Risk factors for adverse outcome after superior cavopulmonary anastomosis for hypoplastic left heart syndrome

Jan Hinnerk Hansen a,1, Anselm Uebing a,1, Anke K. Furck a, Jens Scheewe b, Olaf Jung a, Gunther Fischer a, Hans-Heiner Kramer a,*

a Department of Congenital Heart Disease and Paediatric Cardiology, University Hospital of Schleswig-Holstein, Campus Kiel, Arnold-Heller-Str.3, Haus 9, 24105 Kiel, Germany
b Department of Thoracic and Cardiovascular Surgery, University Hospital of Schleswig-Holstein, Campus Kiel, Kiel, Germany

Received 22 November 2010; received in revised form 10 February 2011; accepted 16 February 2011

Abstract

Objective: Outcome of staged palliation for hypoplastic left heart syndrome (HLHS) has improved over the past decades. We sought to evaluate the outcome of the second palliative procedure, the superior cavopulmonary anastomosis (SCPA), in a single-centre cohort and to identify risk factors for adverse outcome.

Methods: Full data on all 119 HLHS patients who underwent SCPA in our centre between January 1996 and December 2007 were analysed.

Results: Early adverse outcome (death or cardiac transplant within 30 days after surgery or before hospital discharge) was 3.4%. Late adverse outcome (death or transplant after hospital discharge but before the next operative procedure) was 8.7%. Postoperative complications occurred in 30% of patients (n = 36), with transient arrhythmia (n = 11; 9%) and pulmonary artery stenosis or thrombosis (n = 10; 8%) being the most common. The presence of more than moderate tricuspid valve regurgitation after surgery proved to be a strong predictor of late adverse outcome (odds ratio (OR) 16.5 (4.4—62.6), \( P < 0.001 \)). SCPA at less than 4 months of age did not increase the risk for adverse outcome (OR 1.2 (0.4—3.6), \( P = 0.78 \)) but increased the risk for postoperative complications (OR 6.3 (2.3—14.9), \( P < 0.001 \)).

Conclusions: SCPA can nowadays be performed in HLHS patients with low mortality. However, more than moderate tricuspid valve regurgitation should be targeted at surgery as it is a risk factor for adverse outcome such as death or need for cardiac transplant. SCPA should ideally be performed in children older than 4 months to minimise the risk of postoperative complications.

Keywords: Superior cavopulmonary anastomosis; Outcome; Risk factors; Hypoplastic left heart syndrome

1. Introduction

The three-staged surgical palliation can nowadays be regarded as an established treatment strategy for hypoplastic left heart syndrome (HLHS) [1]. The construction of an anastomosis between the superior vena cava (SVC) and the pulmonary artery (PA) is the second step in this approach and follows the initial Norwood operation. Conversion of the source of pulmonary blood flow from a systemic to PA shunt to a superior cavopulmonary anastomosis (SCPA) reduces systemic right ventricular (RV) volume load [2], and this way allows time for the resolution of RV hypertrophy prior to the Fontan operation [3,4]. Moreover, it improves coronary blood flow [5] and ends the vulnerable time after the Norwood operation with its risk for sudden cardiac death. Although interstage mortality from stage one to stage two has constantly been reduced over the last decade [6], the optimal timing of the second stage palliation for HLHS needs to be defined.

We aimed to identify potential risk factors for adverse early and longer-term outcome of this procedure and paid particular attention to age at operation and the presence and severity of tricuspid regurgitation.

2. Methods

2.1. Patients

The study population consisted of all 119 HLHS patients who underwent SCPA between January 1996 and December 2007 at the Department of Congenital Heart Disease and Paediatric Cardiology, University Hospital Schleswig-Holstein, Kiel, Germany. In this period, a Norwood operation was performed on 157 HLHS patients of whom 123 survived. Three patients were awaiting SCPA at the time of data analysis and one patient underwent cardiac transplantation. The departmental HLHS database was reviewed to assess patient, haemodynamic, echocardiographic, procedural...
and morphologic determinants of outcome. All patients had classic HLHS as defined by the Nomenclature Working Group of the International Society of Nomenclature of Paediatric and Congenital Heart Disease [7]. Informed consent for anonymised data analysis was obtained for all patients. The local research ethics committee approved the study protocol.

2.2. Preoperative cardiac catheterisation

All patients underwent preoperative cardiac catheterisation. From this study the RV end diastolic pressure (RVEDP), central venous pressure (CVP) in the SVC, arterial oxygen saturation (SaO2) and the size of the central PA were collected. To quantify PA size, the Nakata index was calculated as previously described [8].

2.3. Echocardiography

Patients were assigned to distinct anatomic subgroups (mitral and aortic stenosis, MA/AA; mitral atresia and aortic stenosis, MA/AS; mitral stenosis and aortic atresia, MS/AA and mitral and aortic stenosis, MS/AS) based on the echocardiography performed prior to the Norwood operation, as previously described [6].

Data on RV function and tricuspid valve function were taken from the echocardiograms recorded on the day before and 2 weeks after surgery. Experienced investigators performed all echocardiograms. RV function was subjectively assessed from multiview two-dimensional echocardiography and graded as good, mildly, moderately or severely impaired. Tricuspid valve regurgitation was quantified using Doppler echocardiographic techniques. The degree of tricuspid regurgitation was also graded semiquantitatively as previously described by Ohye et al. as absent, mild, mild to moderate, moderate to severe or severe [9]. A corresponding numerical grading from 1 to 5 or 1 to 4 was used for statistical analysis of tricuspid regurgitation and RV function, respectively.

2.4. Surgical technique

All children underwent a modified Norwood operation as an initial palliation. A modified Blalock–Taussig (BT) shunt was used to establish pulmonary perfusion in 117 cases and two patients received an RV to PA conduit. Details on the technique of the initial Norwood operation and the outcome of this procedure have previously been reported in detail [6]. Subsequently, an SCPA using the hemi-Fontan technique described by Bove [10] was established in 114 patients. The remaining five patients received a bidirectional Glenn anastomosis. A bilateral SVC was present in six patients. These patients underwent the hemi-Fontan operation with a bilateral bidirectional SCPA. The SCPA was performed with induction of ventricular fibrillation on cardiopulmonary bypass. Deep hypothermic circulatory arrest (DHCA) was used only when required for associated procedures.

2.5. Postoperative management

Postoperatively, all patients received afterload reduction with sodium nitroprusside and inotropic support with epinephrine and enoximone. Early extubation was aimed for and oral feeding was commenced on the first postoperative day.

The following postoperative data were collected from the database:

1. Mean CVP in the SVC and IVC of the first 24 h in the intensive care unit.
2. Mean arterial SaO2 of the first 24 h in the intensive care unit.
3. Duration and amount of chest tube drainage.
4. Duration of postoperative mechanical ventilation.
5. Use of nitric oxide.

2.6. Outcome measures

According to the definition of the STS Congenital Database Taskforce and the Joint EACTS-STS Congenital Database Committee [11], early adverse outcome of the hemi-Fontan operation was defined as death or cardiac transplantation during the first 30 postoperative days or before discharge from hospital. Death or cardiac transplantation later than 30 days after the operation, if discharged from hospital or after hospital discharge but before completion of the Fontan circulation, was accordingly referred to as late adverse outcome after the procedure. The minimum follow-up period was 2 years (data analysis in January 2010).

Postoperative complications were classified into PA complications (PA thrombosis and PA stenosis requiring re-intervention), cardiac complications (cardiopulmonary resuscitation and arrhythmias) and non-cardiac complications (neurological complications such as seizures, cerebral haemorrhage, cerebral infarct or general intensive care complications such as bleeding leading to haemodynamic compromise requiring immediate blood transfusion or reoperation and sepsis diagnosed according to the criteria of the International Consensus Conference on Pediatric Sepsis) [12]. To analyse the impact of age at SCPA, the study population was divided into two groups according to age (group 1: less than 4 months; group 2: greater than 4 months) as previously performed by Jaquiss et al. [13,14].

2.7. Statistical analysis

Continuous variables are presented as mean ± standard deviation or median and range as appropriate, and categorical data as count and percentages. Selected continuous variables were dichotomised to create categorical variables. Categorical data were analysed with the chi-square or Fisher’s exact test as appropriate. Continuous variables were analysed with the Student’s t-test after testing for equality of variances with the Levene test. Non-parametric tests for two independent samples were performed with the Mann–Whitney U test.

Comparisons between pre- and postoperative TVR and RV function were calculated with McNemar test or marginal homogeneity test as appropriate.

Freedom of adverse outcome (death or transplant) after hemi-Fontan operation until end of the follow-up period was estimated by the Kaplan–Meier method. The Breslow test (generalised Wilcoxon) was used to test equality of distribu-
3. Results

Patient characteristics, including gender, anatomic subtypes, age, weight and body surface area at hemi-Fontan operation as well as preoperative cardiac catheterisation data and surgical data, are summarised in Table 1.

### 3.1. The superior cavopulmonary anastomosis

The median age at operation was 4.4 (1.2–45.0) months. Forty-seven (39.5%) patients were younger than 4 months at the time of the operation. In patients with a bilateral SVC who underwent a bilateral SCPA, cardiopulmonary bypass time and total support time were longer compared to the remainder (181 ± 31 vs 143 ± 32 min, P = 0.006 and 188 ± 27 vs 152 ± 30 min, P = 0.004, respectively).

Additional surgical procedures were performed at the time of surgery on 13 (10.9%) patients, which were tricuspid valve repair in seven, relief of an aortic arch obstruction in five and patch enlargement of a right-sided pulmonary vein in one patient. Cardiopulmonary bypass time and total support time were significantly longer in patients who underwent additional procedures at the time of the SCPA (169 ± 31 vs 143 ± 32 min, P = 0.006 and 175 ± 34 vs 151 ± 29 min, P = 0.008, respectively).

### 3.2. Postoperative course

Data on the mean values of CVP in the SVC and IVC and mean SaO2 of the first 24 postoperative hours are given in Table 1, along with data on the duration and volume of chest tube drainage and the duration of postoperative hospital stay. Inhaled nitric oxide was used in 17 (14.3%) patients. The median duration of nitric oxide administration was 48 (2–250) h.

### 3.3. Outcome of the SCPA

The outcome of the SCPA is summarised in Fig. 1. As many as 105 of 119 patients survived this second palliative procedure without subsequent cardiac transplantation (88.2%). Accordingly, adverse outcome was observed in 14 (11.8%) patients. Early adverse outcome (all death) occurred in 4 (3%) patients and late adverse outcome in 10 (8.7%) (death, n = 8, and cardiac transplantation, n = 2). By January 2010, 95 of the 105 survivors proceeded to Fontan completion (90.5%) and 8 (7.6%) are awaiting this operation. In two patients the hemi-Fontan operation is considered the final palliation.

### 3.4. Risk factors for adverse outcome after the SCPA

The results of the comparison of preoperative, surgical and postoperative variables between the group of patients with and without early or late adverse outcome are given in Table 2. Particularly, age at operation, the number of patients younger than 4 months at SCPA and the number of patients with a bilateral SVC were not different between groups. However, patients with late adverse outcome had longer cardiopulmonary bypass time and more frequently more than moderate tricuspid regurgitation on postoperative echocardiographic assessment. Accordingly, the presence of more than moderate tricuspid valve regurgitation after SCPA proved to be a strong predictor of late adverse outcome after this procedure (odds ratio (OR) 16.5 (4.4–62.6), P < 0.001) and patients with more than moderate tricuspid valve regurgitation had a significantly lower freedom from adverse outcome rate after SCPA than those with less severe tricuspid regurgitation (Fig. 2, Breslow–Wilcoxon test P < 0.001). An age less than 4 months at SCPA did not increase the risk for adverse outcome (OR 1.2 (0.4–3.6), P = 0.78).

### 3.5. Postoperative complications

Postoperative complications after SCPA occurred in 36 (30%) of patients, with transient atrial arrhythmia (n = 11; 9%) and PA stenosis or thrombosis requiring early reoperation (n = 10; 8%) being the most common. Eight (7%) patients required cardiopulmonary resuscitation after surgery and in 14 (12%) patients, non-cardiac complications occurred.
3.6. Risk factors for postoperative complications

Overall, postoperative complications occurred more often in patients who received their SCPA at an age less than 4 months (OR 6.3 (2.7—14.9), \(P < 0.001\)). Accordingly, age and weight of patients with postoperative complications were significantly lower (3.5 (1.5—9.9) vs 4.7 (1.2—45) months and 5.0 ± 0.8 vs 5.6 ± 1.3 kg, \(P < 0.0001\) and \(P = 0.012\), respectively). Furthermore, patients with postoperative complications had lower \(\text{SaO}_2\) over the first 24 postoperative hours (71 ± 7 vs 67 ± 5.5%, \(P < 0.0001\)) and were more likely to show significantly impaired RV function after the operation (OR 2.4 (1.4—12.1), \(P = 0.009\)).

Patients with PA complications tended to have smaller PAs on preoperative angiocardiographic assessment (Nakata index 111 ± 12 vs 121 ± 27, \(P = 0.07\)) and the mean CVP in the SVC over the first 24 h was significantly higher (15.0 ± 2.8 vs 13.2 ± 1.3 mmHg, \(P = 0.02\)). PA complications did not occur in one of the patients who underwent a bilateral bidirectional SCPA.

3.7. Impact of age on the postoperative course after SCPA

Forty-seven (39%) patients underwent SCPA at less than 4 months of age. Age at SCPA was inversely related to the year of operation, indicating that we performed the second palliative procedure earlier in recent years (\(r = 0.32, P < 0.001\)). Early or late adverse outcome was not more likely in patients younger than 4 months (OR 1.2 (0.4—3.6), \(P = 0.78\)). Younger patients were more cyanotic (70 ± 6 vs 77 ± 4%, \(P < 0.001\)), had a higher postoperative CVP in the SVC (9.2 ± 2.4 vs 7.8 ± 1.8 mmHg, \(P = 0.02\)) but had no longer duration of mechanical ventilation (18 (4—527) vs 13 (2—113) h, \(P = 0.15\)) or pleural drainage (65 (8—365) vs 8 (18—319) h, \(P = 0.32\)). However, severely impaired RV function on
preoperative and postoperative echocardiographic assessment was more common in these patients compared with the remainder (8 of 47 vs 3 of 72, \( P < 0.02 \), and 12 of 47 vs 5 of 72, \( P = 0.005 \)), whereas cardiopulmonary bypass time was similar (152 \( \pm \) 37 vs 141 \( \pm \) 29 min, \( P = 0.10 \)).

Patients younger than 4 months at SCPA were more likely to suffer postoperative complications compared to patients who received the second palliative operation at an age above 4 months (OR 6.3 (2.7–14.9), \( P < 0.001 \)). Postoperative complications occurred in 25 (53%) of the younger patients compared with 11 (15%) patients of the older group. This difference relates to a higher incidence of cardiac complications other than PA thrombosis or stenosis and non-cardiac complications (24 (51%) vs 9 (12%), \( P < 0.001 \)). The incidence of PA complications was not statistically different between the groups of patients younger and older than 4 months at the time of SCPA (6 (13%) vs 4 (6%), \( P = 0.19 \)).

3.8. Tricuspid regurgitation and RV function before and after hemi-Fontan operation

Data of the semiquantitative assessment of tricuspid regurgitation and RV function are given in Tables 3 and 4.

Table 3. Comparison of pre- and postoperative tricuspid regurgitation.

<table>
<thead>
<tr>
<th>Preoperative TR</th>
<th>Postoperative RVF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Normal, n</td>
</tr>
<tr>
<td>to moderate</td>
<td>12</td>
</tr>
<tr>
<td>Moderate</td>
<td>Mildly impaired, n</td>
</tr>
<tr>
<td>to severe</td>
<td>9</td>
</tr>
<tr>
<td>Severe</td>
<td>Moderately impaired, n</td>
</tr>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>Severely impaired, n</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Total, n</td>
</tr>
</tbody>
</table>

Marginal homogeneity testing did not reveal differences between pre- and postoperative tricuspid regurgitation. After the SCPA, tricuspid valve function improved in 22 (18.5%), remained unchanged in 69 (38%) and deteriorated in 28 (23.5%) of patients. Tricuspid valve repair was attempted in seven patients at the time of the SCPA and resulted in a reduction of tricuspid regurgitation in four patients. In three of seven patients, tricuspid valve function remained unchanged \( (n = 2) \) or became worse \( (n = 1) \). RV function deteriorated significantly after the SCPA (marginal homogeneity test \( P = 0.004 \)). RV function improved in only 8 (7%) patients, remained unchanged in 84 (71%) and deteriorated in 26 (22%) patients.

4. Discussion

This single-centre analysis of outcome of the SCPA in HLHS patients reports a follow-up period of 14 years and shows that early adverse outcome (death within 30 days after surgery or before hospital discharge) occurred in 3.4% and late adverse outcome (death or transplant after hospital discharge but before the next operative procedure) in 8.7% of patients. The presence of at least moderate to severe tricuspid regurgitation on postoperative echocardiographic assessment was found to be a strong predictor of late adverse outcome. Overall, postoperative complications were more likely in children who underwent surgery at less than 4 months of age.

The incidence of late adverse outcome after SCPA was comparable to that found by Jaquiss et al. \( [13] \) who reported an overall rate of late death or cardiac transplant of 7% after the second step of the surgical palliation of HLHS. However, no early death is reported in their series using a superior bidirectional Glenn shunt as cavopulmonary anastomosis rather than the hemi-Fontan technique, which we used in the majority of our patients.

We found tricuspid regurgitation to be a risk factor for late adverse outcome after the SCPA and also showed that volume unloading of the RV with this operation alone does not reduce the degree of tricuspid valve regurgitation. Therefore, tricuspid valve repair should be attempted at the time of SCPA if more than moderate regurgitation is present. Ohye et al. \( [9] \) could show that tricuspid valve repair can be
accomplished with satisfactory results in the majority of patients. In our series, valve function improved after repair in four of seven patients.

Based on semiquantitative echocardiographic assessment, RV function did not improve after SCPA. Three factors might explain this finding. First, postoperative echo assessment was performed only 2 weeks after the operation and full recovery of RV function might not have ensued at that time. Second, cardiopulmonary bypass might negatively impact on postoperative RV function. Third, volume unloading of the RV with SCPA might mask any improvement in intrinsic, load-independent RV function. Therefore, longer-term follow-up studies, ideally using load-independent measures of RV function, are needed to delineate any potential impact of the SCPA operation on RV function.

Younger age at SCPA was not associated with an increased incidence in adverse outcomes such as death or cardiac transplant. However, children younger than 4 months of age at this procedure had a higher CVP in the SVC and lower SaO2 early after the operation. These findings are in line with a previous report by Jaquiss et al. [13]. However, in discrepancy to these authors, we could not find any differences regarding the duration and amount of chest tube drainage, duration of mechanical ventilation and hospital stay. This difference might be explained by a general difference in postoperative management as, overall, the duration of mechanical ventilation and chest tube drainage were shorter and the hospital stay was longer in our series.

The main difference we found between younger and older patients was the higher incidence of postoperative complications in younger patients. However, this did not result in a higher incidence of adverse outcome or prolongation of hospital stay. Nevertheless, this increased risk for postoperative complications after an early SCPA operation has to be taken into consideration when deciding on the timing of the second step of the surgical palliation of HLHS and needs to be balanced against the potential benefit of early RV unloading and a shorter BT-shunt period in HLHS patients.

The ambition to reduce interstage mortality between the initial Norwood and the subsequent SCPA operation has led to the introduction of a home surveillance programme in our department in 2005. This programme certainly contributed to both, an earlier SCPA operation and an elimination of interstage mortality [6]. Therefore, one might decide for an earlier second palliative operation even on the expense of an increased risk of postoperative complications in selected cases deemed to be at a particular risk for interstage mortality.

As opposed to a superior bidirectional cavopulmonary anastomosis, the hemi-Fontan operation comprises patch enlargement of the left PA. However, the incidence of PA complications such as PA stenosis or thrombosis in our series is in the range of that reported for a superior bidirectional cavopulmonary anastomosis [15]. PA complications were reported to be more common in younger patients after a bidirectional cavopulmonary anastomosis procedure [15]. However, in our series of HLHS patients, who predominantly underwent SCPA using the hemi-Fontan technique, a younger age at operation was not associated with an increased risk for PA complications. This fact suggests that the hemi-Fontan technique is particularly appealing when aiming to perform the second palliative step early.

The presence of a bilateral SVC was reported to be associated with an increased risk of thrombus formation and limited growth of the central PAs after the establishment of a bilateral bidirectional SCPA [16]. A bilateral vena cava was only present in six patients of our series and we could not demonstrate a negative impact on outcome after the hemi-Fontan procedure. However, a bilateral bidirectional SCPA operation is surgically more demanding due to smaller caval veins and the need of a second anastomosis. This is represented by the longer cardiopulmonary bypass and total support time needed for this procedure.

RV function after the operation was worse in our subgroup of patients operated at less than 4 months of age. This difference probably relates to the fact that early operation was intended in some patients to volume-unload the impaired RV hoping for RV functional improvement of and certainly does not reflect a different response of the RV myocardium to an earlier operation. The fact that preoperative RV function was also worse in younger children further supports this conjecture.

4.1. Study limitations

RV function and the severity of tricuspid regurgitation were assessed semiquantitatively. Unfortunately, contemporary echocardiographic measures of ventricular function such as tissue Doppler or speckle tracking imaging were not available for all patients. To delineate between the effect of RV unloading and the effect of cardiopulmonary bypass on intrinsic RV function, additional follow-up studies using modern imaging modalities are warranted. Furthermore, postoperative echo assessment of RV function was performed only 2 weeks after the SCPA operation and full recovery of RV function might not have ensued at that time.

It was not possible to obtain sufficient data on the detailed anatomy of the tricuspid valve in all patients with significant tricuspid regurgitation. Therefore, we cannot compare the outcome of the hemi-Fontan operation between patients with an inherent anatomic defect of the tricuspid valve with those with annular dilatation only.

4.2. Conclusions

The SCPA can be established with low mortality in patients with HLHS. However, more than moderate tricuspid valve regurgitation should be targeted at surgery as it is a risk factor for adverse outcome such as death or need for cardiac transplant. The second palliative procedure of the palliation of HLHS patients should ideally be performed in children older than 4 months in order to minimise the risk of postoperative complications. However, as the incidence of adverse outcome and PA complications and the duration of postoperative medical treatment were not higher in younger patients, it seems justified to perform this procedure earlier in selected patients deemed to be at a particular risk for interstage death.

References


