ischaemic time was 277.3 ± 95.4 min (Table 2).
The CPB time was significantly shorter in the CM vs the HLHS
group (one-way analysis of variance; P = 0.001; Supplementary
data, Table S5). The donor ischaemic time was similar in the
HLHS and CM patients.

### Thirty-day survival, RV failure, ECMO and VAD support

Thirty-day survival in the HLHS patients was 100%. In compar-
ison, 30-day survival for the CM group was: 151/154 (98.1%).
Median intensive care unit (ICU) length of stay (LoS) in the
HLHS and CM groups was respectively: 7.2 days (r: 3.0–191.3)
and 10.4 days (r: 1.2–234.9 days); Table 3.

In the HLHS group, four patients had early postoperative RV
failure. None of these, however, had preoperative PHT. Two of
sixteen patients required preoperative ECMO support, though
only one of these was in a patient with isolated RV failure. None
of the patients with RV failure had required pre-OHT ECMO or
VAD support. All four patients with RV failure survived. Median
total ischaemic time in the RV failure patients was 302 min
(r: 285–365 min); this was compared with non-RV failure HLHS
patient ischaemic time of 279 min (r: 75–441 min).

In the CM group, 30/154 patients had postoperative RV failure.
In turn, 12/30 patients had preoperative PHT. One of these 12
patients had required pre-OHT LVAD; 2 had been bridged with
preoperative ECMO and 1 required post-OHT ECMO support.
Overall, therefore, there was no significant difference in the inci-
dence of RV failure between groups (χ²; P = 0.802).

### Early and mid-term survival; multivariate regression; Glenn vs Fontan

A cumulative Kaplan–Meier survival analysis showed that the
1- and 5-year survivals for the palliated HLHS patients were 100
and 87.5%, respectively. This compares with 95.4%/88.9% for the
1- and 5-year survivals in the CM group (P = 0.393; log-rank;
Fig. 1). In contrast to the steady attrition of the CM patients over
time only a single patient in the HLHS group had died by
5-years of follow-up. As the numbers of patients within the
HLHS group alone was small, an analysis of risk factors for sur-
vival was performed using Cox proportional hazards multiple re-
gression including all 201 patients (Table 4). Only age emerged
as a statistically significant factor. In the present analysis, it was
not possible to demonstrate any statistically significant differ-
ences in survival between transplanted Glenn vs Fontan patients
as there had been only one death in the latter group.

### DISCUSSION

This study has examined early and mid-term outcomes for
patients with prior surgical palliation of HLHS who have under-
gone OHT. Good 30-day survival of 100% was observed in the
patients, with 100 and 87.5% 1- and 5-year Kaplan–Meier sur-
vival statistic respectively. Further, these results compared fa-
avourite with and were not statistically different, from those of
patients with CM undergoing OHT. Ischaemic times were similar
between HLHS and CM patients, though CPB times were signifi-
cantly longer in the HLHS patients, reflecting the need for addi-
tional dissection time and reconstruction of PAs. The incidence of
post-OHT RV failure was no higher in patients with palliated
HLHS, nor was the requirement for post-OHT ECMO support.
HLHS or acquired CM undergoing orthotopic heart transplantation. Figure 1: Kaplan–Meier survival plots for patients with surgically palliated HLHS or acquired CM undergoing orthotopic heart transplantation.

Survival

We observed a 1- and 5-year Kaplan–Meier survivals in the HLHS patients of 100 and 87.5%, respectively. This was not significantly different from that observed for the CM group. Over a similar 11-year period at our institution, 103 patients underwent Norwood I palliation for HLHS, with 29 patients progressing to Fontan completion. The 1-year Kaplan–Meier survival following Glenn in the HLHS patients was 87.1%; 1-year survival post-Fontan was 95.5% (unpublished observations). Interestingly, we observed a steady attrition in the CM patients, while the initial survival in the HLHS group did not decline markedly until ~5 years. In a recent report of 116 paediatric patients transplanted for CHD, overall Kaplan–Meier 5-year survival was 72.7% [12]. Survival in HLHS patients with prior surgical palliation was worse than for HLHS patients undergoing primary OHT, though this just failed to reach statistical significance. On univariate analysis, risk factors for survival included MCS, longer CPB time and ischaemic time and heterotaxy [12]. In our multivariable regression analysis, only age emerged as being significant, although the number of patients with heterotaxy was small and this factor had not therefore been entered into the model.

Huebler et al. [13] have recently reported their large single institution results for paediatric heart transplantation, although their study incorporated patients from 1986 and only four patients with a diagnosis of HLHS. Furthermore, these investigators found a significant era effect, with far better outcomes in the post-2000 era. We have previously reported similar era effects from our own institution [14]. Our 30-day survival of 100% in the HLHS patients demonstrates that good outcomes for OHT in palliated HLHS patients can be achieved in the modern era. These data compare favourably with the small number of other series in the literature [5, 6, 9]. Further, the ICU LoS for the HLHS patients in our series was not significantly different compared with the CM patients.

Jacobs et al. [8], undertook a single centre study of OHT in failed HLHS palliation patients, though with only seven patients and from 1995 to 2005. The 30-day mortality was 4.34% for primary OHT for HLHS vs 25% for rescue transplantation in palliated HLHS. In a more recent report, the same institution has reported results for OHT in children with CHD and included 116 patients from 1995, though only 9 were rescue transplants in those with palliated HLHS [12]. Overall operative mortality was 12.6%. Survival in HLHS with prior surgical palliation was worse than those with primary OHT, though this just failed to reach statistical significance [12]. Kanter et al. [7], studied outcomes in 417 paediatric patients undergoing OHT from 1985 to 2005. Operative mortality was 13.0% for primary transplantation for HLHS and 11.9% in patients with CHD. These investigators included nine patients with failed surgical palliation of HLHS in the latter group.

Table 4: Multivariate Cox regression analysis for survival (all 201 patients)

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>95.0% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis (HLHS, CM, CHD)</td>
<td>0.949</td>
<td>0.694–1.300</td>
<td>0.746</td>
</tr>
<tr>
<td>CPB time</td>
<td>1.000</td>
<td>0.996–1.004</td>
<td>0.932</td>
</tr>
<tr>
<td>ABO mismatch</td>
<td>0.877</td>
<td>0.098–7.886</td>
<td>0.907</td>
</tr>
<tr>
<td>Weight ratio</td>
<td>0.923</td>
<td>0.530–1.609</td>
<td>0.779</td>
</tr>
<tr>
<td>Age at Tx</td>
<td>1.097</td>
<td>1.006–1.197</td>
<td>0.037</td>
</tr>
<tr>
<td>Sex</td>
<td>1.141</td>
<td>0.508–2.559</td>
<td>0.750</td>
</tr>
<tr>
<td>Ischaemic time</td>
<td>0.999</td>
<td>0.994–1.004</td>
<td>0.604</td>
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<tr>
<td>RV failure</td>
<td>1.349</td>
<td>0.483–3.770</td>
<td>0.568</td>
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<tr>
<td>Preoperative PHT</td>
<td>2.527</td>
<td>0.784–8.148</td>
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*P < 0.05.

OHT post-Glenn vs post-Fontan

It has been suggested that Fontan patients undergoing OHT are at greater risk compared with those with Glenn circulations and that they die sooner. Jayakumar et al. [5] reported outcomes for OHT following the Glenn or Fontan procedure, though a hypoplastic LV was present in only 12/35 patients in their study group. Overall 1-year survival was 71.5% and 5-year survival was 67.5%, though patients were included from 1984 to 2001 and as such reflect outcomes from a prior era [5]. Patients with OHT post-Fontan were found to have worse outcomes compared with Glenn patients, as in our study, though this was not statistically significant. Kanter et al. [6] have examined outcomes for OHT in patients with failing Fontans. The cohort included patients from 1988, with 27 Fontan patients. 1- and 5-year Kaplan–Meier survivals in the Fontan patients were 81.5 and 65.5%, respectively, with a cluster of deaths in the first 6 months after OHT that was not observed in the present study [6]. In this study by Kanter et al., only 2/27 Fontan patients undergoing OHT had a prior preserved ventricular function with PLE [6]. Interestingly, the presence of PLE in itself did not affect overall 1-year survival following OHT and all patients with PLE who survived OHT had a resolution of PLE as in the single patient in our study with PLE who underwent OHT [6]. Although only one patient in the present study had PLE and failure of Fontan physiology with preserved systemic ventricular function, other investigators have reported a significantly worse post-OHT survival in patients with Fontan circulations and PLE, with Jayakumar et al.
One study of outcomes of listing for OHT in paediatric patients <18 years of age with a failed Fontan reviewed 70 transplanted patients across 17 centres [15]. One-year Kaplan–Meier survival was 76%. Importantly, patients who were transplanted <6 months from the time of the Fontan were at higher risk [15]. In our series, none of the Fontan patients had been transplanted within 6 months of the Fontan procedure, although it should be stated that only 4/16 HLHS patients undergoing OHT in our series had prior Fontan circulations. It should be noted that our institution does not currently offer MCS for patients with failing Fontan circulations, although this policy may be reviewed in the future. We treat failing Fontan patients with intensified medical therapy. A small number of reports in the literature do, however, cite the use of MCS in failing Fontan circulations, though with variable outcomes, and this has recently been reviewed [16]. In addition to early survival, a key further outcome of interest is the incidence of RV failure post-OHT.

Post-OHT RV failure and circulatory support

We found a 25% incidence of RV failure in the HLHS patients following OHT that was comparable across groups, although the CM group had a slightly lower incidence of 19.5% ($\chi^2; P = 0.802$). Very few studies have reported on the specific occurrence of RV failure post-OHT in the paediatric population. In their study of 35 patients with Glenn or Fontan circulations who had been transplanted, Jayakumar et al. [5] reported a single death directly attributable to RV failure, representing 10% of deaths within 6 weeks of transplant. Tjang et al. [17] have more recently examined a cohort of 116 paediatric heart transplants from 1989 and reported RV failure as cause of 30-day mortality in 7% of patients. It is not clear as to why the incidence of RV failure is higher in our population. One factor that may be important is the graft ischaemic time, though Tjang et al. [17] certainly report a comparable mean ischaemic time of 212.1 ± 47.6 min, while Jayakumar et al. [5] report a mean ischaemic time of 4.7 ± 1.5 h. Total graft ischaemic times in our study were similar for HLHS and CM patients. One further factor that is likely to play a major role in the incidence of post-OHT RV failure is the presence of preoperative PHT.

In our previous report, we studied the incidence of RV failure in 129 patients from 2000 to 2006 and found a similar 25% incidence of RV failure [10]. Of patients with elevated PVR, 75% progressed to RV failure. Interestingly, elevated PVR, though not an RV failure as such, was associated with a poorer survival. In the present study, none of the HLHS patients with RV failure post-OHT had pre-existing PHT. In the CM group, 40% of those with RV failure had PHT pre-transplant. In one published study, none of the patients with Glenn or Fontan circulations coming forward for transplant had elevated PVR [5]. Importantly, difficulties arise in the interpretation of PVR measurements in patients with Glenn and particularly Fontan circulations in the setting of a low cardiac output, non-pulsatile pulmonary blood flow and presence of collaterals [6]. Indeed, it has been our institutional policy not to routinely catheterize all HLHS patients prior to transplantation. In the last 3 years, newer techniques at our institution, such as magnetic resonance imaging assessment of pulmonary blood flow, are being evaluated to more accurately identify PHT in HLHS patients coming forward for cardiac transplantation. Once RV failure has become established following OHT, however, MCS may be required.

In the present series, post-transplant ECMO was required in 2/16 of the HLHS patients, though only one of these had isolated RV failure following transplant. Both of these patients survived. Tissot et al. have reported on their series of 28 paediatric patients requiring post-OHT ECMO support, with 86% <1 year of age. Twenty three of these patients had CHD and only 5 had CM, out of a total of 310 transplants in the study period [18]. Nineteen of twenty-three CHD patients had variants of HLHS and 6/23 CHD patients had previous corrective or palliative surgery. ECMO was required for isolated RV failure in 56%. There was no significant difference in survival within the CHD groups for HLHS vs non-HLHS. Risk factors for ECMO-supported patients at the time of OHT were lower weight, lower age and greater graft ischaemic time [18]. In our study, the two HLHS patients requiring post-transplant ECMO were 3.6 and 6.8 years of age, though they did have graft ischaemic times markedly longer than the mean ischaemic time for the HLHS group as a whole: 318 and 305 min (vs mean for HLHS group: 240.2 ± 72.4 min).

Study limitations and conclusions

The retrospective, single-centre nature of this study may limit the power of the statistical inferences that may be made. Further, the number of patients with palliated HLHS is small. Importantly, the HLHS patients represent a heterogeneous population of patients and as alluded to above, the evaluation of pre-transplant PVR in patients with single ventricle circulations is likely to be difficult and may perhaps underestimate the number of patients with PHT. Detailed data on morbidity and QoL of the transplanted HLHS patients including functional status, somatic growth and neurodevelopmental and psychological and social well-being have not been analysed and this will be an important area for further study.

Despite these limitations, our results suggest that good outcomes following OHT in surgically palliated HLHS are achievable in the contemporary era, with an incidence of RV failure and post-transplant ECMO support that is similar following OHT for acquired cardiomyopathies. We suggest that re-evaluation of the optimal strategy and timing for managing high-risk Glenn or Fontan candidates may be required in view of these findings and that appropriate and timely assessment and listing for transplantation be performed in those with failing palliated hypoplastic left heart.

SUPPLEMENTARY MATERIAL

Supplementary material is available at EJCTS online.

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