The Impact of Length of Post-Operative Ventilator Support on Outcome of the Arterial Switch Operation – Report from a Single Institute

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Background: The arterial switch operation (ASO) is the gold-standard surgical procedure for transposition of the great arteries (TGA) in newborns and small infants. The goal of this current study is to describe the postoperative respiratory care and the current outcomes of the patients that underwent ASO for TGA at our institute.

Method: We retrospectively enrolled 28 patients (23 males and 5 females) with TGA, who underwent ASO in this institution between January 2006 and December 2008, and analyzed some parameters. The outcome measurements were length of ventilator support, re-intervention rate and survival during hospitalization.

Results: Ages and body weights at ASO were 17.2 ± 32.3 days (median, 5 days; range, 0-158 days) and 3.1 ± 0.6 kg (median, 3; 1.3-5 kg), respectively. Partial cardio-pulmonary bypass (CPB) time was 231.8 ± 56.9 (163.0-377.0) minutes, total CPB time 192.8 ± 56.1 (134.0-308.0) minutes and aortic cross-clamp time 125.3 ± 36.0 (62.0-194.0) minutes. In this cohort, the mean ventilator duration was 12.8 ± 14.3 days (median, 7; range, 2-61) for all patients and 11.2 ± 11.3 days (median, 7; range, 3-50) for survivors. Yearly report showed that median ventilator duration was 17.5 days and survival was 73% in 2006, 8.6 days of ventilation and 100% survival in 2007, and 6.4 days of ventilation and 91% survival in 2008. Multivariate analysis showed patients with aortic coarctation had longer ventilation durations, possibly related to increased lung fluid caused by cardiopulmonary bypass and increased left ventricular afterload. A higher re-intervention rate was found in patients with ventilation support > 14 days (p < 0.05).

Conclusion: Ventilation duration shortened and survival rate increased gradually from 2006 to 2008. Patients with aortic coartation had longer ventilator support. Cardiorespiratory investigation or intervention was indicated in patients who required ventilation support more than 14 days postoperatively.

Key Words: Arterial switch operation • Mechanical ventilation • Respiratory care • Transposition of great arteries

INTRODUCTION

Transposition of great arteries (TGA) is a congenital heart defect in which the anatomical relationship of the great arteries is reversed. Severe cyanosis usually is evident soon after birth and some communication between the arterial and venous circulations is mandatory to sustain life. Without surgery, TGA is incompatible with life. Surgery with the aim of setting both circulations in series offers the only hope for long-term survival. The arterial switch operation (ASO) has become the preferred surgical procedure for TGA in newborns and small infants since its introduction by Jatene in 1975 and later modification by Lecompte. With recent advances in
perioperative management and surgical techniques, the surgical results are promising. In this study, we focused on respiratory care in the intensive care unit (ICU) and finding risk factors of prolonged ventilator dependence, and also to characterize their impact on outcomes.

PATIENTS AND METHODS

Study population
From January 2006 to December 2008, a review of the medical records identified 28 patients (23 males and 5 females) who had congenital d-TGA and underwent ASO in this institution, constituting the study population. The patients who had TGA variations and underwent procedures other than ASO, for example, the Rastelli operation, Senning procedure, or Fontan operation, were excluded from this study.

Among the 28 patients, palliative procedures prior to definitive ASO (aortoplasty and pulmonary artery banding) were performed in two patients. All patients underwent preoperative echocardiography, and 16 underwent balloon atrial septostomy (BAS). Prostaglandin infusions were administered to 25 patients.

Operative techniques and postoperative management
Hypothermic cardiopulmonary bypass (CPB) was applied in all patients. Myocardial protection was achieved by multidose, cold-blood cardioplegia. The atrial septal defect or ventricular septal defect (VSD) was repaired through an atriotomy, under deep hypothermic circulatory arrest, if necessary. The coronary arteries were translocated first, and the neo-aorta was anastomosed. After reconstitution of the neo-aorta was finished, the neo-pulmonary artery was reconstructed. After weaning off CPB, the sternum was kept open and stented with a partial syringe. A silicone membrane was sutured to the skin edges with continuous prolene stitches and covered with iodine impregnated adhesive plastic drape. Postoperative inotropic support included dopamine (5 μg/kg/min), milrinone (0.5-0.7 μg/kg/min) and low-dose epinephrine to treat low cardiac output syndrome. Extracorporeal membrane oxygenation (ECMO) was instituted in patients who failed to wean from CPB or who had severely low cardiac output syndrome after surgery.

Patients were ventilated with a pressure-controlled ventilator, and the initial settings were as follows: ventilation rate of 30-33 ventilations/min, inspiratory time of 0.5 seconds, peak inspiratory pressure (PIP) of 21-23 cmH₂O, peak end expiratory pressure (PEEP) of 4 cmH₂O, and oxygen fraction of 0.6. The settings were later adjusted according to blood gas analyses and chest radiography. Fentanyl and pancuronium infusion were used for analgesia and sedation before sternal closure. After approximation of the sternum and stabilization of hemodynamics, midazolam or propofol were infused continuously and the patients started to wean from the ventilators. Additionally, intensive chest care and airway hygiene were given to the patients. Extubation was done when the patients had stable hemodynamics and the ventilator settings could be lowered to a flow rate of 12 ventilations/min, PIP of less than 18 cmH₂O, and FiO₂ of less than 0.4. Before extubation, we gave intravenous dexamethasone (0.2 mg/kg) to patients who had been ventilated for more than 7 days.

Statistical analysis
The results are presented as means ± standard deviations or medians, when appropriate. Statistical analyses were performed utilizing Student’s t test. Multivariate linear regression was done to identify the significant factors related to ventilation duration. An event-free curve was estimated by Kaplan-Meier analysis, and Cox regression analysis was used to examine the statistical differences between the curves. A p-value of < 0.05 was considered significant.

RESULTS

Clinical characteristics
In this study group, associated VSD was found in 32% (9/28) of patients and coarctation was found in 18% (5/28) of them. One patient had situs solitus and dextrocardia. Ages and body weights at ASO were 17.2 ± 32.3 days (median, 5 days; range, 0-158 days) and 3.1 ± 0.6 kg (median, 3; 1.3-5 kg), respectively. Partial CPB time was 231.8 ± 32.3 minutes, total CPB time 192.8 ± 56.1 minutes, total CPB time 125.3 ± 36.0 minutes. Six patients (21%) required ECMO support in the post-
operative period, and four were successfully weaned off ECMO.

**ICU course and outcomes**

Four patients died in the ICU. The ICU survival rate was 86%. The sternum was closed 1.8 ± 0.7 (median, 2; range, 0-4) days after surgery. The mean ventilator duration was 12.8 ± 14.3 days (median, 7; range, 2-61) for all patients and 11.2 ± 11.3 days (median, 7; range, 3-50) for survivors. The ICU stay was 18.3 ± 20.1 days (median, 11; range, 2-97) for all patients and 10.0 ± 6.7 days (median, 8; range, 5-42) for survivors. Seven patients (25%) required re-intervention, which included VSD repair in two patients, balloon angioplasty of great vessels in four patients, and coarctation repair in one patient. Additionally, there was one late death due to hypoxic-ischemic encephalopathy after cardiopulmonary resuscitation in the postoperative course. The final survival rate was 82%.

**Predictors of prolonged dependence on ventilation**

We further analyzed the predictors of prolonged ventilator support. Preoperative BAS did not affect the ventilator days. The ventilation days were not correlated with body weight or age at operation, as shown in Figure 1. Figure 2 shows that the bypass duration (both partial and total) was associated with ventilator duration required after operation (p = 0.032 and 0.019, respectively). The presence of VSD and coarctation were also associated with longer periods of ventilator use. Finally, multivariate analysis revealed that coarctation was an independent predictor of prolonged ventilator use (p = 0.002).

![Figure 1. (A) The relationship between body weight and ventilator days. (B) The relationship between age at operation and ventilator days.](image-url)
Clinical significance of prolonged ventilator use

In this cohort, seven patients required prolonged ventilator use (> 14 days). These patients required more re-intervention, as listed in Figure 3. These patients also had complicated ICU courses, as shown in Table 1.

Improving outcomes

When we compared the outcomes over the years, we found significantly improved surgical results, including decreased ECMO use, shorter ventilation durations and ICU stays, and improved ICU and hospital survival (Table 2). There was only one death after 2007 and the baby was a 1.3-kg premature infant.

DISCUSSION

We characterized the postoperative ventilation course after ASO since 2006, during which ventilator use (days) shortened over the years. Furthermore, cardiorespiratory investigation or intervention was performed more frequently in patients who required ventilator support for more than 14 days in the postoperative period.

ASO was performed through a median sternotomy with the patient on CPB. After CPB, lung compliance was altered due to increased fluid in the lungs. The impact of this on the patient was diminished lung capacity to perform gas exchange, which resulted in the need for increased ventilator support. Pulmonary vascular resistance increased after CPB, which in turn affected right ventricular function. Also, the inflammatory response during CPB results in pulmonary derangements, which manifest as decreased functional residual capacity, compliance, and gas exchange, as well as increased pulmonary vascular resistance and pulmonary artery pressure.7,8 Additionally, when patients are placed on CPB, the lungs have a sudden and significant decrease in antegrade flow via the pulmonary artery. This relative ischemia results in significant clinical pulmonary dysfunction.9 The above phenomena explain the relation-

Table 1. Complications of patients requiring prolonged ventilator dependence

<table>
<thead>
<tr>
<th>No</th>
<th>Ventilator days</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>Postop ECMO, large residual VSD</td>
</tr>
<tr>
<td>2</td>
<td>55</td>
<td>Postop ECMO, coronary insufficiency</td>
</tr>
<tr>
<td>3</td>
<td>19</td>
<td>Postop ECMO, severe pulmonary stenosis, RV failure</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>Severe supravalvular aortic stenosis</td>
</tr>
<tr>
<td>5</td>
<td>14</td>
<td>Postop ECMO, hypoxic ischemic encephalopathy</td>
</tr>
<tr>
<td>6</td>
<td>61</td>
<td>Chylothorax, severe pulmonary stenosis</td>
</tr>
<tr>
<td>7</td>
<td>50</td>
<td>Left phrenic nerve palsy</td>
</tr>
</tbody>
</table>

ECMO, extracorporeal membrane oxygenation; RV, right ventricle; VSD, ventricular septal defect.
ship between the bypass time and the postoperative ventilation duration.

After ASO, ICU provides a safe homeostatic environment at minimal metabolic cost. All infants are sedated by continuous fentanyl infusion and are paralyzed with continuous pancuronium infusion for at least 24 hours postoperatively. The sternum is unapproximated to avoid cardiac tamponade because the extensive anatomic dissection, long suture lines, and long CPB for ASO predispose patients to significant bleeding. Furthermore, a closed chest creates “thoracic tamponade syndrome”, in which pulmonary resistance increases greatly; thereafter, the aforementioned “wet lung” after CPB worsens.

Postoperative respiratory support should optimize oxygen delivery, avoid unnecessary oxygen consumption from spontaneous respiration, and improve carbon dioxide elimination. Positive pressure ventilation primarily affects cardiac output by increasing intrathoracic pressure and altering lung volume, which decreases both ventricular preload and afterload. However, positive pressure ventilation with a short inspiratory time prevents the decrease in left ventricular filling and maximizes cardiac output. According to literature, gradual weaning from the ventilator usually takes place over a 12- to 24-hour period, followed by extubation on about postoperative day 3. However, weaning took 12.8 ± 14.3 (median, 7; 2-61 days) in our study, probably because we closed the sternum 1 to 3 days after operation. Weaning process could only be initiated after chest closure. Furthermore, ventilation duration significantly shortened after 2007, with decrease to 5.2 days for survivors in 2008. In multivariate analysis, patients with aortic coarctation had longer postoperative ventilation durations than those with other defects. One possible reason for this could be organ injury caused by longer CPB times required for aortoplasty. One patient whose aortic coarctation was not diagnosed initially still had a long ventilation duration, due possibly to increased left ventricular afterload, which made weaning more difficult. We also had seven patients with ventilation durations of more than 2 weeks (Table 2 and Figure 3), five of whom had significant residual cardiac defects which necessitated repeat operations in the immediate postoperative ICU course, or in the follow-up period. One had phrenic nerve palsy, which made the patient unable to separate from the positive pressure ventilator. Therefore, we suggest that after ASO, patients who depend more than 2 weeks of ventilation also require further cardiopulmonary investigations to correct residual cardiac defects or respiratory problems.

With modern CPB, improved surgical techniques and perioperative care, the current operative mortality for ASO is low and the results are satisfactory. The early outcome for TGA with an intact ventricular septum is now comparable to that of tetralogy of Fallot and isolated VSD. Hutter et al reported that the mortality rate was 4% for complex TGA and 0% for simple TGA. Freed et al. also reported only one patient died in a cohort of consecutive 88 TGA patients (1.1%). Our results were not as satisfactory as those of the above studies. This could be explained by our relatively low patient volumes. According to Hirsch et al, hospital mortality for ASO is a function of institutional volume; for an institution with less than 10 patients yearly, the

Table 2. Comparison of surgical outcomes by year

<table>
<thead>
<tr>
<th>Year</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
</tr>
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<tbody>
<tr>
<td>N</td>
<td>11</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Partial CPB duration (min)</td>
<td>247.7 ± 62.1</td>
<td>196.3 ± 35.2</td>
<td>235.3 ± 56.7</td>
</tr>
<tr>
<td>Total CPB duration (min)</td>
<td>209.7 ± 46.2</td>
<td>162.5 ± 27.9</td>
<td>192.5 ± 37.3</td>
</tr>
<tr>
<td>Aortic cross clamp duration (min)</td>
<td>139.1 ± 40.0</td>
<td>100.0 ± 23.8</td>
<td>126.9 ± 32.5</td>
</tr>
<tr>
<td>Post-op ECMO use (N)</td>
<td>5</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Overall median ventilation duration (days)</td>
<td>17.5</td>
<td>8.6</td>
<td>6.4</td>
</tr>
<tr>
<td>Median ventilation duration for survivors (days)</td>
<td>6.5</td>
<td>8.5</td>
<td>4.5</td>
</tr>
<tr>
<td>ICU survival (%)</td>
<td>73</td>
<td>100</td>
<td>91</td>
</tr>
<tr>
<td>Re-intervention (%)</td>
<td>46</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>Final hospital survival (%)</td>
<td>64</td>
<td>100</td>
<td>90</td>
</tr>
</tbody>
</table>

ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.
hospital mortality is greater than 3.2%.20 We have improved outcomes for ASO at our hospital since 2007, when ventilator duration shortened (8.6 days vs. 17.5 days) and hospital survival improved (100% vs. 72.7%) in comparison to 2006. In the most recent 2 years, only one patient died after ASO, and this infant was premature, weighing only 1.3 kg.

CONCLUSION

After ASO, ventilator duration decreased gradually from 17.5 days in 2006 to 8.6 days in 2007, and 6.4 days in 2008). Patients with concomitant aortic coarctation required longer period of ventilator support. Further cardiorespiratory investigation or intervention is indicated in patients who depend ventilator support for more than 14 days in the postoperative period.

REFERENCES