OPEN

ASAIO Journal 2020

The Effect of Additional Stepwise Venous Inflow on Differential Hypoxia of Veno-Arterial Extracorporeal Membrane Oxygenation

Jin Gu Lee,* Namo Kim,† Kyoung Shik Narm,‡ Jee Won Suh,* Jisung Hwang,† Hyo Chae Paik,* and Young Chul Yoo†

Use of femoral-femoral veno-arterial (VA) extracorporeal membrane oxygenation (ECMO) for cardiopulmonary support during lung transplantation can be inadequate for efficient distribution of oxygenated blood into the coronary circulation. We hypothesized that creating a left-to-right shunt flow using veno-arterio-venous (VAV) ECMO would alleviate the differential hypoxia. Total 10 patients undergoing lung transplantation were enrolled in this study. An additional inflow cannula was inserted into the right internal jugular (RIJ) vein for VAV ECMO. During left one-lung ventilation using a 1.0 inspired oxygen fraction (FiO_2), the left-to-right shunt flow was incrementally increased from 0 to 500, 1,000, and 1,500 ml/min. The arterial oxygen partial pressure (PaO_2) and oxygen saturation (SaO_2) were measured at the proximal ascending aorta and right radial artery. The ascending aorta gas analysis revealed that six patients had a PaO_2/FiO_2 ratio less than 200 mm Hg at a 0 ml/min shunt flow. The PaO_2 (SaO_2) values were 48.5 ± 14.8 mm Hg (80.9 ± 11.6%) at the ascending aorta and 77.8 ± 69.7 mm Hg (83.3 ± 13.2%) at the right radial artery. As the left-to-right shunt flow rate increased over 1,000 ml/min, the PaO_2 and SaO_2 values for the ascending aorta and right radial artery significantly increased. In conclusion, femoral-femoral VA ECMO can produce suboptimal coronary oxygenation in patients unable to tolerate one-lung ventilation. A left-to-right shunt using VAV ECMO can alleviate the differential hypoxia. *ASAIO Journal* 2020; 66:803–808.

Key Words: differential hypoxia, left-to-right shunt, lung transplantation, oxygenation, veno-arterio-venous extracorporeal membrane oxygenation

Veno-veno (VV) and veno-arterial (VA) extracorporeal membrane oxygenation (ECMO) are gaining acceptance as potentially effective options for use in high-mortality situations and as tools that can replace the cardiopulmonary bypass (CPB) machine and support surgery requiring CPB use.[1] Although CPB has been the standard technique used for intraoperative cardiorespiratory support during lung transplantation (LTX),[2] results of various studies indicate that VA ECMO can be used as a substitute for CPB to provide intraoperative hemodynamic support during LTX.[3–7] Compared with CPB, VA ECMO is more versatile and results in better postoperative outcomes.[3,6,8]

During use of femoral-femoral VA ECMO for the patient with respiratory failure accompanied by severe hemodynamic impairment, the patient may develop upper body hypoxemia called differential hypoxia.[9,10] The application of an additional inflow cannula to the RIJ vein to add left-to-right shunt might alleviate myocardial depression or cerebral infarct by supplying sufficient oxygen.[11] Studies performed in the intensive care unit (ICU) setting have revealed the efficacy of providing a left-to-right shunt during ECMO support.[9,10,12,13] We hypothesized that differential hypoxia may occur in patients undergoing LTX using femora-femoral VA ECMO, and planned to assess the extent of hypoxemia by sampling the blood at the proximal ascending aorta adjacent to the coronary artery. To our knowledge, there have been no studies that directly measured oxygenation at the coronary artery level using femoral-femoral VA ECMO in patients who require respiratory and hemodynamic support. The objective of this study was to evaluate whether creating a left-to-right shunt flow using veno-arterio-venous (VAV) ECMO would alleviate the differential hypoxia that can occur in patients undergoing LTX.

Materials and Methods

Patients

The protocol for this single-center, prospective clinical trial complies with the Declaration of Helsinki and was approved by the institutional review board (number: 4-2016-0124) at Severance Hospital, Yonsei University Health System, Seoul, Republic of Korea. The study was registered at www.clinicaltrials.gov (NCT02859194).

From the *Department of Thoracic and Cardiovascular Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea; †Department of Anesthesiology and Pain Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea; and ‡Department of Thoracic and Cardiovascular Surgery, Eulji University Hospital, Daejeon, Republic of Korea.

Submitted for consideration August 2018; accepted for publication in revised form June 2019.

Disclosure: The authors have no conflicts of interest to report.

This study was conducted by departmental sources only.

Drs. Lee and Kim contributed equally to this work.

Drs. Paik and Yoo are corresponding authors contributed equally to this work.

Drs. Paik and Yoo takes responsibility for the content of the manuscript, including the data and analysis; and also conceptualized, designed the study, and carried out the initial analyses. Drs. Narm, Suh, and Hwang carried out the data collection. Drs. Lee and Paik provided the study materials. Drs. Lee and Kim contributed substantially to the data analysis and interpretation and writing of the manuscript. All authors approved the final manuscript as submitted.

Correspondence: Hyo Chae Paik, Department of Thoracic and Cardiovascular Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea, (03722) 50-1 Yonsei-ro, Seodaemun-gu, Seoul, Republic of Korea. Email: HCPAIK@yuhs.ac; and Young Chul Yoo, Department of Anesthesiology and Pain Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea, (03722) 50-1 Yonsei-ro, Seodaemun-gu, Seoul, Republic of Korea. Email: SEAOYSTER@yuhs.ac.

DOI: 10.1097/MAT.0000000000001052

Ten patients scheduled for LTX between May 2016 and September 2016 were consecutively enrolled in the study. Each patient provided written informed consent before enrollment. Patients greater than or equal to 20 years of age and scheduled for an isolated double LTX with ECMO support were considered eligible. Patients with a history of coronary artery disease or any type of arrhythmia were excluded from the trial.

Anesthetic and Study Protocol

Immediately after arrival at the operating theater, right radial artery cannulation and routine hemodynamic monitoring were achieved and followed by insertion of a pulmonary artery catheter (Swan-Ganz CCOmbo; Edwards Lifesciences, Irvine, CA). No premedication was given to patients. Induction of anesthesia was achieved using midazolam (0.5 mg/kg), sufentanil (1.0–3.0 μg/kg), and rocuronium bromide (1 mg/kg). Anesthesia was maintained using a 0.4–1.5vol% end-tidal concentration of sevoflurane and a continuous sufentanil (0.3–0.5 μg/kg/h) infusion to achieve a bispectral index score of 40–60. Mechanical ventilation was maintained using a 6 ml/kg tidal volume with a 5 mm Hg positive end-expiratory pressure. Respiratory frequency was adjusted to maintain an end-tidal carbon dioxide concentration approximately 40 mm Hg and an inspired oxygen fraction of 1.0 until the ECMO was initiated for the operation. A multiplane transesophageal echocardiography (TEE) probe (6TC; GE, Vingmed Ultrasound AS, Horten, Norway) was inserted after induction of anesthesia.

Insertion of peripheral VA ECMO was commenced after induction of anesthesia. Before initiation of the ECMO cannulation, a single, unfractionated heparin bolus targeting an activated clotting time between 160 and 180 seconds was administered. Veno-arterial ECMO using the Bioline heparin-coated Quadrox PLS circuit system (Maquet Cardiopulmonary, Hirrlingen, Germany) primed with 0.8 L acetated Ringer's solution (Plasma Solution A Inj.; CJ Pharma, Seoul, Korea) was performed with femoral artery-femoral vein cannulation. An arterial cannula (15–17 Fr), which was used for the arterial inflow, was inserted into the common femoral artery *via* the percutaneous route using the cut-down method, followed by cannula (20–24 Fr) insertion into the common femoral vein for the venous outflow. Upon switching to VAV ECMO, an additional arterial inflow cannula (15–17 Fr) was inserted into the RIJ vein. A Y connector was used to connect this additional inflow cannula to the existing inflow circuit. The venous and additional inflow cannula positions were adjusted using TEE guidance. The tip of the femoral vein cannula was adjusted between the inferior vena cava and right atrial junction. The tip of the additional inflow RIJ vein cannula lay approximately at the superior vena cava and the right atrium junction. A vascular clamp device and the Novaflow c Ultrasonic Flowcomputer (NovaLung GmbH, Heilbronn, Germany) were used to regulate inflow to the RIJ vein. During the study period, the FiO_2 of the ECMO was maintained at 1.0 and the sweep gas rate was adjusted according to a carbon dioxide partial pressure ($PaCO_2$) result from the arterial blood gas analysis (ABGA) of approximately 40 mm Hg. A pediatric cardioplegia catheter was placed and fixed at the proximal ascending aorta to collect blood samples for gas analysis. The samples were used to evaluate coronary artery oxygenation.

Surgical exposure was achieved using a clamshell incision, and the surgery was performed in right-to-left order. The crystalloid solution infusion rate was 6–8 ml/kg/h. Norepinephrine and vasopressin were used to maintain mean arterial pressure between 60 and 80 mm Hg during the operation. Milrinone was administered to patients with pre-existing or newly developed right ventricular (RV) failure or moderate to severe pulmonary hypertension. During the operation, the pulmonary artery catheter was withdrawn by approximately 5 cm to prevent interference with anastomosis. Packed red blood cells and cell saver salvaged blood were transfused when the hematocrit was less than 27%. Use of transfusion of fresh frozen plasma and platelets was consistent with institutional guidelines.[14]

Outcome Assessments

The primary outcome was to evaluate the effect of left-to-right shunt on oxygenation during femoral-femoral VA ECMO. During the right lung operation with left one-lung ventilation (OLV), ECMO, and ventilatory FiO_2 were fixed at 1.0 and the RIJ cannula inflow was increased from 0 ml/min to 1,500 ml/min by 500 ml/min increments, as referenced by previous study[9] (0–500, 1,000, and 1,500 ml/min). Five minutes after each flow rate increase, hemodynamic variables, respiratory variables, and cerebral oxygen saturation (rSO_2) were recorded, and blood samples were collected from the right radial artery, proximal ascending aorta, and pulmonary artery. Arterial oxygen partial pressure (PaO_2), $PaCO_2$, and oxygen saturation (SaO_2) were measured at the right radial artery and proximal ascending aorta. Venous oxygen partial pressure and mixed oxygen saturation (SvO_2) were measured at the pulmonary artery. Hemodynamic variables included heart rate, mean arterial pressure, mean pulmonary artery pressure, and peripheral oxygen saturation (SpO_2) at the right index finger. Respiratory variables included the peak airway pressure. During the experimental periods, total ECMO flow was maintained at approximately 60 ml/kg/min. After the study protocol was completed, additional inflow rate was maintained at 500 ml/min until the end of the operation.

Statistical Analysis

The data were collected from ten consecutively enrolled patients. Results for the baseline characteristics of the study participants were presented as mean ± standard deviation values for continuous variables; frequencies (percentages) were used for categorical variables. The Student's t-test or paired t-test was used for analysis of continuous variables and χ^2 or Fisher's exact test for categorical variables, as appropriate. SPSS software (Version 23.0; SPSS Inc., Chicago, IL) was used for all statistical analysis and *p* values of less than 0.05 were considered statistically significant.

Results

Individual data points of PaO_2 of proximal ascending aorta at baseline, 500 ml/min, 1,000 ml/min, and 1,500 ml/min of additional flow were connected and demonstrated by a line graph (**Figure 1**). The groups were divided by a single straight line graphed by the regression model of each data point, which met the baseline at the point of P/F ratio of 180 mm Hg. This was cross-checked by k-means cluster analysis, and the results of calculated average of the two groups at baseline were 48.5 mm

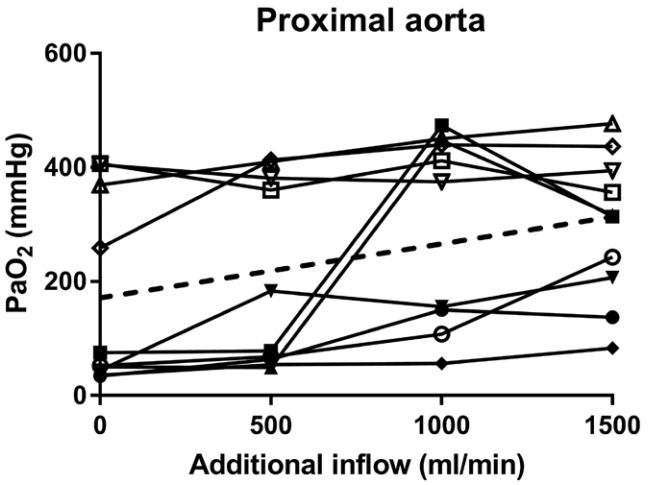

Figure 1. Changes of arterial oxygen partial pressure (PaO_2) at the proximal aorta according to the changes of additional inflow. A single dotted line was graphed by using the regression model of each data point.

Hg and 359.8 mm Hg, respectively. The result average of the two groups was 204.2 mm Hg. Accordingly, the data were analyzed using a ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen (P/F ratio) less than 200 group and a P/F ratio greater than or equal to 200 group.

The results indicated that except for pulmonary function, the demographic variables were comparable between the two groups (**Table 1**). The results for the hemodynamic variables and peak airway pressure after an increase to additional ECMO flow indicated that there were no significant between-group differences (**Table 2**).

In the P/F ratio less than 200 group, the mean SpO_2 was 81% with no shunt flow but increased to 96%, 97%, and 99%, respectively, with the incremental increase in shunt flow from 500 to 1,500 ml/min (**Table 3**). The only statistically significant difference in SpO_2 occurred at the 1,500 ml/min shunt flow rate. Cerebral oxygen saturation was comparable between different shunt flow rates. After the left-to-right shunt flow rate was increased to 1,000 ml/min and 1,500 ml/min, PaO_2 and SaO_2 from the ascending aorta, and radial artery were significantly increased, compared with no shunt flow. After a shunt flow rate increase to 500 ml/min, between-group differences in pulmonary artery oxygen partial pressure and mixed venous oxygen saturation were statistically significant, compared with no shunt flow. At 1,500 ml/min shunt flow, the *p* values for PaO_2 from the ascending aorta and the radial artery, and for the SvO_2, were more statistically significant ($p = 0.004$, 0.007, and 0.008, respectively) than the *p* values at a 1,000 ml/min shunt flow ($p = 0.046$, 0.040, and 0.018, respectively).

Four patients with a P/F ratio greater than or equal to 200 had no significant differences in SpO_2, rSO_2, oxygen partial pressure (PO_2), and SO_2 from the proximal aorta, radial artery, and pulmonary artery.

Discussion

This study was the first to directly measure the oxygenation level near the coronary circulation during femoral-femoral VA ECMO using femoral artery-femoral vein cannulation during LTX. The study revealed that femoral-femoral VA ECMO may produce suboptimal coronary oxygenation in patients who are unable to tolerate OLV. A small left-to-right shunt using VAV ECMO can prevent differential hypoxia and maintain coronary and cerebral oxygenation.

Extracorporeal membrane oxygenation use is associated with lower heparin doses and reduced blood activating surface due to lack of a venous reservoir and additional suction lines.[3] Thus, compared with CPB, coagulopathy, and inflammatory cascades are attenuated when ECMO is used. Extracorporeal

Table 1. Patients' Characteristics

	All Patients (n = 10)	P/F Ratio < 200 (n = 6)	P/F Ratio ≥ 200 (n = 4)
Age (years)	54.7 ± 9.5	53.3 ± 12.0	56.8 ± 4.6
Sex (male/female), n (%)	7/3	5/1	2/2
Body surface area (m^2)	1.64 ± 0.19	1.63 ± 0.20	1.66 ± 0.21
Height (cm)	165.2 ± 7.7	167.2 ± 6.5	162.3 ± 9.3
Weight (kg)	59.0 ± 11.9	57.5 ± 12.6	61.4 ± 12.1
Results of transthoracic echocardiography			
Ejection fraction (%)	62.7 ± 5.5	63.3 ± 6.1	61.8 ± 5.0
E/E′	9.2 ± 2.7	8.7 ± 2.3	10.0 ± 3.6
Right ventricular systolic pressure	47.4 ± 17.3	52.8 ± 14.9	39.3 ± 19.4
Type of disease			
Idiopathic pulmonary fibrosis	8	5	3
ARDS	1	1	
COPD	1		1
Preoperative pulmonary function test			
FVC (L)	1.50 ± 0.44	1.66 ± 0.46	1.31 ± 0.38
FVC (%, predicted)	41.1 ± 8.0	44.6 ± 9.3	37 ± 3.3
FEV1 (L)	1.23 ± 0.51	1.52 ± 0.41	0.86 ± 0.37
FEV1 (%, predicted)	46.3 ± 17.1	56.6 ± 13.5	33.5 ± 11.8*
FEV1/FVC ratio (%)	81.7 ± 20.2	92.0 ± 3.1	68.8 ± 25.9*
DL_{CO} (%, predicted)	28.3 ± 9.5	25.8 ± 7.9	33.5 ± 13.4

Values are expressed as the numbers of patients with percentage, mean ± SD. *p < 0.05 compared to P/F ratio < 200 group.

ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; DL_{CO}, diffusion capacity of lung for carbon monoxide; E/E', peak early diastolic transmitral inflow velocity (E) / peak early diastolic mitral annular velocity (E'); FEV1, forced expiratory volume in one second; FVC, forced vital capacity; SD, standard deviation.

Table 2. Results of Hemodynamic Variables and Peak Airway Pressure After Increase of Additional ECMO Flow

	Additional ECMO Flow Through Right Internal Jugular Vein			
Left-to-Right Shunt Flow	0 ml/min	500 ml/min	1,000 ml/min	1,500 ml/min
P/F ratio < 200				
Heart rate	110 ± 6	111 ± 6	109 ± 10	114 ± 7
Mean arterial pressure	83 ± 8	75 ± 8	73 ± 12	74 ± 8
Mean pulmonary artery pressure	23 ± 4	21 ± 6	27 ± 8	29 ± 11
Cardiac index	3.2 ± 0.2	3.0 ± 0.4	2.8 ± 0.6	2.7 ± 0.6
Peak airway pressure	38 ± 6	32 ± 8	36 ± 7	36 ± 6
P/F ratio ≥ 200				
Heart rate	90 ± 12	88 ± 11	89 ± 11	92 ± 14
Mean arterial pressure	91 ± 24	77 ± 28	71 ± 13	75 ± 14
Mean pulmonary artery pressure	11 ± 6	13 ± 0	14 ± 3	16 ± 6
Cardiac index	2.5 ± 0.5	2.6 ± 0.6	2.6 ± 0.6	2.8 ± 0.7
Peak airway pressure	33 ± 7	36 ± 9	37 ± 8	36 ± 6

Values are expressed as mean ± SD.
ECMO, extracorporeal membrane oxygenation; SD, standard deviation.

membrane oxygenation use can easily be extended to postoperative care (*i.e.,* during postoperative graft dysfunction).[3] Because these advantages result in better outcomes,[8] some European and North American centers changed their primary intraoperative cardiopulmonary support technique from CPB to ECMO.[3–7] Since 2013, our institution has performed LTX using the peripheral ECMO technique.[15]

Peripheral VA ECMO, especially femoral-femoral VA ECMO, does not always guarantee oxygenation of distal organs. The blood coming from the ECMO meets the blood coming from the left ventricle from the opposite direction; they combine in a "mixing zone."[16,17] The left ventricular blood oxygen content is unknown, which presents a risk of profound heart and brain hypoxemia when the mixing zone is located distal to the carotid arteries. Some animal studies have found that use of peripherally cannulated ECMO systems results in adequate cerebral and coronary tissue oxygenation.[18] However, clinical studies have found that patients experience stroke and post apoplectic intracerebral bleeding or severe myocardial necrosis.[19] In addition, hypoxia causes acute hypoxic pulmonary vasoconstriction of small muscular pulmonary arteries[20] and substantially increases pulmonary vascular resistance,

Table 3. Comparison of Oxygenation at Each Site With Increasing Left-to-Right Shunt Flow Using VAV ECMO

	Additional ECMO Flow Through Right Internal Jugular Vein			
Left-to-Right Shunt Flow	0 ml/min	500 ml/min	1,000 ml/min	1,500 ml/min
P/F ratio < 200				
SpO_2	81 ± 18	96 ± 4	97 ± 4	99 ± 3*
rSO_2 (left)	47 ± 13	51 ± 7	46 ± 6	46 ± 8
rSO_2 (right)	39 ± 13	45 ± 11	40 ± 7	41 ± 5
PO_2				
Aorta	48.5 ± 14.8	78.0 ± 39.3	236.2 ± 178.9*	216.7 ± 94.2*
Radial artery	77.8 ± 69.7	93.7 ± 54.5	149.5 ± 121.5*	242.4 ± 112.4*
Pulmonary artery	37.6 ± 4.5	50.2 ± 5.7*	57.4 ± 5.3*	66.5 ± 10.9*
SO_2				
Aorta (%)	80.9 ± 11.6	93.0 ± 5.8	97.7 ± 3.8*	99.1 ± 1.2*
Radial (%)	83.3 ± 13.2	94.9 ± 3.6	96.9 ± 3.1*	99.1 ± 1.3*
SvO_2 (%)	72.4 ± 7.3	85.1 ± 3.6*	88.7 ± 4.0*	92.5 ± 2.4*
P/F ratio ≥ 200				
SpO_2	99.8 ± 0.5	98.8 ± 2.5	99 ± 2	99.8 ± 0.5
rSO_2 (left)	50 ± 5	50 ± 5	45 ± 7	44 ± 11
rSO_2 (right)	54 ± 11	49 ± 11	43 ± 8	39 ± 3
PO_2				
Aorta	359.8 ± 49.6	391.0 ± 25.0	419.1 ± 33.8	416 ± 52
Radial artery	370.1 ± 65.8	419.6 ± 28.8	398.9 ± 44.0	433.7 ± 36.9
Pulmonary artery	46.2 ± 8.6	68.6 ± 21.3	84.8 ± 28.6	94.2 ± 23.3
SO_2				
Aorta (%)	99.9	99.9	99.9	99.9
Radial (%)	99.9	99.9	99.9	99.9
SvO_2 (%)	82.7 ± 14.1	921 ± 4.1	94.6 ± 4.9	95.8 ± 2.1

Values are expressed as mean ± SD.
*$p < 0.05$ compared with the value of 0 ml/min shunt flow.
ECMO, extracorporeal membrane oxygenation; P/F, ratio of arterial oxygen partial pressure to inspired oxygen fraction; PO_2, oxygen partial pressure; rSO_2, cerebral oxygen saturation; SD, standard deviation; SO_2, oxygen saturation; SpO_2, peripheral oxygen saturation; SvO_2, mixed venous oxygen saturation; VAV, veno-arterio-venous.

eventually contributing to increased RV afterload.[21] For these reasons, femoral-femoral VA ECMO may not sufficiently mitigate the pre-existing burden of RV dysfunction if hypoxia persists, which may make difficult to wean from ECMO after surgery.

There have been some studies of alleviation of the differential hypoxia resulting from VA ECMO in the ICU setting. Stöhr *et al.*[13] found that in patients undergoing ECMO therapy for acute respiratory distress syndrome, converting to VAV ECMO from VV or VA modality conferred a survival benefit compared with the VV and VA ECMO configurations. The study by Moravec *et al.*[12] revealed that two patients with cerebral hypoxemia under VA ECMO circumstances were successfully treated after changing to VAV ECMO. Veno-arterio-venous ECMO can be a hybrid ECMO that can overcome the shortcomings of VV ECMO and VA ECMO.

Consistent with the results of animal[22,23] and clinical studies,[9,13] we found that the VAV ECMO-associated left-to-right shunt provided sufficient oxygenation in a less invasive and relatively safe manner in patients with a P/F ratio less than 200 who did not tolerate OLV during femoral-femoral VA ECMO. This can be considered as a way of inducing the redistribution of oxygen delivery rather than increasing the amount of oxygen since the total flow remains the same. Unlike the findings by Ius *et al.*[9], we found that a minimal flow of 1,000 ml/min provided sufficient oxygenation through RIJ catheter inflow. This result was consistent with the findings by Moravec *et al.*[12] that indicated that a flow of 1,200 ml/min through the additional inflow catheter provides sufficient oxygen during VAV ECMO in patients who cannot tolerate the VA or VV ECMO modalities. They recommended using a large-bore catheter (≥ 16 Fr) to maintain greater than or equal to 1,500 ml/min of additional flow in patients who require a high cardiac output through the VAV ECMO. However, if enough oxygen is supplied at a flow rate of 1,000 ml/min as in our study, it should be reconsidered whether these recommendations are necessary. The risk of hemorrhage is a disadvantage of VAV ECMO,[9,11,24] but we have found little difference between results using VAV ECMO and our previous experience with VA ECMO techniques.[15]

The reason why the rSO_2 was well maintained, despite low oxygen levels in proximal aorta, is presumably since the mixing zone was located between the proximal part of head vessels and coronary artery ostium. This suggests that cerebral oxygenation is relatively well preserved in femoral-femoral VA ECMO. This also indicates that it is not accurate to predict the SaO_2 of coronary artery by monitoring rSO_2 or ABGA of the right hand in patients receiving LTX under femoral-femoral VA ECMO. As shown in our study results, the mean PaO_2 of radial artery was 77.8 mm Hg, but the average PaO_2 of aorta level was only 48.5 mm Hg in P/F ratio less than 200 group when the left-to-right shunt flow was 0 ml/min. Therefore, even if the PaO_2 of the radial artery under VA ECMO is measured upper normal value, coronary oxygenation could be inadequate if a "watershed" is formed between the coronary artery ostium and the supra-aortic branches of the ascending aorta. There are few methods available to directly assess coronary artery oxygenation; similar to the case report by Hoeper *et al.*[25], only the TEE can be considered as a tool to assess cardiac function.

The differential hypoxia associated with peripheral VA ECMO might not occur during central VA ECMO. The central ECMO cannulation technique is structurally similar to CPB, so all organs can receive sufficient oxygenation. It also reduces groin wound complications and peripheral vascular problems. However, during LTX, central ECMO has some limitations. The drainage catheter at right atrium can interfere with the surgical field, hinder efficient operation. Furthermore, donor lung can be exposed to prolonged ischemia due to delays in the thoracic surgery steps, which are performed after initiation of central ECMO. In addition, central VA ECMO can make it difficult to maintain ECMO after surgery. In contrast, the peripherally inserted VA ECMO can reduce the ischemia and operation time and is easier to convert to postoperative ECMO support to manage primary graft dysfunction.

This study had several limitations. Although we showed that femoral-femoral VA ECMO may cause insufficient oxygenation in the cerebral or coronary circulation, we were not able to elucidate the cause of failure OLV or differential hypoxia. Preoperative lung function and cardiac function variables were not significantly different between those groups, except for forced expiratory volume in one second (FEV1) and FEV1/forced vital capacity ratio. The pathophysiologic changes that were caused by OLV (*e.g.*, intrapulmonary shunt changes or hypoxic pulmonary vasoconstriction) seem to be more relevant for explaining the differential hypoxia, compared with the results of the various preoperative examinations. Second, because the objective of this study was to identify the level of oxygenation near the coronary circulation and the effect of left-to-right shunt during LTX with VA ECMO, no follow-up and comparison was performed to evaluate postoperative heart function and graft function. Further investigation is warranted to compare the overall cardiac function before and after surgery to confirm the outcomes of VAV ECMO-provided left-to-right shunt.

In conclusion, our study revealed the presence of suboptimal coronary oxygenation using a peripheral VA ECMO application in patients unable to tolerate OLV during LTX. We suggest that creating a small left-to-right shunt using VAV ECMO is a valid method for intraoperative support of hemodynamics and respiratory function during LTX; this method prevents the differential hypoxia resulting from peripheral VA ECMO.

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