Veno-Right Ventricular Extracorporeal Membrane Oxygenation for Thoracic Surgery*

An Experimental Study in Dogs

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Background: Although the indications for extracorporeal membrane oxygenation (ECMO) have been extended, ECMO has yet to be used as a respiratory support system during thoracic surgery. The purpose of this experimental study was to investigate whether veno-right ventricular (veno-RV) ECMO can be used for thoracic surgery without mechanical ventilation.

Methods: Acute experimental study: Veno-RV ECMO as total lung support was maintained for 60 min without mechanical ventilation in six dogs. A venous drainage cannula was inserted in the superior cavoatrial junction through the right femoral vein and a venous return cannula was inserted in the right ventricle through the right jugular vein. The veno-RV ECMO system comprised a centrifugal pump and membrane oxygenator. Survival model: After veno-RV ECMO had been established in three dogs, a two-ring thoracic tracheal segment was resected and the tracheal ends were anastomosed by video-assisted thoracic surgery without ventilation.

Results: In the acute study, when the veno-RV ECMO flow was maintained at 100 mL/kg/min, all six dogs remained hemodynamically stable and the arterial oxygen saturation was maintained at more than 98%, despite total lung collapse. In the survival study, all three dogs made an uneventful postoperative recovery.

Conclusion: Video-assisted tracheal surgery can be performed without conventional respiratory support. Veno-RV ECMO as total lung support may become an alternative respiratory management device for thoracic surgery.

Key words: thoracic surgery; total lung support; tracheal reconstruction; veno-right ventricular extracorporeal membrane oxygenation

Abbreviations: AP = arterial pressure; BE = base excess; ECMO = extracorporeal membrane oxygenation; FA = femoral artery; HCO₃⁻ = bicarbonate; HR = heart rate; LA = left atrium; LAP = left atrial blood pressure; PA = pulmonary artery; PAP = pulmonary artery pressure; SfaO₂ = femoral arterial saturation of oxygen; SintO₂ = oxygenator inlet saturation of oxygen; SlaO₂ = left atrial saturation of oxygen; SpaO₂ = pulmonary arterial saturation of oxygen; veno-RV = veno-right ventricular

In 1976, Bartlett et al1 reported the first successful use of extracorporeal membrane oxygenation (ECMO) for neonatal respiratory failure and ever since, ECMO has been used widely for children and adults suffering severe respiratory failure. Whether ECMO is effective when the lungs are totally collapsed is unknown, however. Although the indications for extracorporeal membrane oxygenation (ECMO) have been extended, ECMO has yet to be used as a respiratory support system during thoracic surgery. If ECMO can maintain satisfactory oxygenation without mechanical lung ventilation, it would enable the endobronchial tube to be removed and simplify difficult airway reconstruction surgery.

Therefore, the first experiment was undertaken to investigate the pulmonary hemodynamics and physiology in order to determine the feasibility of using ECMO during lung collapse and in the second
experiment, the applicability of ECMO as an alternative to direct operative endobronchial tube ventilation during video-assisted tracheal reconstruction was assessed.

Materials and Methods

Acute Experimental Preparation

Six mongrel dogs weighing 17 to 24 kg were used in the acute phase of the study. They were premedicated with 1M ketamine hydrochloride, 40 mg/kg body weight. A left radial vein was cannulated for fluid and drug administration and the dogs were anesthetized by administering 5 mg/kg of sodium pentobarbital and 0.1 mg/kg of pancuronium bromide through the cannula. Then, tracheal intubation with a No. 7 endotracheal tube was carried out and the lungs were ventilated mechanically using a volume-cycle respirator (model 671; Shinano Inc; Tokyo, Japan) with an inspired oxygen fraction of 0.4. Ventilation was adjusted to maintain the blood pH and oxygen levels within satisfactory ranges, determined by measuring arterial blood gas levels. The routine respiration rate was 20 breaths/min and the tidal volume was 20 mL/kg body weight. Additional doses of sodium pentobarbital and pancuronium bromide were administered as required to maintain anesthesia. After anesthesia induction, a catheter was inserted in the right femoral artery (FA) for continuous arterial BP measurement and arterial oxygen saturation analysis. A Swan-Ganz catheter (Baxter Healthcare Corp; Santa Ana, Calif) was placed in the pulmonary artery (PA) through a branch of the right jugular vein for mean pulmonary artery pressure (mean PAP) measurement and blood sampling. Through a fifth left intercostal lateral thoracotomy, an IV line catheter (18G IV line; Togo Medikit Co Ltd; Tokyo, Japan) was inserted into the left atrium (LA) from the left atrial appendage for mean left atrial blood pressure (LAP) monitoring and blood sampling.

Veno-Right Ventricular ECMO

After administering IV heparin, 300 IU/kg, the right femoral vein was exposed and a 22F percutaneous venous cannula (Togo Medikit Co Ltd; Tokyo, Japan) was inserted directly over a guideewire to serve as the drainage cannula. The tip of this venous cannula was positioned at the superior cavoatrial junction. An 18F wire-reinforced venous cannula (William Harvey venous cannula; Bard Inc; Billerica, Mass), used as the outflow cannula, was passed into the right ventricle across the tricuspid valve through the right jugular vein. The position of this return cannula was confirmed by directed palpation through a sixth right intercostal thoracotomy. The inflow and outflow cannula lines were connected to a perfusion circuit comprising a Nikkiso centrifugal pump (HPM-15; Nikkiso Co; Tokyo, Japan) and a membrane oxygenator (Midflow D705; Dideco Co; Mirandola, Italy). A flow probe was attached to the distal outlet line of the pump, and blood flow was measured using an electromagnetic flow meter (Nikkiso Co). The system (total priming volume, 250 mL) was primed with 0.9% w/v normal saline solution. A diagram of the veno-right ventricular (veno-RV) ECMO system is shown in Figure 1. The animals were subjected to moderate hypothermic veno-RV ECMO. The maximum possible blood flow rate was maintained, generally 100 mL/kg/min, and the blood/oxygen gas ratio in the oxygenator was maintained at 1:2. During veno-RV ECMO, the nasopharyngeal temperature of each animal was maintained at 30 to 31°C using a heat exchange machine, and the

FIGURE 1. Diagram of the veno-RV ECMO system, which consists of a centrifugal pump and a membrane oxygenator.

Acute Experimental Protocol

The pump was started with the aim of reaching a blood flow rate of 100 mL/kg/min. Once stable bypass conditions were established, the ventilator was disconnected to collapse the lungs, and veno-RV ECMO was performed without mechanical lung ventilation for 1 h; blood gas levels and hemodynamics were investigated. The hemodynamic parameters, heart rate (HR), mean femoral arterial pressure (AP), mean pulmonary arterial pressure (PAP) and mean LAP, were monitored continuously. Blood samples were obtained from the oxygenator inlet and outlet lines, LA, PA, and FA before veno-RV ECMO (baseline) and then 15, 30, 45, and 60 min after starting veno-RV ECMO without lung ventilation support. Blood samples were then analyzed (AB-510; Radiometer; Copenhagen, Denmark). After veno-RV ECMO was performed for 1 h, the lungs were mechanically ventilated again (as before veno-RV ECMO); a blood sample was obtained 15 min after ventilation was restarted. No vasoactive drugs were administered during or after veno-RV ECMO. After the animals were sacrificed by IV injection of potassium chloride, all the lungs were excised rapidly and preserved immediately in 10% w/v formaldehyde for hematoxylin-eosin staining.

Survival Model

Three mongrel dogs weighing 25 to 35 kg were used for the survival study. They were anesthetized and ventilated as de-
scribed above. The experiment was performed under sterile conditions. The dogs received a preoperative dose of cefazolin sodium, 30 mg/kg, through a cannula in the left radial vein. After a catheter was inserted in the right FA for continuous BP and arterial oxygen saturation measurement, a 10-mm flexible thoracoscope attached to a video monitoring system (Fujinon electronic video endoscope system 400 series; Fuji Photo Optical Co Ltd; Saitama, Japan) was inserted into the right chest cavity through a 12-mm trocar in the seventh right intercostal space. A second incision in the third right intercostal space and a 3-cm anterolateral right minithoracotomy in the sixth intercostal space were made for surgical manipulation. After systemic heparinization with 100 IU/kg of IV heparin, the animals were subjected to moderate hypothermic veno-RV ECMO at a flow rate equivalent to 100 mL/kg/min, and the active clotting time was maintained within a range of 250 to 300 s.

Operative Procedures

The entire trachea was dissected by means of a port access using 10-mm scissors, 5-mm grasping forceps, and a cherry dissector. Two 2-0 PDS II stay sutures (Ethicon Inc; Somerville, NJ) were placed on the medial line of the distal and proximal tracheal wall. Once veno-RV ECMO had been established, the endotracheal tube was opened to the air to deflate the lungs and mechanical ventilation was stopped during veno-RV ECMO. A two-ring tracheal section was removed during video-assisted thoracic surgery. After observing the tracheal wall edges carefully to ensure bleeding had stopped, the distal and proximal tracheal ends were anastomosed using the full-layer continuous running suture technique with 3-0 PDS II sutures (Ethicon Inc). Adequate visualization was possible, even through the endoscopic instruments. The tracheal anastomosis line was examined carefully with warm saline solution to ensure that there was no bleeding or air leakage.

Upon completion of the procedure, each animal was rewarmed to 35°C and weaned from the veno-RV ECMO, the lungs were allowed to inflate with mechanical ventilation, and the veno-RV ECMO system was disconnected after 30 min of bypass weaning. After removing the veno-RV ECMO cannulas, the right jugular and right femoral veins were repaired with 6-0 Prolene sutures (Ethicon Inc). All blood that remained in the venous tubing and the oxygenator after veno-RV ECMO was collected and rein fused.

Next, the chest was irrigated with normal saline solution, a 28F chest drainage tube was inserted into the thorax through the trocar hole, and a suction device was connected. The wound was closed in layers and the skin was sutured in a subcuticular fashion. Each animal was allowed to breathe spontaneously; once it could breathe room air with adequate oxygenation, the chest drainage tube was removed, and the animal was weaned from ventilation and extubated.

Hemodynamic measurements and blood samples were obtained under control conditions, during veno-RV ECMO, and up to the end of the experiment. The initial base excess (BE) was corrected to within the normal range by IV sodium bicarbonate administration and further corrections were made, as necessary, up to the end of the experiment. The animals were given 20 mg/kg of 1M cefazolin sodium postoperatively and then maintained for 14 days on a daily dose of 40 mg/kg of amoxicillin, an oral antibiotic drug. Sixty days after surgery, each dog underwent fiber bronchoscopic examination under anesthesia induced with IM ketamine.

Statistical Analysis

Each value is expressed as the mean±SD. The data were compared with the paired t test, and differences were considered significant at p<0.05.

Animal Care

The experimental protocol was approved by the Animal Care and Use Committee of Saga Medical School. The animals received humane care in compliance with the “Principles of Laboratory Animal Care,” formulated by the National Society for Medical Research, and the “Guide for the Care and Use of Laboratory Animals,” published by the National Institutes of Health (NIH publication No. 86-23, revised 1985).

Results

Acute Experimental Study

The mean weight of the 6 dogs was 20.1±1.0 kg. Veno-RV ECMO remained stable throughout the 1-h experiment. During veno-RV ECMO, the mean nasopharyngeal temperature was 29±2°C and the extracorporeal blood flow rate was 100 mL/kg/min without respiratory ventilation.

The oxygen saturation levels of the PA (SpO₂), LA (SlaO₂), FA (SfaO₂) and oxygenator inlet (SintO₂) during the acute experiment are shown in Figure 2. SpO₂ increased during veno-RV ECMO compared with the level before veno-RV ECMO (p=0.05) and was maintained at more than 99% during veno-RV ECMO. After the oxygenator was disconnected, the SpO₂ level decreased to that recorded before veno-RV ECMO. Despite total lung collapse during veno-RV ECMO, both SfaO₂ and SlaO₂ were maintained at more than 98% and there was no significant difference between them. There was also no significant difference between SpO₂ and SfaO₂ during veno-RV ECMO and, therefore, the aorta was perfused with blood that had been oxygenated by the veno-RV ECMO system. SintO₂, which represents the mixed venous blood oxygen saturation during veno-RV ECMO, was elevated from 69.9±7.4% at baseline to 78.6±23.8% 15 min after veno-RV ECMO, and satisfactory oxygenation of >80% was maintained thereafter despite total lung collapse during veno-RV ECMO.

The changes in pH, PAco₂, bicarbonate (HCO₃⁻) levels, and BE are presented in Table 1. Up to the end of the acute experiment, none of these parameters underwent significant changes during veno-RV ECMO compared with measurements taken prior to veno-RV ECMO.

The HR, mean PAP, mean LAP, and mean AP values at each measurement time are shown in Figure 3. Despite the use of veno-RV ECMO, the mean PAP remained below 25 mm Hg and the values before and
during veno-RV ECMO did not differ significantly; the mean AP and LAP were maintained at greater than 100 mm Hg and less than 10 mm Hg, respectively, during veno-RV ECMO. There were no significant differences between the HR, mean AP, or mean LAP values measured before and during veno-RV ECMO. Therefore, the systemic and pulmonary hemodynamics of all the dogs remained stable during veno-RV ECMO support. Additionally, 60 min after the start of veno-RV ECMO, all the animals were weaned easily from veno-RV ECMO without inotropic support. Histopathologic examination of tissues stained with hematoxylin-eosin demonstrated neither pulmonary edema nor intra-alveolar hemorrhage at the end of this acute study (Fig 4).

Survival Model

Three dogs (mean weight, 29.3±3.4 kg) underwent video-assisted tracheal reconstruction using veno-RV ECMO. Moderate hypothermic (33°C) veno-RV ECMO was maintained at 100 mL/kg/min for 30 min without lung mechanical ventilation during tracheal reconstruction. Hemodynamic stability and satisfactory oxygenation of the FA was achieved during this procedure (Table 2). Despite video-assisted thoracic surgery, tracheal reconstruction without direct intraoperative endobronchial tube ventilation could be performed with satisfactory visualization (Fig 5). Heparinization caused no bleeding problems, and no complications resulted from this incidental use of extracorporeal circulation. On completion of this procedure, the animals were weaned easily from veno-RV ECMO without inotropic support and they were all hemodynamically stable. The tracheal tube was removed 6 h after the operation. No dog died of hypoxia after being taken off the bypass and the postoperative recovery was uneventful. Sixty weeks after the operation, all three

Table 1—Changes in Femoral Arterial Blood Gas Values Before Veno-RV ECMO, During Veno-RV ECMO, and After Restarting Ventilation in the Acute Experiment (n=6)*

<table>
<thead>
<tr>
<th></th>
<th>Before Veno-RV ECMO</th>
<th>15 min</th>
<th>30 min</th>
<th>45 min</th>
<th>60 min</th>
<th>After Restarting Ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin, g/dL</td>
<td>13.3±2.4</td>
<td>10.7±3.0</td>
<td>11.3±2.7</td>
<td>10.3±3.6</td>
<td>10.1±2.7</td>
<td>10.2±3.12</td>
</tr>
<tr>
<td>pH</td>
<td>7.40±0.09</td>
<td>7.45±0.07</td>
<td>7.46±0.08</td>
<td>7.48±0.13</td>
<td>7.46±0.11</td>
<td>7.48±0.07</td>
</tr>
<tr>
<td>PaCO₂, mm Hg</td>
<td>27.2±5.11</td>
<td>34.3±9.24</td>
<td>33.9±9.94</td>
<td>29.3±4.76</td>
<td>23.7±7.26</td>
<td>34.2±6.36</td>
</tr>
<tr>
<td>HCO₃⁻, mEq/L</td>
<td>19.5±3.17</td>
<td>28.7±4.73</td>
<td>23.3±5.58</td>
<td>23.8±4.91</td>
<td>23.2±2.81</td>
<td>26.6±2.35</td>
</tr>
<tr>
<td>BE, mEq/L</td>
<td>-5.5±4.91</td>
<td>1.8±3.43</td>
<td>0.2±5.06</td>
<td>0.5±4.79</td>
<td>0.7±4.15</td>
<td>4.8±0.59</td>
</tr>
</tbody>
</table>

*There were no significant differences in the hemoglobin, pH, PaCO₂, HCO₃⁻, or BE values before veno-RV ECMO, during veno-RV ECMO, and after restarting ventilation. Each value represents the mean±SD.
dogs were examined using fiber bronchoscopy, which revealed no evidence of stenosis at the anastomosis sites (Fig 6).

**DISCUSSION**

ECMO has been used with simple veno-venous access using two catheters or a double-lumen catheter. However, if ECMO is used with veno-venous access and with no contribution from the lungs supplied by mechanical ventilation, ECMO could not achieve satisfactory oxygenation and provide total lung support. This is because it is impossible to achieve a bypass flow nearly equal to the cardiac output with ECMO using the veno-venous cannulation technique without significant recirculation of oxygenated blood.

This problem is described in the article by Wet-terberg and Steen. In an attempt to overcome it, Koul et al4 carried out ECMO using veno-right ventricle cannulation access with the aim of minimizing the possible recirculation of the oxygenated blood in the extracorporeal circuit; they demonstrated that veno-RV ECMO could provide effective total lung support. Although Koul et al4 showed that veno-RV ECMO was effective, they applied dead space ventilation (volume-controlled ventilation, 1 L/min; frequency, 20/min; positive end-expiratory pressure, 5 cm H2O; fraction of inspired oxygen, 0.21) during veno-RV ECMO. The efficacy of veno-RV ECMO without mechanical ventilation under conditions of complete lung collapse were unknown.

Therefore, the aim of our acute experiment was to determine whether veno-RV ECMO can provide total lung support and satisfactory arterial oxygenation without use of dead space ventilation. We found that, despite total lung collapse, the PA and FA oxygen saturation levels were similar and the SfaO2 was maintained at more than 98% throughout the period of veno-RV ECMO. Although we expected the pulmonary vascular resistance to rise significantly during lung deflation, no significant hemodynamic parameter changes were observed during veno-RV ECMO or after ventilation was restarted. Furthermore, hemodynamic stability could be maintained until the end of this acute experimental study, all the lungs appeared normal macroscopically, and no microscopic lung edema was detected. These results indicate that veno-RV ECMO without dead space ventilation is a safe and useful total lung support system for 60 min.

Hitherto, main airway surgery has been tradition-ally performed via a standard thoracotomy with direct operative endobronchial tube ventilation. Direct lung ventilation is a widely accepted method of
respiratory support, as it is simple to use. However, it is not easy to obtain an adequate operative view or achieve adequate arterial oxygenation during difficult procedures, such as tracheal carina reconstruction. The results of our acute experimental study suggest that airway surgery can be performed without conventional respiratory support by using veno-RV ECMO, which easily maintained adequate arterial oxygenation. Although veno-RV ECMO may be needed for longer than 1 h when dealing with lung injuries, most airway anastomosis procedures can be performed within 1 h. Therefore, veno-RV ECMO without additional respiratory support may become a total respiratory support system used during airway reconstruction.

The long-term survival study in dogs demonstrated the successful use of veno-RV ECMO as a new ventilation support system during thoracic surgical procedures, such as video-assisted tracheal reconstruction. To the best of our knowledge, the use of veno-RV ECMO as a total lung support system during thoracic surgery without mechanical ventilation has not been reported. In the survival model, despite total lung collapse, tracheal anastomosis by video-assisted surgery was performed with adequate arterial oxygenation in all three dogs and no major complications resulted from the use of this ECMO system. Although this model has several limitations, the results of the long-term survival experiment indicate that surgical procedures on the airway are possible using the veno-RV ECMO system.

These experiments on dogs have demonstrated that a perfusion cannula can be placed in the right

**Figure 5.** Thoracoscopic view of the tracheal anastomosis. SVC = superior vena cava.

**Figure 6.** Fiber bronchoscopic findings 60 weeks after video-assisted tracheal reconstruction. There is no stenosis at the anastomotic site.
ventricle through the tricuspid valve during veno-RV ECMO without complications. Furthermore, the position of the cannula in the superior cavoatrial junction can be confirmed by direct palpation with a finger inserted through the sixth right minithoracotomy space. In the clinical setting, this veno-RV ECMO system could be installed promptly under fluoroscopic guidance using an internal guide wire catheter, such as a Swan-Ganz catheter, and percutaneous respiratory support could be implemented rapidly.

In our acute study, satisfactory arterial oxygenation and hemodynamic stability could be achieved during veno-RV ECMO with total lung collapse for 1 h. However, veno-RV ECMO does not provide circulatory support, and hemodynamic stability must be assured before starting veno-RV ECMO. Patients in a hemodynamically unstable condition at the time of cannulation should not be subjected to veno-RV ECMO.

Cardiac arrhythmias and right ventricular endocardial injury are thought to be the major risks of using veno-RV ECMO because a perfusion cannula is placed in the right ventricle through the tricuspid valve. In our acute experimental study, however, satisfactory arterial oxygenation and hemodynamic stability without arrhythmias or right ventricular failure were achieved throughout veno-RV ECMO with totally collapsed lungs for 1 h in all six dogs.

In conclusion, introduction of the veno-RV ECMO system is a simple surgical technique. The use of veno-RV ECMO for respiratory support may be valuable for thoracic surgery in areas where airway reconstruction is difficult. The results of our study indicate that in the future, it may be possible to perform thoracic surgery without conventional respiratory support.

REFERENCES