Temporary venovenous extracorporeal membrane oxygenation after cardiopulmonary bypass in minimally invasive cardiac surgery via right minithoracotomy

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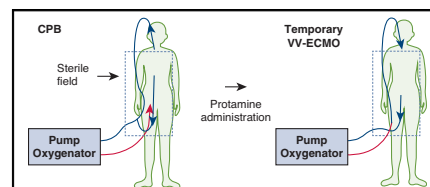
ABSTRACT

Objectives: In minimally invasive cardiac surgery, it can be difficult at times to maintain adequate oxygenation with single-lung ventilation after weaning from cardiopulmonary bypass (CPB), and intermittent double-lung ventilation is required during hemostasis. Venovenous extracorporeal membrane oxygenation (VV-ECMO) after weaning from CPB eliminates the necessity of overinflation of the left lung and intermittent double-lung ventilation and enables secure and fast hemostasis. We investigated the effectiveness and safety of temporary VV-ECMO in MICS.

Methods: Between May 2018 and March 2021, 149 patients underwent temporary VV-ECMO during minimally invasive cardiac surgery in our institutions. After weaning from CPB, the arterial circuit was reconnected to the right internal jugular venous cannula, the femoral venous cannula was pulled down by 20 cm, and VV-ECMO was established using the CPB machine and cannulas. After starting VV-ECMO, we administered protamine and performed hemostasis. Operative data and outcomes were retrospectively reviewed.

Results: The mean VV-ECMO time and flow were 26 ± 13 minutes and 2.38 ± 0.40 L/m², respectively. There was no thrombus in the CPB circuit, including the oxygenator. The trans-oxygenator pressure gradient index at the end of VV-ECMO significantly correlated with that at the start of VV-ECMO ($r = 0.88$; 95% CI, 0.79-0.94; $P = .01$). The 30-day mortality rate was 2.0%. The incidences of unilateral pulmonary edema, prolonged ventilation, and re-exploration for bleeding were 2.7%, 5.4%, and 2.0%, respectively.

Conclusions: Temporary VV-ECMO is safe and useful to maintain single-lung ventilation without overinflation after weaning from CPB for secure and fast hemostasis in minimally invasive cardiac surgery. No thrombotic event was found during temporary VV-ECMO without heparinization. (JTCVS Techniques 2023;20:99-104)

Temporary VV-ECMO after weaning from CPB to assist with single-lung ventilation.

CENTRAL MESSAGE

Temporary venovenous extracorporeal membrane oxygenation is a useful option to maintain single-lung ventilation after weaning from cardiopulmonary bypass in minimally invasive cardiac surgery.

PERSPECTIVE

Temporary venovenous extracorporeal membrane oxygenation is feasible and useful to maintain single-lung ventilation after weaning from cardiopulmonary bypass for secure and fast hemostasis in minimally invasive cardiac surgery. Thrombus formation is not clinically problematic even after neutralization of heparin.

Minimally invasive cardiac surgery (MICS) via a right minithoracotomy requires single-lung ventilation for secure hemostasis of the surgical field after weaning from cardiopulmonary bypass (CPB). However, single-lung ventilation occasionally requires overinflation of the left lung or intermittent double-lung ventilation to maintain sufficient oxygenation. Overinflation could cause lung injury, and intermittent double-lung inflation during hemostasis

Abbreviations and Acronyms
CPB   = cardiopulmonary bypass
MICS   = minimally invasive cardiac surgery
PMEA   = poly-2-methoxyethyl acrylate
TEE   = transesophageal echocardiography
trans-PG = trans-oxygenator pressure gradient
VV-ECMO   = venovenous extracorporeal membrane
            oxygenation

forces a surgeon to suspend the hemostatic procedure, which may increase the amount of bleeding and prolong the operation time. Thus, we introduced temporary venovenous extracorporeal membrane oxygenation (VV-ECMO) following CPB withdrawal and protamine administration by using the same CPB machine, circuit, and cannulas to maintain single-lung ventilation during hemostasis. Here we describe the method of temporary VV-ECMO and report operative data and outcomes.

PATIENTS AND METHODS

Between May 2018 and March 2021, 467 patients underwent MICS via a right minithoracotomy at Tokyo Bay Urayasu Ichikawa Medical Center and Toranomon Hospital. Among them, 149 patients received intraoperative temporary VV-ECMO following CPB withdrawal and protamine administration during hemostasis. The indications for temporary VV-ECMO were limited to patients with impaired respiratory function in our early experience, and then expanded to patients with normal respiratory function. During the first 20 months (from May 2018 to December 2019), we selected patients for temporary VV-ECMO by preoperative respiratory function test and intraoperative single-lung test before CPB. We implemented temporary VV-ECMO for patients with preoperative respiratory dysfunction, and those who required high-level oxygen, high airway pressure, or intermittent double-lung ventilation during single-lung ventilation test before the establishment of CPB. During this period, we recognized that this method was safe and that some patients required intermittent double-lung ventilation after weaning from CPB, although they passed preoperative and intraoperative respiratory tests. Then, during the next 15 months (from January 2020 to March 2021), we expanded the indications of this method to patients passing tests who were likely to need intermittent double-lung ventilation (eg, smoking history, obesity, anemia, and long CPB time). ECMO use in our MICS cases increased from 21% (52 out of 242 cases) in the first 20 months (from May 2018 to December 2019) to 43% (97 out of 225 cases) in the next 15 months (from January 2020 to March 2021).

We retrospectively reviewed those 149 cases and evaluated the safety of temporary VV-ECMO use in MICS via a right minithoracotomy. The institutional review board approved the study (No. 2024; June 22, 2020 at Toranomon Hospital; No. 569, July 17, 2020 at Tokyo Bay Urayasu Ichikawa Medical Center), and written informed consent was waived given the retrospective nature of this work.

Anesthesia and CPB

All cases were performed under general anesthesia. A double-lumen endotracheal tube and transesophageal echocardiography (TEE) were routinely used. A 15Fr or 17Fr cannula was percutaneously inserted into the right internal jugular vein and heparinized during anesthesia induction. The tip of the cannula was placed in the superior vena cava under TEE guidance. This cannula was extended using a curved extension tube and connected to the CPB venous circuit branch in the sterile surgical field after draping the patient. Another venous cannula (18Fr-24Fr) was inserted through the common femoral vein and placed in the right atrium, and then an arterial cannula (15Fr-21Fr) was inserted through the common femoral or right axillary artery. The CPB was established with a centrifugal pump and vacuum-assist venous drainage. For the CPB circuit, including tubing, reservoir, and oxygenator, we used the Capiox series (Terumo Corporation), which is coated with poly-2-methoxyethyl acrylate (PMEA). If the patient was unlikely to tolerate single-lung ventilation well, a minithoracotomy was made after the CPB was established. Otherwise, CPB was started before the pericardial incision. While the patient was on CPB, both lungs were deflated, and no positive end-expiratory pressure was applied during the respiratory arrest.

### VV-ECMO and Respirator Setting After CPB Weaning

After intracardiac procedures were done and the aorta was unclamped (except for some beating-heart surgery cases), double-lung ventilation was resumed during temporary CPB weaning for TEE assessment. Once favorable TEE findings were confirmed, CPB was resumed, ventilation was discontinued, and the left atrial and aortic root vents were removed. Then, single-lung ventilation was resumed, the femoral venous cannula was pulled out from the right atrium by 20 cm and moved into the inferior vena cava to avoid recirculation (Figure 1). After weaning off CPB, the arterial line was disconnected from the femoral/axillary arterial cannula and reconnected to the internal jugular vein to establish VV-ECMO using the CPB machine and circuit. The full dose of protamine was administered to neutralize heparin upon withdrawal from CPB. The reservoir was left in the ECMO circuit. The ECMO flow was maintained at 2 to 3 L/minute by monitoring the pulse oximeter and arterial blood gas. The pump inlet pressure was maintained at -30 mm Hg and higher, and the outlet pressure was kept between 180 and 220 mm Hg. Our typical ventilator setting during VV-ECMO was the pressure-regulated volume control mode with a positive end-expiratory pressure of 0-3 cm H_2O, a low tidal volume of 6 mL/kg (or low inspiratory pressure <20-25 cm H_2O), a respiratory rate of 8 to 10 breaths per minute, and a fraction of inspired oxygen of 1.0. We used auxiliary nitric oxide inhalation for patients with impaired respiratory function or right ventricular dysfunction. After all the intrathoracic procedures, including hemostasis, pericardial closure, chest tube placement, and irrigation were done, we resumed double-lung ventilation and discontinued VV-ECMO.

Data Collection and Definition

Preoperative patient characteristics, operative details and perioperative outcomes were retrieved from the electronic medical records at 2 hospitals. We also collected detailed VV-ECMO data, including pre- and postoxygenator pressure, trans-oxygenator pressure gradient (trans-PG), ECMO flow, and trans-PG index (ie, trans-PG/ECMO flow). Unilateral pulmonary edema was defined as a new unilateral pulmonary edema on chest radiography and computed tomography after the operation. Prolonged ventilation was defined as mechanical ventilation support for 48 hours or longer after surgery. A stroke was defined as an acute episode of focal or global neurological dysfunction lasting more than 24 hours and confirmed by neuroimaging procedures, and/or neurologists or neurosurgical specialists. Perioperative myocardial infarction was defined as new ischemic symptoms or new ischemic signs, and elevated cardiac biomarkers (preferable creatine kinase-MB fraction) within 72 hours after the index procedure, consisting of at least 1 sample postprocedure with a peak value exceeding 5 times the upper reference limit for creatine kinase-MB fraction. Acute kidney injury was defined as a postoperative creatinine >2.0 mg/dL, more than double the preoperative level, or requiring new dialysis.

Statistical Analysis

Changes in the trans-PG index were compared using linear mixed-effect models with random intercepts. Estimations of 95% CI were based on 1000
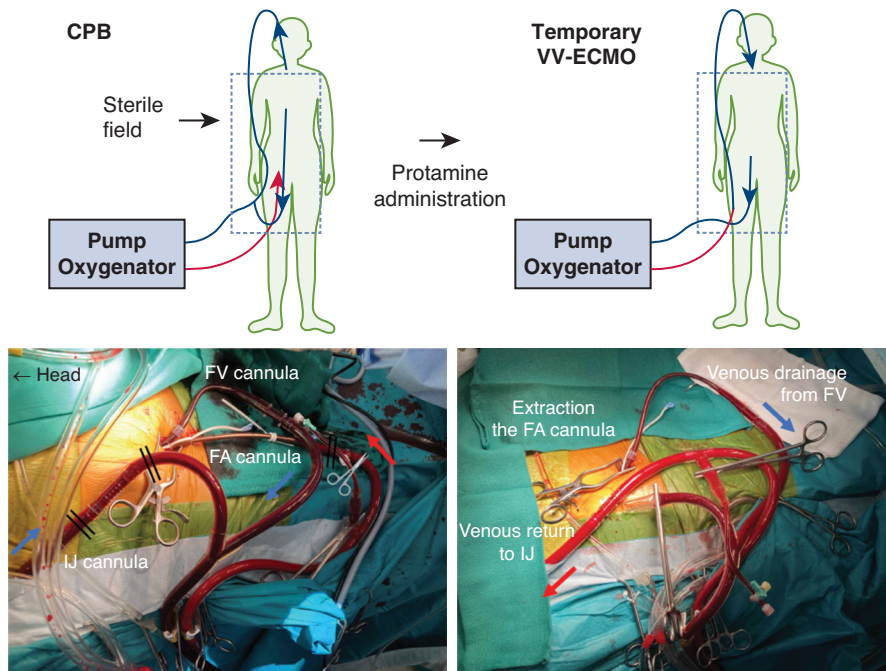
FIGURE 1. Overview of the cardiopulmonary bypass (*CPB*) and venovenous extracorporeal membrane oxygenation (*VV-ECMO*) circuits. The upper panel illustrates the transition from a regular CPB to VV-ECMO. *Red and blue lines* indicate the arterial and venous circuits, while the *arrow* coincides with the direction of blood. Two venous cannulae inserted from the right internal jugular (*IJ*) vein and femoral vein (*FV*) are used to establish a VV-ECMO. After weaning off CPB, we reconnect the arterial tube to the IJ vein cannula (*lower panels*). To avoid recirculation, the FV cannula is pulled out about 10 to 20 cm. *FA*, Femoral artery.

bootstrap samples.[1] For associations, we used a 2-sided test. All analyses were performed with the SPSS statistical package version 25.0 (IBM-SPSS Inc).

Ethical Statement

The institutional review board approved the study (No. 2024. June 22, 2020 at Toranomon Hospital; No. 569, July 17, 2020 at Tokyo Bay Urayasu Ichikawa Medical Center), and written informed consent was waived given the retrospective nature of this work.

RESULTS
Patient Background and Operative Data

Baseline characteristics are summarized in Table 1. The mean age was 64 years, and women accounted for 47%. Spirometry pulmonary function tests showed a restrictive pattern in 34% of patients and an obstructive pattern in 21%. The operative data are shown in Table 2. The majority of procedures were mitral valve surgery (84%) with a mean CPB time of 149 minutes and aortic crossclamp time of 101 minutes. Beating heart surgery without aortic crossclamping was performed in 11 patients who had poor ventricular function or a history of previous cardiac surgery.

VV-ECMO

The mean VV-ECMO time was 26 ± 13 minutes, with a range of 6 to 74 minutes. The flow rate during VV-ECMO averaged 2.4 ± 0.4 L/min/m^2. The lowest oxygen saturation

during VV-ECMO averaged $95.6\% \pm 4.1\%$. One patient (0.7%) required double-lung ventilation during VV-ECMO. We did not experience increased perfusion pressure, thrombus formation in the ECMO circuit, or need for the ECMO circuit exchange in any patients. All patients were successfully weaned from VV-ECMO. No significant change was observed in the indexed trans-PG during VV-ECMO (Figure 2).

Operative Outcomes

Operative outcomes are shown in Table 3. Three patients died within 30 days after surgery. The causes of death included multiple organ failure due to severe left ventricular dysfunction after emergency mitral valve replacement for acute mitral regurgitation with cardiogenic shock, ventricular wall rupture after redo mitral valve replacement, and nonobstructive mesenteric ischemia after mitral valve repair in a high-risk patient. No death was related to intraoperative VV-ECMO. Unilateral pulmonary edema occurred in 4 patients, but because the severity of pulmonary edema was relatively mild, all 4 patients made a full recovery after respiratory management with high positive end-expiratory pressure for a few days. Eight patients required long-term mechanical ventilation (>48 hours). There were 3 cases requiring re-exploration for bleeding. Two of them had postoperative coagulopathy due to

TABLE 1. Patient Characteristics

Variable	Result
Age (y)	64 ± 14
Female	71 (47.7)
Body surface area (m^2)	1.7 ± 0.2
Hypertension	65 (43.6)
Atrial fibrillation	66 (44.3)
Estimated glomerular filtration rate (mL/min/1.73 m^2)	64 ± 21
NYHA class III or IV	17 (11.4)
Left ventricular ejection fraction (%)	60 ± 10
Spirometry*	
FEV1 (% predicted)	
< 30%	0
30%-50%	3 (2.7)
50%-70%	34 (30.9)
>70%	73 (66.4)
Forced vital capacity (% predicted)	
<25%	0
25%-50%	1 (0.9)
50%-75%	20 (18.2)
> 75%	89 (80.9)
EuroSCORE II (%)	2.7 ± 4.8

Values are presented as n (%) or mean ± SD. *NYHA*, New York Heart Association; *FEV$_1$*, forced expiratory volume in 1 second; *EuroSCORE II*, European System for Cardiac Operative Risk Evaluation II. *Number of patients with data available was 110.

TABLE 2. Operative data

Variable	Result
Procedure	
Mitral valve surgery	
Isolated	69 (46.3)
Combined	56 (37.6)
Tricuspid valve surgery	38 (25.5)
Maze or PV isolation	26 (17.4)
Others	1 (0.7)
Isolated tricuspid valve surgery	13 (16.1)
Others	11 (7.4)
Cannular size	
Femoral vein (Fr)	
18	6 (4.0)
20	29 (19.5)
22	68 (45.6)
24	46 (30.9)
Internal jugular vein (Fr)	
15	108 (72.5)
17	41 (27.5)
Total operation time (min)	218 ± 50
Duration of cardiopulmonary bypass (min)	149 ± 45
Duration of aortic crossclamping (min)	101 ± 46
Intraoperative blood transfusion	56 (37.6)

Values are presented as n (%) or mean ± SD. *PV*, Pulmonary vein.

postoperative venoarterial ECMO and intra-aortic balloon pump support. The other patient developed bleeding after the removal of temporary ventricular lead on postoperative day 2, and this patient was receiving intravenous heparin for a mechanical prosthetic valve. Neither of these postoperative bleeding complications was associated with temporary VV-ECMO. There was no patient with postoperative stroke or myocardial infarction.

DISCUSSION

To the best of our knowledge, this is the first report of intraoperative temporary VV-ECMO use during hemostasis after CPB weaning in minimally invasive cardiac surgery. Conversion from CPB to VV-ECMO was quick and simple, not requiring any additional equipment or major modification of the CPB circuit in our setting.

One major concern of our method is potential thromboembolism or hemorrhagic events, which are associated with the excessive activation of the coagulation/fibrinolysis system, complement cascades, and contact phase system secondary to VV-ECMO use after protamine administration. The safety of VV-ECMO for respiratory failure under low-dose anticoagulant therapy has been proposed.[2,3] Kurihara and colleagues[4] reported VV-ECMO without anticoagulation and there was no significant difference in survival rate in the group without anticoagulation compared with the group with anticoagulation. Rather, there was less gastrointestinal bleeding, oxygenator exchange, and blood transfusion in the group without anticoagulation therapy. However, there are no reports of VV-ECMO after CPB weaning and protamine administration in cardiac surgery. In our clinical experience of temporary VV-ECMO, there were no cases of oxygenation failure, clot/thrombus in the circuit, or circuit exchange during VV-ECMO, and no cases of postoperative stroke or myocardial infarction. Furthermore, there was no significant change in the indexed trans-PG during VV-ECMO. The oxygenator has an integrated filter that can catch thrombi larger than 32 μm, so if a thrombus forms in the circuit, the indexed trans-PG is expected to increase. An arterial filter prevents potential pulmonary thrombosis, and we only need to discontinue VV-ECMO and resume double-lung ventilation if any problems arise in the oxygenator or ECMO circuit. Thus, we believe that there is no primary concern about the safety of our method, and it may be a new option for VV-ECMO.

We used an open circuit with a blood reservoir. This can regulate the circulating blood volume and maintain stable ECMO flow. However, the risk of formation of thrombi in the circuit still deserves consideration. There is no doubt that the successful use of temporary VV-ECMO benefited from the excellent coating technologies for extracorporeal circulation. We used the CPB circuit coated by PMEA.
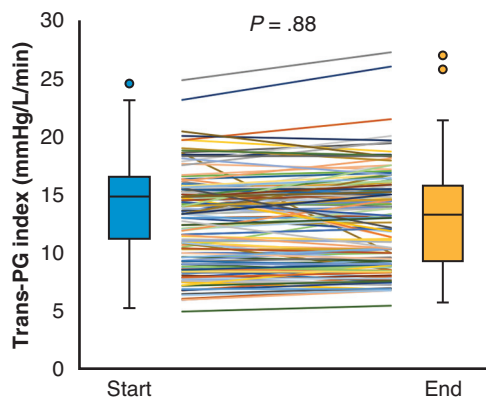
FIGURE 2. Change of trans-oxygenator pressure gradient (*trans-PG*) index during venovenous extracorporeal membrane oxygenation (VV-ECMO) in overall patients. No significant changes were observed in the trans-PG index between the start and the end of VV-ECMO. The *P* values were based on the linear mixed-effect model. Lines trace the values at the start and at the end of VV-ECMO for each patient. *Boxes* contain the lower and upper quartiles, whereas *whiskers* represent the minimum and maximum values of nonoutliers. *Extra dots* represent outliers, which are located outside 1.5 times the interquartile range above the upper quartile and below the lower quartile.

PMEA has been reported to have platelet- and protein-sparing and anti-inflammatory effects, and to and exhibit excellent biocompatibility noninferior to the heparin coating.[5-9]

Ventilator-induced lung injury, including unilateral pulmonary edema, is an infrequent but potentially lethal complication after the lateral minithoracotomy approach. Although the causes are still unclear, repetitive collapse and inflation of the lung, overdistension, and increased airway pressures are possible mechanisms underlying ventilator-induced lung injury.[10-12] For example, suppose the respiratory condition deteriorates while relying on single-lung ventilation: In that case, anesthesiologists

TABLE 3. Operative outcomes

Pulmonary	Result
Unilateral pulmonary edema	4 (2.7)
Mechanical ventilation for >48 h	8 (5.4)
Pneumonia	3 (2.0)
Re-exploration for bleeding	3 (2.0)
Postoperative stroke	0 (0.0)
Perioperative myocardial infarction	0 (0.0)
Postoperative new atrial fibrillation	26 (17.4)
Acute kidney injury	12 (8.1)
Postoperative ICU stay (d)	1 (1, 2)
30-d mortality	3 (2.0)

Values are presented as n (%) or median (25th, 75th percentiles). *ICU*, Intensive care unit.

need to increase the ventilation volume and pressure. In some situations, excessive pressure stress must be applied to the lungs. Temporary VV-ECMO can eliminate the possibility of falling into such a situation. Just as we reduced tidal volume and kept ventilation pressure low while using VV-ECMO, it may reduce the risk of ventilation-induced lung injury. Anesthesiologists have a lot of things to do after weaning from CPB, such as respiratory management, hemodynamic management, coagulation control, and TEE assessment. Temporary VV-ECMO frees anesthesiologists from respiratory management, which we think is among the benefits of this method.

Some studies reported that long CPB time and long surgery were risk factors for unilateral pulmonary edema after minimally invasive cardiac surgery.[13-16] It could be considered that long CPB time and long surgery may result in unilateral pulmonary edema due to longer single-lung ventilation time. Because one must consider the possibility that the use of temporary VV-ECMO may prolong single-lung ventilation without intermittent double-lung ventilation, increasing the risk of causing unilateral pulmonary edema, we make sure to perform double-lung ventilation during TEE assessment before complete discontinuation of CPB. In our study, the incidence of unilateral pulmonary edema was 2.7% (4 out of 149) and all of those cases had mild pulmonary edema. The reported incidence of unilateral pulmonary edema after minimally invasive cardiac surgery is between 1.6% and 25%.[13-16]

There are several limitations in the present study. First, this was a single-arm study with no control group. We did not compare the outcomes of this cohort with those of patients undergoing minimally invasive cardiac surgery without VV-ECMO, because the patients' and operation profiles differed greatly between the 2 groups. Additionally, we did not conduct a hematologic or microscopic examination to check the effect of ECMO on the coagulation/fibrinolysis system and the complement cascade.

A future task is to build hematologic evidence for VV-ECMO use. Specifically, the changes over time in the following measurements should be compared between patients who use and those who do not use temporary VV-ECMO: β-thromboglobulin or platelet IV, which are markers for platelet activation and degranulation; glycoprotein Ib as a platelet membrane disorder marker; and thrombin/antithrombin III complex or fibrin monomer as a thrombin formation marker. In addition, it is also necessary to investigate the plasmin/α2-plasmin inhibitor complex; fibrin/fibrinogen degradation product; or D-dimer as a marker for fibrinolysis, and C4, C2, C3, C5, and CH50 as a marker for complement activation. We also hope that issues regarding the permissible time of VV-ECMO, appropriate flow rate, and hematocrit value, will be investigated in the near future.

CONCLUSIONS

Temporary VV-ECMO is a helpful option to assist with single-lung ventilation after weaning from CPB in lateral minithoracotomy for cardiac surgery. Thrombus formation is not clinically problematic even after protamine administration.

Conflict of Interest Statement

Dr Tabata is a consultant for Terumo Corporation. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of insterest.

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