**의학석사 학위논문**

# 체외 막 산소요법을 시행한 환자에서 체외 막 산소요법 연관 합병증이 병원 내 사망률에 미치는 영향

**Impact of Extracorporeal membrane oxygenation-related complications on in-hospital mortality of Extracorporeal membrane oxygenation patients**

**울산대학교 대학원**

**의학과**

**이상아**

# Impact of Extracorporeal membrane oxygenation-related complications on in-hospital mortality of Extracorporeal membrane oxygenation patients

지도교수 조용필

이 논문을 의학석사 학위 논문으로 제출함

2022년 2월

울산대학교 대학원

의학과

이상아

이상아의 의학석사 학위 논문을 인준함

심사위원 이승환 인

심사위원 조용필 인

심사위원 정성호 인

울산대학교 대학원

2022년 2월

**Abstract**

**Objective:** To assess the predictors of extracorporeal membrane oxygenation (ECMO)-related vascular and cerebrovascular complications among adult patients and to test the hypothesis that ECMO-related complications are associated with higher in-hospital mortality rates.

**Summary Background Data:** Although ECMO is a well-established treatment for supporting severe cardiopulmonary failure, the morbidity and mortality of patients requiring ECMO support remain high. Evaluating and correcting potential risk factors associated with any ECMO-related complications may improve care and decrease mortality.

**Methods:** This single-center, retrospective study included 856 ECMOs administered via cannulation of the femoral vessels of 769 patients: venoarterial (VA) ECMO (n = 709, 82.8%) and venovenous (VV) ECMO (n = 147, 17.2%). The study outcomes included the occurrence of ECMO-related vascular and cerebrovascular complications and in-hospital death. The association of ECMO-related complications with the risk of in-hospital death was analyzed.

**Results:** The incidences of ECMO-related vascular and cerebrovascular complications were 20.2% and 13.6%, respectively. The overall in-hospital mortality rate was 48.7%: 52.8% among VA ECMOs and 29.3% among VV ECMOs. Multivariable analysis indicated that age ($P < 0.01$), cardiopulmonary cerebral resuscitation ($P < 0.01$), continuous renal replacement therapy ($P < 0.01$), and initial platelet count [$< 50 \times 10^3/\mu L$ ($P = 0.02$) and $50–100 \times 10^3/\mu L$ ($P < 0.01$)] were associated with an increased risk of in-hospital death. ECMO-related vascular and cerebrovascular complications were not independently associated with higher in-hospital mortality rates among either VA or VV ECMOs.

**Conclusions:** ECMO-related vascular and cerebrovascular complications were not associated with an increased risk of in-hospital death among adult patients.

**ABBREVIATIONS AND ACRONYMS**

AVF = arteriovenous fistula; CPCR = cardiopulmonary cerebral resuscitation; CKD = chronic kidney disease; CT = computed tomography; CRRT = continuous renal replacement therapy; CAD = coronary artery disease; DVT = deep venous thrombosis; ECLS = extracorporeal life support; ECMO = extracorporeal membrane oxygenation; ECPR = extracorporeal cardiopulmonary resuscitation; Hb = hemoglobin; MCS = mechanical circulatory support; PAOD = peripheral arterial occlusive disease; PLT = platelet; VA = venoarterial; VV = venovenous

**Contents**

**List of figures and tables**

## Introduction

Recent technical advances have led to increasingly wider adoption of extracorporeal membrane oxygenation (ECMO) for temporary mechanical cardiopulmonary support for patients whose heart and lungs can no longer provide adequate physiologic support.[1–5] ECMO can be either venoarterial (VA) for systemic circulatory support—oxygenation and circulatory support—or venovenous (VV) for gas exchange without hemodynamic support—oxygenation only.[1–3] Currently, ECMO is a well-established treatment for temporarily supporting patients with severe cardiopulmonary failure. However, despite increasing experience with ECMO and recent technical improvements, the morbidity and mortality among patients undergoing ECMO support remain high. Vascular and cerebrovascular complications during ECMO support—with reported rates of 30% to 60% of patients[7–9]—are common among high-risk patient, including those who are critically ill, exposed to anticoagulation, and susceptible to coagulopathy and platelet (PLT) dysfunction.[6] These complications can arise from various contributing factors.[10–13]

We aimed to identify predictors of ECMO-related vascular and cerebrovascular complications among adult patients and to test the hypothesis that ECMO-related complications are associated with an increased risk of in-hospital death.

## Methods

### *Study Design and Study Sample*

In this single-center, retrospective, observational study, we analyzed the data extracted from the prospectively collected ECMO registry of the patients ≥18 years of age who underwent ECMO at our hospital to support severe cardiac and/or pulmonary failure. Further clinical details were obtained from retrospective reviews of patient medical records.

Between January 2015 and December 2019, 868 ECMO patients were screened for inclusion in this study. The exclusion criteria were as follows: (1) ECMO implanted at other hospitals (n = 50), (2) only central ECMO implantation without peripheral cannulation (n = 40), and (3) ECMO running time less than 20 minutes (n = 9).[3,10,11] Our analysis was not performed on a per-patient basis but on a per ECMO basis. Among included patients, 9 underwent both VA and VV ECMOs and were included in both the VA and VV ECMO groups. A total of 856 ECMOs—administered via cannulation of the femoral vessels—from 769 patients were included in the final analysis. Eligible ECMO procedures were stratified into 2 groups according to the mode of ECMO: VA ECMO (n = 709, 82.8%) and VV ECMO (n = 147, 17.2%) (**Figure 1**).

For all consecutive patients, we entered the following data into an Excel (Microsoft Corp., Redmond, WA, USA) database for retrospective analysis: demographics, underlying diseases, risk factors of

interest (including history of cardiovascular disease and interventions), clinical characteristics, laboratory profiles, indications for ECMO support, ECMO-related complications, in-hospital deaths, and causes of death. We alsdo collected and analyzed ECMO data from the ECMO records: running time, cannula size, and placement of distal perfusion catheter.

***Study Protocol Approvals, Registrations, and Patient Consent***

Approval for data collection and publication was obtained from the institutional review board at our hospital (IRB No. 2020-0793), which waived the requirement for written informed consent because of the study's retrospective design. All methods were performed in accordance with the relevant guidelines and regulations.

***ECMO Protocol***

ECMO was administered using a standard protocol.[4,14–17] Because of the heterogeneity of our study sample, there were no predefined indications for ECMO support. The decision to administer ECMO was made by each physician but usually followed general recommendations in the Extracorporeal Life Support Organization (ELSO) guidelines.[16,17] In most, if not all, cases, the cannulation was performed using a percutaneous technique, preferably guided by ultrasonography. If percutaneous cannulation failed, direct cut down cannulation was done. The heparin bolus was given at any time after the main wire was placed. Two ECMO systems were used—the QUADROX PLS System (Maquet Cardiopulmonary AG, Rastatt, Germany) and the CAPIOX EBS System (Terumo Cardiovascular Systems Corporation, Tokyo, Japan)—with each system having its own oxygenator, pump, and console. Most patients were anticoagulated with unfractionated heparin except those who had contraindications for heparinization. The target range of activated clotting time and activated partial thromboplastin time on ECMO were 150 to 180 seconds and 60 to 80 seconds, respectively. ECMO weaning could be considered if the level of oxygen or carbon dioxide was adequate without any evidence of low cardiac output after 1 to 2 hours of interruption of gas flow in VV ECMO or with low ECMO flow (< 1.5 L/min), low gas flow (< 2 L/min), and ECMO $FiO_2$ 30 to 40%, and after 5 minutes of pump controlled retrograde trial off in VA ECMO.

***Definitions and Study Outcomes***

The study outcomes included the occurrence of ECMO-related vascular (defined as thromboembolic, bleeding, deep venous thrombosis [DVT], and cannula-related local vascular complications) and cerebrovascular complications, and in-hospital death. Thromboembolic complications—both in the patient or the circuit—were defined as a medical diagnosis of limb ischemia, intracardiac or aortic thrombosis, or visible thrombosis of the oxygenator and circuits.[1,4] Bleeding complications were defined as loss of more than 2 g/dL hemoglobin (Hb) in 24 hours or a bleeding rate of more than 20 mL/kg/d, blood transfusion more than 10 mL/kg/d, or any bleeding requiring radiologic intervention or

surgical treatment.[4] DVT was defined as a medical diagnosis of venous thrombosis using ultrasonography or computed tomographic (CT) scan, or pulmonary embolism using CT angiography of the pulmonary arteries or a ventilation-perfusion lung scan. Cannula-related local vascular complications included pseudoaneurysm, arteriovenous fistula, and arterial dissection. Cerebrovascular complications were defined as either embolic or hemorrhagic strokes reported on CT scan with no other potential cause, confirmed by an expert neurologist.[6]

Data on all outcomes were centrally reviewed and blindly adjudicated by 2 experienced independent physicians. For quality control, second reviews were conducted by other physicians blinded to the original adjudicated results. Every event of each outcome was analyzed individually. Then, the association of ECMO-related vascular and cerebrovascular complications with the risk of in-hospital death was analyzed.

***Statistical Analysis***

Continuous variables are reported as mean and standard deviation or median and interquartile range based on their distribution. Categorical variables are presented as count and proportion (%). All of the outcomes were binary variables; thus, multivariable logistic regression was used to investigate the explanatory variables and outcomes. To account for the clustering effect within each patient, we used the generalized estimation equation method to make inferences about the regression coefficients. To select the variables to be included in the multivariable model, we considered the statistical significance ($P < 0.1$) from the univariable analysis, clinical knowledge, multicollinearity between the variables, as well as the parsimony of the model to avoid overfitting. $P$ values $\leq 0.05$ were considered statistically significant for individual tests. All analyses were conducted using R 4.0.4 (R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/).

## Results

***Clinical Characteristics and Outcomes***

Among the study sample of 856 ECMOs, the VA ECMO group consisted of 709 ECMOs (82.8%), and the VV ECMO group consisted of 147 ECMOs (17.2%). The baseline and clinical characteristics of the study sample are presented in **Table 1**. Four-hundred sixty-one of 856 ECMOs (53.9%) were successfully weaned, and the weaning rate was significantly higher in the VV ECMO group (51.6% vs 64.6%, $P < 0.01$). The in-hospital mortality rate was 48.7% (52.8% in VA ECMO group and 29.3% in VV ECMO group, $P < 0.01$). Although patients in the VA ECMO group were more likely to have medical comorbidities than those in the VV ECMO group, the mean durations of hospitalization and intensive care unit admission were longer in the VV ECMO group. The incidences of ECMO-related vascular and cerebrovascular complications were 20.2% and 13.6%, respectively. The rate of ECMO-

related vascular complications was significantly higher in the VA ECMO group (21.7% vs 12.9%, $P$ = 0.02), whereas there was no significant difference in the incidence of ECMO-related cerebrovascular complications between the 2 groups (14.5% vs 8.8%, $P$ = 0.09) (**Table 2**). For the analyses of the individual components of ECMO-related vascular complications, the rate of thromboembolic complications was significantly higher in the VA ECMO group (7.3% vs 1.4%, $P$ = 0.01), and there was no significant difference in the bleeding (9.2% vs 8.2%, $P$ = 0.82) and DVT (2.0% vs 2.0%, $P$ > 0.99) rates between the 2 groups. Limb ischemia (n = 54) was the only thromboembolic complications, and in the VA ECMO group, we had to perform 6 major amputations (6/709, 0.8%) because of limb ischemia. An antegrade distal perfusion catheter to augment extremity perfusion was selectively placed in 31.6% of the VA ECMOs (224/709) for patients with peripheral arterial occlusive disease (PAOD) or in whom we suspected limb ischemia after ECMO implantation; 10.3% of these patients (23/224) eventually developed limb ischemia, among whom we performed 5 major amputations. Despite the higher rates of in-hospital death and ECMO-related complications in the VA ECMO group, there was no difference in the rate of in-hospital death caused by ECMO-related complications between the 2 groups (6.1% vs 2.3%, $P$ = 0.49) (**Table 1**). According to the indications for ECMO support, the in-hospital mortality rates are presented in **Supplemental Table 1**.

***Variables Associated With ECMO-related Vascular and Cerebrovascular Complications***

Multivariable analysis adjusting for confounding variables indicated that PAOD (odds ratio [OR], 3.28; 95% confidence interval [CI], 1.02–10.58; $P$ = 0.047) and ECMO running time (OR, 1.02; 95% CI, 1.01–1.03; $P$ < 0.01) were negative independent risk factors for ECMO-related vascular complications associated with VA ECMO, whereas past history of coronary artery disease (CAD) (OR, 0.93; 95% CI, 0.88–0.99; $P$ = 0.03) had a protective effect on the occurrence of vascular complications (**Table 3**). In terms of the incidence of the individual components of ECMO-related vascular complications associated with VA ECMO, age (OR, 0.98; 95% CI, 0.95–1.00; $P$ = 0.02) and continuous renal replacement therapy (CRRT) (OR, 5.27; 95% CI, 1.66–16.77; $P$ < 0.01) were associated with an increased risk of thromboembolic complications (**Supplemental Table 2**), whereas ECMO running time (OR, 1.01; 95% CI, 1.00–1.02; $P$ < 0.01), arterial cannula size (OR, 0.79; 95% CI, 0.63–0.99; $P$ = 0.04), initial Hb level < 8.0 g/dL (OR, 4.19; 95% CI, 2.21–7.96; $P$ < 0.01), and PLT count (50–100 × $10^3/\mu L$) (OR, 2.07; 95% CI, 1.13–3.79; $P$ = 0.02) were associated with bleeding complications (**Supplemental Table 3**). For VV ECMO, the univariable analysis identified that female sex (OR, 2.99; 95% CI, 1.01–8.86; $P$ = 0.048), past history of chronic kidney disease (CKD) (OR, 0.00; 95% CI, 0.00–0.00; $P$ < 0.01), ECMO running time (OR, 1.02; 95% CI, 1.01–1.04; $P$ < 0.01), and initial Hb level < 8.0 g/dL (OR, 4.93; 95% CI, 1.21–20.07; $P$ = 0.03) were associated with an increased risk of ECMO-

related vascular complications (**Supplemental Table 4**). The low number of events (n = 19) precluded the execution of multivariable analysis.

The univariable analysis for the incidence of ECMO-related cerebrovascular complications associated with VA ECMO identified no significant risk factors (**data not shown**). For the variables associated with ECMO-related cerebrovascular complications in VV ECMO, univariable analysis indicated diabetes mellitus (OR, 3.80; 95% CI, 1.10–13.15; $P = 0.04$), PAOD (OR, 0.00; 95% CI, 0.00–0.00; $P < 0.01$), past history of CKD (OR, 7.59; 95% CI, 1.87–30.75; $P < 0.01$), and cardiopulmonary cerebral resuscitation (CPCR) (OR, 0.00; 95% CI, 0.00–0.00; $P < 0.01$) were independent predictors of an increased risk of cerebrovascular complications (**Supplemental Table 5**): multivariable models could not be performed due to the low number of events (n = 13).

***Association Between ECMO-related Complications and the Risk of In-hospital Death***

Among a total of 856 ECMOs from 769 patients, the overall in-hospital mortality rate was 48.7% (417/856): 52.8% among VA ECMOs (374/709) and 29.3% among VV ECMOs (43/147). For both VA and VV ECMOs, multivariable analysis indicated that age (OR, 1.03; 95% CI, 1.01–1.04; $P < 0.01$), CPCR (OR, 1.42; 95% CI, 1.12–1.79; $P < 0.01$), CRRT (OR, 3.57; 95% CI, 2.59–4.93; $P < 0.01$), initial PLT count $< 50 \times 10^3/\mu L$ (OR, 1.60; 95% CI, 1.10–2.33; $P = 0.02$) and initial PLT count $50–100 \times 10^3/\mu L$ (OR, 1.24; 95% CI, 1.07–1.44; $P < 0.01$)] were associated with higher in-hospital mortality rates (**Table 4**). Among VA ECMOs, multivariable analysis indicated that age (OR, 1.02; 95% CI, 1.01–1.04; $P < 0.01$), CRRT (OR, 2.93; 95% CI, 2.06–4.17; $P < 0.01$), and initial PLT count ($50–100 \times 10^3/\mu L$) (OR, 1.64; 95% CI, 1.06–2.54; $P = 0.03$) were negative independent risk factors for in-hospital death (**Table 5**), whereas among VV ECMOs, age (OR, 1.03; 95% CI, 1.00–1.06; $P = 0.03$) and CRRT (OR, 5.48; 95% CI, 2.46–12.23; $P < 0.01$) were associated with an increased risk of in-hospital death (**Table 6**). In these analyses for all ECMOs, VA ECMOs, and VV ECMOs, ECMO-related vascular and cerebrovascular complications were not associated with higher in-hospital mortality rates.

## Discussion

Although ECMO is a complex and high-risk therapy,[18,19] this modality has been increasingly adopted after the landmark CESAR (Conventional Ventilatory Support versus Extracorporeal Membrane Oxygenation for Severe Adult Respiratory Failure) trial, in which ECMO appeared to be superior to ventilator use in the adult population.[19] Whereas VV ECMO replaces failing lungs, VA ECMO replaces both the heart and lungs. To date, few randomized controlled trials have investigated ECMO administration for critically ill patients, and the evidence supporting current ECMO guidelines is weak[20]; however, the indications for ECMO support have continued to evolve over the past decade.[3] Regarding VA ECMO, the primary indication has shifted from post-cardiotomy shock to multifactorial cardiogenic

shock and/or cardiac arrest.[3] The proportion of post-cardiotomy shock patients supported by VA ECMO decreased from 56.9% in 2002 to 37.9% in 2012. During this same period, the number of adult patients with cardiopulmonary failure supported by VA ECMO substantially increased.[21] VV ECMO is mainly used to support patients who suffer from severe acute respiratory distress syndrome[22] or as a bridging strategy to lung transplantation.[23] In our analysis, the proportion of post-cardiotomy shock patients supported by VA ECMO was 20.3%, and there were various other indications for ECMO support.

Despite increasing experience with ECMO and recent technical advances, the morbidity and mortality of patients receiving ECMO remain high, with variations between centers, patient subgroups, and indications.[6,24,25] ECMO outcome are influenced not only by factors independent of ECMO (severity and type of patient illness, and other organ support) but also by potential ECMO-related complications.[6] Evaluations and clarification of the impact of correctable ECMO-related complications on outcomes could inform safer care and improve outcomes. However, because of the lack of randomized trials, observational series may provide some useful information on factors associated with morbidity and mortality.

ECMO-related complications may be mechanical (relating to the ECMO circuit components) or medical.[26] Recent technical improvements—the introduction of centrifugal pumps, low-resistance polymethylpentene membranes, and modern heparin-coated surfaces, for example—could reduce mechanical complications and hemolysis, but medical complications frequently occur, including vascular and neurological complications.[6] In our analysis, for both modes of ECMO, ECMO-related vascular complications were the commonest, followed by cerebrovascular complications.

For ECMO support, cannulation under systemic anticoagulation with a large cannula is critically important and known to be associated with vascular complications, particularly among small women or in association with high systemic vascular resistance.[3] In our study, for VA ECMOs, PAOD and ECMO running time were negative independent risk factors for ECMO-related vascular complications associated with VA ECMO, whereas past history of CAD had a protective effect on the occurrence of vascular complications, maybe due to previous use of antiplatelet agents or statins. It is generally stated that unless the vessel is at least 1 to 2 mm larger than the cannula in arterial cannulation for VA ECMO, there is an increased risk of limb ischemia; however, the size of the cannula required for ECMO cannulation is not clearly defined in currently available publications, and it is usual practice to select a cannula that will yield optimal support for a given patient.[3] Currently, the use of prophylactic antegrade perfusion catheters is recommended to reduce the incidence of limb ischemia[27,28]; Lamb et al.[27] found that 0 of 55 patients with distal perfusion catheters placed prophylactically developed limb ischemia, and Juo et al.[28] calculated a relative risk ratio of 0.41 with a distal perfusion catheter in a meta-analysis. In our study, we selectively used a distal perfusion catheter in 31.6% of VA ECMOs (224/709) for high-

risk patients with limb ischemia, and 10.3% of them (23/224) eventually developed limb ischemia. Among the 485 ECMOs that did not use distal perfusion catheters, there was a 6.0% limb ischemia rate (29/485). Further studies are needed to better understand the role of an antegrade catheter for augmenting extremity perfusion in the prevention of limb ischemia.

Patients under ECMO support are typically anticoagulated and prone to bleeding. For optimal blood oxygen saturation, Hb should be maintained between 8 and 10 g/dL,[3] and transfusions may be required. Bleeding complications, ranging in incidence from 10 to 30%,[6,29,30] are treated by reducing the dosage of heparin (or direct thrombin inhibitor) or stopping anticoagulation. A previous study suggested that it is safe to stop anticoagulation for up to 3 days in circumstances of anticoagulation intolerance.[31]

The causes of cerebrovascular complications—ischemic and hemorrhagic strokes—are multifactorial, with thromboembolic events, systemic anticoagulation, and hemodynamic instability thought to contribute.[32] The presence of the circuit adds risk secondary to particles, bubbles, or emboli, which may be inadvertently infused into the arterial circuit. Furthermore, thrombi can form spontaneously in the left atrium and left ventricle due to the low-flow state. The incidence of neurological complications reported in the literature is highly variable (between 4% and 37%).[6,32] It may vary by ECMO indications, types of cannulation, and patient comorbidities.

Given the different indications for ECMO support and the diversity of each patient's underlying disease, deaths among ECMO patients are usually multifactorial; potential predictors of death include older age, female sex, longer support time, decreased cardiac function at baseline,[33] high lactate concentration, peripheral vascular disease, chronic obstructive lung disease, renal dysfunction,[34,35] stroke, infection, hypoglycemia, alkalosis,[36] device insertion during CPCR, and decreased urine output.[37] In our study, we found that ECMO-related vascular and cerebrovascular complications are common: 20.2% and 13.6% of ECMOs were associated with ECMO-related vascular and cerebrovascular complications, respectively. Older age, CPCR, CRRT, and initial PLT count were associated with higher in-hospital mortality rates. However, similar to the previous study by Bisdas et al.,[38] which found that vascular complications were not associated with mortality in a cohort of 174 VV and VA ECMOs, our study indicated that ECMO-related vascular and cerebrovascular complications were not associated with an increased risk of in-hospital death associated with either VA or VV ECMO.

Our study had important limitations that should be acknowledged. First, although ECMO data and patient characteristics were collected prospectively, this was a retrospective study subject to selection bias, and some clinical information was not available from the medical records. Second, this was a single-center study with a relatively small sample size, precluding detailed subgroup analyses, which are likely to be underpowered for some outcomes. Furthermore, because of various indications for ECMO support, we could not analyze the relationship between indications for ECMO support and

outcomes. Third, we used alternative definitions to those used by previous publications. The lack of standard definitions means that there are varying indications for ECMO support and definitions of ECMO-related complications between studies; therefore, we cannot directly compare our results with previously published data. Fourth, given the small sample size and the retrospective study design, this study was likely underpowered to provide robust evidence. Future multicenter studies with larger sample sizes and strict, well-defined indications are required to evaluate the impact of ECMO-related complications on in-hospital mortality.

In conclusion, given the heterogeneity of the study sample—varying indications and underlying diseases—various factors were associated with a higher risk of ECMO-related vascular and cerebrovascular complications. Older age and CRRT were important risk factors for in-hospital death in association with both VA and VV ECMOs. However, ECMO-related vascular and cerebrovascular complications were not associated with an increased risk of in-hospital death.

**REFERENCES**

1. Rihal CS, Naidu SS, Givertz MM, et al. 2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care: Endorsed by the American Heart Assocation, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention. *J Am Coll Cardiol*. 2015;65:e7–26.

2. Burkhoff D, Sayer G, Doshi D, Uriel N. Hemodynamics of Mechanical Circulatory Support. *J Am Coll Cardiol*. 2015;66:2663–2674.

3. Guglin M, Zucker MJ, Bazan VM, et al. Venoarterial ECMO for Adults: JACC Scientific Expert Panel. *J Am Coll Cardiol*. 2019;73:698–716.

4. Ellouze O, Abbad X, Constandache T, et al. Risk Factors of Bleeding in Patients Undergoing Venoarterial Extracorporeal Membrane Oxygenation. *Ann Thorac Surg*. 2021;111:623–628.

5. Naidu SS. Novel percutaneous cardiac assist devices: The science of and indications for hemodynamic support. *Circulation*. 2011;123:533–543.

6. Aubron C, Cheng AC, Pilcher D, et al. Factors associated with outcomes of patients on extracorporeal membrane oxygenation support: a 5-year cohort study. *Crit Care*. 2013;17:R73.

7. Zangrillo A, Landoni G, Biondi-Zoccai G, et al. A metaanalysis of complications and mortality of extracorporeal membrane oxygenation. *Crit Care Resusc*. 2013;15:172–178.

8. Aubron C, DePuydt J, Belon F, et al. Predictive factors of bleeding events in adults undergoing extracorporeal membrane oxygenation. *Ann Intensive Care*. 2016;6:97.

9. Ried M, Sommerauer L, Lubnow M, et al. Thoracic bleeding complications in patients with venovenous extracorporeal membrane oxygenation. *Ann Thorac Surg*. 2018;106:1668–1674.

10. Millar JE, Fanning JP, McDonald CI, et al. The inflammatory response to extracorporeal membrane oxygenation (ECMO): a review of the pathophysiology. *Crit Care*. 2016;20:387.

11. Raiten JM, Wong ZZ, Spelde A, et al. Anticoagulation and transfusion therapy in patients requiring extracorporeal membrane oxygenation. *J Cardiothorac Vasc Anesth*. 2017;31:1051–1059.

12. Heilmann C, Geisen U, Beyersdorf F, et al. Acquired von Willebrand syndrome in patients with extracorporeal life support (ECLS). *Intensive Care Med*. 2012;38:62–68.

13. Murphy DA, Hockings LE, Andrews RK, et al. Extracorporeal membrane oxygenation—hemostatic complications. *Transfus Med Rev*. 2015;29:90–101.

14. Parzy G, Daviet F, Persico N, et al. Prevalence and Risk Factors for Thrombotic Complications Following Venovenous Extracorporeal Membrane Oxygenation: A CT Scan Study. *Crit Care Med*. 2020;48:192–199.

15. Tonna JE, Abrams D, Brodie D, et al. Management of Adult Patients Supported with Venovenous Extracorporeal Membrane Oxygenation (VV ECMO): Guideline from the Extracorporeal Life Support Organization (ELSO). *ASAIO J*. 2021;67:601–610.
16. Richardson ASC, Tonna JE, Nanjayya V, et al. Extracorporeal Cardiopulmonary Resuscitation in Adults. Interim Guideline Consensus Statement From the Extracorporeal Life Support Organization. *ASAIO J*. 2021;67:221–228.
17. Extracorporeal Life Support Organization (ELSO). ELSO guidelines for cardiopulmonary extracorporeal life support, Version 1.4 August 2017. Ann Arbor, MI. www.elso.org. Accessed April 23, 2021.
18. Combes A, Brodie D, Bartlett R, et al., International ECMO Network (ECMONet). Position paper for the organization of extracorporeal membrane oxygenation programs for acute respiratory failure in adult patients. *Am J Respir Crit Care Med*. 2014;190:488–496.
19. van Diepen S, Katz JN, Albert NM, et al., American Heart Association Council on Clinical Cardiology, Council on Cardiovascular and Stroke Nursing, Council on Quality of Care and Outcomes Research; and Mission: Lifeline. Contemporary management of cardiogenic shock: a scientific statement from the American Heart Association. *Circulation*. 2017;136:e232–268.
20. Brunner S, Guenther SPW, Lackermair K, et al. Extracorporeal Life Support in Cardiogenic Shock Complicating Acute Myocardial Infarction. *J Am Coll Cardiol*. 2019;73:2355–2357.
21. McCarthy FH, McDermott KM, Kini V, et al. Trends in U.S. extracorporeal membrane oxygenation use and outcomes: 2002–2012. *Semin Thorac Cardiovasc Surg*. 2015;27:81–88.
22. Davies A, Jones D, Bailey M, et al; Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators: Extracorporeal membrane oxygenation for 2009 influenza A(H1N1) acute respiratory distress syndrome. *JAMA*. 2009; 302:1888–1895.
23. Oh DK, Hong SB, Shim TS, et al. Effects of the duration of bridge to lung transplantation with extracorporeal membrane oxygenation. *PLoS One*. 2021;16:e0253520.
24. Combes A, Leprince P, Luyt CE, et al. Outcomes and long-term quality-of-life of patients supported by extracorporeal membrane oxygenation for refractory cardiogenic shock. *Crit Care Med*. 2008;36:1404–1411.
25. Camboni D, Philipp A, Lubnow M, et al. Support time-dependent outcome analysis for veno-venous extracorporeal membrane oxygenation. *Eur J Cardiothorac Surg*. 2011;40:341–346.
26. Marasco SF, Lukas G, McDonald M, McMillan J, Ihle B. Review of ECMO (extra corporeal membrane oxygenation) support in critically ill adult patients. *Heart, lung & circulation*. 2008;Suppl 4:S41–47.
27. Lamb KM, DiMuzio PJ, Johnson A, et al. Arterial protocol including prophylactic distal perfusion

catheter decreases limb ischemia complications in patients undergoing extracorporeal membrane oxygenation. *J Vasc Surg*. 2017;65:1074–1079.
28. Juo YY, Skancke M, Sanaiha Y, Mantha A, Jimenez JC, Benharash P. Efficacy of distal perfusion cannulae in preventing limb ischemia during extracorporeal membrane oxygenation: a systematic review and meta-analysis. *Artif Organs*. 2017;41:E263–273.
29. Hemmila MR, Rowe SA, Boules TN, et al. Extracorporeal life support for severe acute respiratory distress syndrome in adults. *Ann Surg*. 2004;240:595–605, discussion 605–607.
30. Bartlett RH, Gattinoni L. Current status of extracorporeal life support (ECMO) for cardiopulmonary failure. *Minerva Anestesiol*. 2010;76:534–540.
31. Chung YS, Cho DY, Sohn DS, et al. Is stopping heparin safe in patients on extracorporeal membrane oxygenation treatment? *ASAIO J*. 2017;63:32–36.
32. Nasr DM, Rabinstein AA. Neurologic complications of extracorporeal membrane oxygenation. *J Clin Neurol*. 2015;11:383–389.
33. Murashita T, Eya K, Miyatake T, et al. Outcome of the perioperative use of percutaneous cardiopulmonary support for adult cardiac surgery: factors affecting hospital mortality. *Artif Organs*. 2004;28:189–195.
34. Carroll BJ, Shah RV, Murthy V, et al. Clinical features and outcomes in adults with cardiogenic shock supported by extracorporeal membrane oxygenation. *Am J Cardiol*. 2015;116:1624–1630.
35. Ariyaratnam P, McLean LA, Cale AR, Loubani M. Extra-corporeal membrane oxygenation for the post-cardiotomy patient. *Heart Fail Rev*. 2014;19:717–725.
36. Lan C, Tsai PR, Chen YS, Ko WJ. Prognostic factors for adult patients receiving extracorporeal membrane oxygenation as mechanical circulatory support–a 14-year experience at a medical center. *Artif Organs*. 2010;34:E59–64.
37. Combes A, Leprince P, Luyt CE, et al. Outcomes and long-term quality-of-life of patients supported by extracorporeal membrane oxygenation for refractory cardiogenic shock. *Crit Care Med*. 2008;36:1404–1411.
38. Bisdas T, Beutel G, Warnecke G, et al. Vascular complications in patients undergoing femoral cannulation for extracorporeal membrane oxygenation support. *Ann Thorac Surg*. 2011, 92:626–631.

**FIGURE LEGENDS**

**FIGURE 1. Flow chart of ECMO inclusion**

The analysis included 856 ECMOs from 769 patients who underwent ECMO. Eligible ECMO procedures were stratified into 2 groups according to the type of ECMO: VA ECMO (n = 709, 82.8%) and VV ECMO (n = 147, 17.2%).

*Nine patients underwent both VA and VV ECMOs and were included in both the VA and VV ECMO groups.

ECMO, extracorporeal membrane oxygenation; VA, venoarterial; VV, venovenous

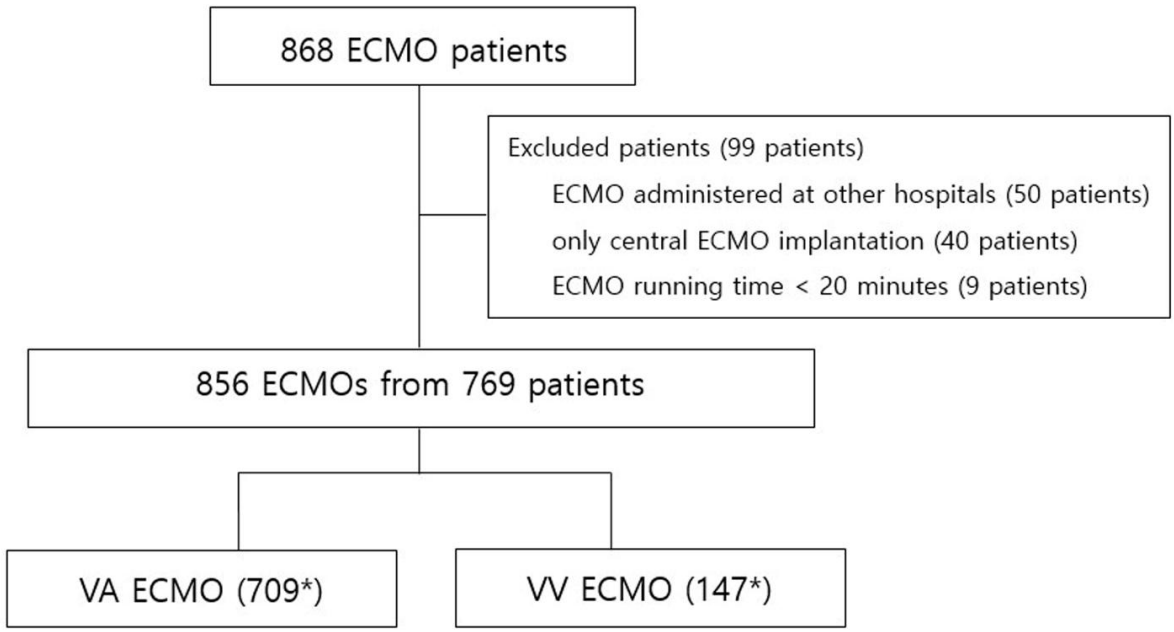

**TABLE 1. Baseline and Clinical Characteristics, Stratified by the ECMO Mode**

| Characteristics | Total | VA ECMO* | VV ECMO* | *P* Value |
|---|---|---|---|---|
| Number of patients | 769 | 639 | 139 | |
| Mean age, y ± SD | 59.4 ± 13.8 | 59.8 ± 14.1 | 57.1 ± 12.5 | 0.04 |
| Male sex | 246 (32.0) | 199 (31.1)† | 50 (36.0) | 0.32 |
| BMI, kg/m$^2$ | 23.5 ± 4.5 | 23.6 ± 4.4 | 23.0 ± 5.0 | 0.18 |
| Risk factor | | | | |
| Hypertension | 336 (43.7) | 291 (45.5) | 48 (34.5) | 0.02 |
| Diabetes mellitus | 219 (28.5) | 194 (30.4) | 26 (18.7) | 0.01 |
| Smoking | 181 (23.5) | 153 (23.9) | 30 (21.6) | 0.63 |
| PAOD‡ | 19 (2.5) | 17 (2.7) | 2 (1.4) | 0.55 |
| Past medical history§ | | | | |
| History of CAD | 164 (21.3) | 157 (24.6) | 7 (5.0) | <0.01 |
| History of CVA | 57 (7.4) | 54 (8.5) | 3 (2.2) | 0.01 |
| History of CKD | 108 (14.0) | 97 (15.2) | 12 (8.6) | 0.06 |
| Use of antiplatelet | 199 (25.9) | 186 (29.1) | 14 (10.1) | <0.01 |
| Use of anticoagulant | 109 (14.2) | 104 (16.3) | 7 (5.0) | <0.01 |
| Characteristics | Total | VA ECMO | VV ECMO | *P* Value |
| Number of ECMOs | 856 | 709 (82.8) | 147 (17.2) | |
| Indications | | | | <0.01 |
| Cardiac failure | 489 (57.1) | 487 (68.7) | 2 (1.4) | |
| Post-cardiotomy shock | 148 (17.3) | 144 (20.3) | 4 (2.7) | |
| Respiratory failure | 184 (21.5) | 57 (8.0) | 127 (86.4) | |
| PTE | 13 (1.5) | 13 (1.8) | 0 (0.0) | |
| Septic shock | 9 (1.1) | 8 (1.1) | 1 (0.7) | |
| Others | 13 (1.5) | 0 (0.0) | 13 (8.8) | |
| CPCR | 313 (36.6) | 304 (42.9) | 9 (6.1) | <0.01 |
| CRRT | 543 (63.4) | 487 (68.7) | 56 (38.1) | <0.01 |
| Arterial cannulation | | | | |
| Cannula size, Fr. | | | | |
| Median (IQR) | - | 15 (15–17) | - | |
| Distal perfusion catheter | - | 224 (31.6) | - | |
| Artery closure | | | | |
| Surgical repair | - | 108 (15.2) | - | |
| Perclosure | - | 50 (7.1) | - | |
| Venous cannulation | | | | |
| Cannula size, out, Fr. | | | | |
| Median (IQR) | - | - | 22 (21–23) | |
| Cannula size, in, Fr. | | | | |
| Median (IQR) | - | - | 18 (17–19) | |

| | | | | |
|---|---|---|---|---|
| Success of ECMO weaning | 461 (53.9) | 366 (51.6) | 95 (64.6) | <0.01 |
| Operation | 104 (12.1) | 79 (11.1) | 25 (17.0) | |
| Hospital stay, d | 56.7 ± 96.6 | 51.7 ± 79.4 | 80.6 ± 153.0 | <0.01 |
| ICU stay, d | 28.2 ± 39.4 | 26.0 ± 37.2 | 38.9 ± 47.4 | <0.01 |
| In-hospital death | 417 (48.7) | 374 (52.8) | 43 (29.3) | <0.01 |
| Cause of death | | | | |
| ECMO-related†† | 24 (5.8) | 23 (6.1) | 1 (2.3) | 0.49 |
| Cardiac failure | 189 (45.3) | 186 (49.7) | 3 (7.0) | <0.01 |
| Respiratory failure | 96 (23.0) | 64 (17.1) | 32 (74.4) | <0.01 |
| Septic shock | 43 (10.3) | 39 (10.4) | 4 (9.3) | >0.99 |
| Cerebrovascular disease | 6 (1.4) | 5 (1.3) | 1 (2.3) | 0.48 |
| Bleeding | 37 (8.9) | 35 (9.4) | 2 (4.7) | 0.41 |
| Others | 22 (5.3) | 22 (5.9) | 0 (0.0) | 0.15 |

Categorical data are given as number (%); continuous data are presented as mean ± standard deviation or median (IQR).

BMI, body mass index; CPCR, cardiopulmonary cerebral resuscitation; CVA, cerebrovascular accident; CKD, chronic kidney disease; CRRT, continuous renal replacement therapy; CAD, coronary artery disease; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range; PAOD, peripheral arterial occlusive disease; PTE, pulmonary thromboembolism; SD, standard deviation; VA, venoarterial; VV, venovenous

*Included 9 patients who underwent both VA and VV ECMOs.

†Included 3 men who underwent both VA and VV ECMOs.

‡PAOD was defined as by a history of surgical or radiologic intervention or an ankle-brachial index ≤ 0.9 prior to ECMO implantation.

§Past medical history prior to ECMO implantation.

CPCR or CRRT prior to ECMO implantation.

††Included ECMO-related vascular and cerebrovascular complications.

**TABLE 2. ECMO-related Vascular and Other Complications, Stratified by ECMO Mode**

| | Total | VA ECMO | VV ECMO | *P* Value |
|---|---|---|---|---|
| Number of ECMOs | 856 | 709 (82.8) | 147 (17.2) | |
| Any complications | 297 (34.7) | 259 (36.5) | 38 (25.9) | 0.02 |
| ECMO-related vascular* | 173 (20.2) | 154 (21.7) | 19 (12.9) | 0.02 |
| Thromboembolic | 54 (6.3) | 52 (7.3)† | 2 (1.4) | 0.01 |
| Bleeding | 77 (9.0) | 65 (9.2) | 12 (8.2) | 0.82 |
| DVT | 17 (2.0) | 14 (2.0) | 3 (2.0) | >0.99 |
| Cannula-related local | 24 (2.8) | 22 (3.1) | 2 (1.4) | 0.37 |
| Pseudoaneurysm | 14 (1.6) | 12 (1.7) | 2 (1.4) | >0.99 |
| AVF | 9 (1.1) | 9 (1.3) | 0 (0.0) | 0.35 |
| Arterial dissection | 1 (0.1) | 1 (0.1) | 0 (0.0) | >0.99 |
| Cerebrovascular | 116 (13.6) | 103 (14.5) | 13 (8.8) | 0.09 |
| Others | | | | |
| Local wound infection | 52 (6.1) | 46 (6.5) | 6 (4.1) | 0.36 |
| Peripheral neurologic | 28 (3.3) | 23 (3.2) | 5 (3.4) | >0.99 |
| Bowel ischemia | 16 (1.9) | 15 (2.1) | 1 (0.7) | 0.40 |
| Pneumothorax | 1 (0.1) | 0 (0.0) | 1 (0.7) | 0.38 |

Values in parentheses are percentages.

AVF, arteriovenous fistula; DVT, deep venous thrombosis; ECMO, extracorporeal membrane oxygenation; VA, venoarterial; VV, venovenous.

*Any event of each ECMO-related vascular complications was included individually.

†Included 6 major amputations as a result of limb ischemia.

**TABLE 3. Factors Associated With ECMO-related Vascular Complications in VA ECMOs**

| | Univariable Analysis | | Multivariable Analysis | |
|---|---|---|---|---|
| | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value |
| Age | 0.99 (0.98–0.99) | 0.03 | 0.99 (0.98–1.01) | 0.34 |
| Female sex | 1.09 (0.73–1.63) | 0.68 | NA | NA |
| BMI | 1.03 (0.97–1.09) | 0.32 | NA | NA |
| Hypertension | 0.72 (0.49–1.05) | 0.09 | 0.78 (0.48–1.26) | 0.31 |
| Diabetes mellitus | 0.76 (0.50–1.17) | 0.21 | NA | NA |
| Smoking | 1.13 (0.73–1.74) | 0.58 | NA | NA |
| PAOD | 2.80 (1.05–7.51) | 0.04 | 3.28 (1.02–10.58) | 0.047 |
| History of CAD | 0.95 (0.61–1.47) | 0.81 | 0.93 (0.88–0.99) | 0.03 |
| History of CVA | 1.08 (0.55–2.11) | 0.82 | NA | NA |
| History of CKD | 1.33 (0.81–2.20) | 0.26 | NA | NA |
| CPCR | 1.45 (0.88–2.39) | 0.15 | NA | NA |
| CRRT | 1.70 (1.10–2.62) | 0.02 | 1.48 (0.91–2.38) | 0.11 |
| ECMO running time (10 hours) | 1.02 (1.01–1.03) | <0.01 | 1.02 (1.01–1.03) | <0.01 |
| Arterial cannula size | 0.96 (0.83–1.12) | 0.63 | NA | NA |
| Initial Hb (ref. ≥ 10.0 g/dL) | | 0.04 | | 0.21 |
| <8.0 g/dL | 2.94 (1.27–6.80) | 0.01 | 2.50 (0.90–6.97) | 0.08 |
| 8.0–10.0 g/dL | 1.17 (0.67–2.04) | 0.58 | 1.03 (0.54–1.95) | 0.93 |
| Initial PLT (ref. ≥100 × $10^3$/μL) | | 0.16 | | |
| <50 × $10^3$/μL | 1.69 (0.56–5.10) | 0.36 | NA | NA |
| 50–100 × $10^3$/μL | 1.41 (0.94–2.10) | 0.10 | NA | NA |

BMI, body mass index; CPCR, cardiopulmonary cerebral resuscitation; CVA, cerebrovascular accident; CKD, chronic kidney disease; CI, confidence interval; CRRT, continuous renal replacement therapy; CAD, coronary artery disease; ECMO, extracorporeal membrane oxygenation; Hb, hemoglobin; NA, not applicable; OR, odds ratio; PAOD, peripheral arterial occlusive disease; PLT, platelet; ref., reference range; VA, venoarterial.

**TABLE 4. Factors Associated With In-hospital Mortality in Both VA and VV ECMOs**

| | Univariable Analysis | | Multivariable Analysis | |
|---|---|---|---|---|
| | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value |
| Age | 1.02 (1.01–1.03) | <0.01 | 1.03 (1.01–1.04) | <0.01 |
| Female sex | 1.23 (0.91–1.67) | 0.18 | NA | NA |
| BMI | 1.01 (0.99–1.03) | 0.65 | NA | NA |
| Hypertension | 1.56 (1.17–2.09) | <0.01 | 1.16 (0.82–1.64) | 0.41 |
| Diabetes mellitus | 1.41 (1.03–1.94) | 0.03 | 0.97 (0.65–1.46) | 0.89 |
| Smoking | 0.91 (0.65–1.28) | 0.60 | NA | NA |
| PAOD | 0.60 (0.24–1.51) | 0.28 | NA | NA |
| History of CAD | 1.21 (0.85–1.71) | 0.29 | NA | NA |
| History of CVA | 1.62 (0.92–2.84) | 0.095 | 1.18 (0.60–2.35) | 0.63 |
| History of CKD | 1.52 (1.00–2.31) | 0.051 | NA | NA |
| CPCR | 1.19 (1.08–1.32) | <0.01 | 1.42 (1.12–1.79) | <0.01 |
| CRRT | 3.93 (2.89–5.35) | <0.01 | 3.57 (2.59–4.93) | <0.01 |
| ECMO running time (10 hours) | 1.00 (1.00–1.00) | 0.051 | 1.00 (1.00–1.01) | 0.07 |
| Initial Hb (ref. ≥ 10.0 g/dL) | | <0.01 | | 0.03 |
| <8.0 g/dL | 1.24 (1.08–1.42) | <0.01 | 1.06 (0.91–1.24) | 0.47 |
| 8.0–10.0 g/dL | 1.18 (1.08–1.30) | <0.01 | 1.08 (0.96–1.22) | 0.19 |
| Initial PLT (ref. ≥100 × $10^3$/μL) | | <0.01 | | 0.12 |
| <50 × $10^3$/μL | 1.37 (1.14–1.64) | <0.01 | 1.60 (1.10–2.33) | 0.02 |
| 50–100 × $10^3$/μL | 1.18 (1.09–1.27) | <0.01 | 1.24 (1.07–1.44) | <0.01 |
| ECMO-related vascular complications | 1.00 (0.85–1.17) | 0.95 | | |
| Thromboembolic | 1.25 (0.99–1.58) | 0.06 | 1.09 (0.75–1.59) | 0.66 |
| Bleeding | 1.21 (0.98–1.50) | 0.08 | 1.03 (0.71–1.48) | 0.89 |
| Cerebrovascular complications | 1.27 (0.97–1.67) | 0.08 | 1.16 (0.57–2.32) | 0.69 |

BMI, body mass index; CPCR, cardiopulmonary cerebral resuscitation; CVA, cerebrovascular accident; CKD, chronic kidney disease; CI, confidence interval; CRRT, continuous renal replacement therapy; CAD, coronary artery disease; ECMO, extracorporeal membrane oxygenation; Hb, hemoglobin; NA, not applicable; OR, odds ratio; PAOD, peripheral arterial occlusive disease; PLT, platelet; ref., reference range; VA, venoarterial; VV, venovenous.

**TABLE 5. Factors Associated With In-hospital Mortality in VA ECMOs**

| | Univariable Analysis | | Multivariable Analysis | |
|---|---|---|---|---|
| | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value |
| Age | 1.02 (1.01–1.03) | <0.01 | 1.02 (1.01–1.04) | <0.01 |
| Female sex | 1.34 (0.95–1.90) | 0.095 | 1.48 (0.98–2.22) | 0.06 |
| BMI | 1.01 (0.98–1.03) | 0.71 | NA | NA |
| Hypertension | 1.50 (1.09–2.06) | 0.01 | NA | NA |
| Diabetes mellitus | 1.26 (0.89–1.79) | 0.19 | NA | NA |
| Smoking | 0.92 (0.64–1.33) | 0.67 | NA | NA |
| PAOD | 0.60 (0.23–1.58) | 0.30 | NA | NA |
| History of CAD | 1.01 (0.70–1.46) | 0.95 | NA | NA |
| History of CVA | 1.57 (0.86–2.85) | 0.14 | NA | NA |
| History of CKD | 1.42 (0.90–2.23) | 0.13 | NA | NA |
| CPCR | 1.22 (1.02–1.46) | 0.03 | 1.53 (0.47–4.97) | 0.48 |
| CRRT | 3.44 (2.44–4.84) | <0.01 | 2.93 (2.06–4.17) | <0.01 |
| ECMO running time (10 hours) | 1.00 (1.00–1.00) | 0.48 | NA | NA |
| Arterial cannula size | 1.00 (0.94–1.07) | 0.90 | NA | NA |
| Initial Hb (ref. ≥10.0 g/dL) | | <0.01 | | 0.06 |
| <8.0 g/dL | 1.32 (1.05–1.65) | 0.02 | 1.01 (0.52–1.97) | 0.97 |
| 8.0–10.0 g/dL | 1.26 (1.10–1.45) | <0.01 | 1.05 (0.75–1.46) | 0.78 |
| Initial PLT (ref. ≥100 × $10^3$/μL) | | <0.01 | | 0.06 |
| <50 × $10^3$/μL | 1.66 (1.23–2.22) | <0.01 | 1.92 (0.47–7.86) | 0.36 |
| 50–100 × $10^3$/μL | 1.36 (1.19–1.56) | <0.01 | 1.64 (1.06–2.54) | 0.03 |
| ECMO-related vascular complications | 0.85 (0.67–1.08) | 0.19 | NA | NA |
| Thromboembolic | 1.30 (0.94–1.80) | 0.11 | NA | NA |
| Bleeding | 1.18 (0.83–1.67) | 0.35 | NA | NA |
| Cerebrovascular complications | 1.00 (0.94–1.07) | 0.25 | NA | NA |

BMI, body mass index; CPCR, cardiopulmonary cerebral resuscitation; CVA, cerebrovascular accident; CKD, chronic kidney disease; CI, confidence interval; CRRT, continuous renal replacement therapy; CAD, coronary artery disease; ECMO, extracorporeal membrane oxygenation; Hb, hemoglobin; NA, not applicable; OR, odds ratio; PAOD, peripheral arterial occlusive disease; PLT, platelet; ref., reference range; VA, venoarterial.

**TABLE 6. Factors Associated With In-hospital Mortality in VV ECMOs**

| | Univariable Analysis | | Multivariable Analysis | |
|---|---|---|---|---|
| | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value |
| Age | 1.02 (0.99–1.05) | 0.18 | 1.03 (1.00–1.06) | 0.03 |
| Female sex | 0.93 (0.44–1.94) | 0.84 | NA | NA |
| BMI | 0.99 (0.90–1.08) | 0.80 | NA | NA |
| Hypertension | 1.35 (0.65–2.82) | 0.42 | NA | NA |
| Diabetes mellitus | 1.63 (0.68–3.92) | 0.27 | NA | NA |
| Smoking | 0.83 (0.35–1.99) | 0.68 | NA | NA |
| PAOD | Not calculable | | | |
| History of CAD | 0.80 (0.15–4.29) | 0.80 | NA | NA |
| History of CVA | Not calculable | | | |
| History of CKD | 1.50 (0.45–5.01) | 0.51 | NA | NA |
| CPCR | 1.06 (0.34–3.26) | 0.92 | NA | NA |
| CRRT | 4.77 (2.24–10.17) | <0.01 | 5.48 (2.46–12.23) | <0.01 |
| ECMO running time (10 hours) | Not calculable | | | |
| Initial Hb (ref. ≥ 10.0 g/dL) | Not calculable | | | |
| <8.0 g/dL | | | | |
| 8.0–10.0 g/dL | | | | |
| Initial PLT (ref. ≥100 × $10^3$/μL) | | 0.40 | | |
| <50 × $10^3$/μL | 8.37 (0.38–183.14) | 0.18 | NA | NA |
| 50–100 × $10^3$/μL | 1.34 (0.37–4.93) | 0.66 | NA | NA |
| ECMO-related vascular complications | 2.61 (0.65–10.44) | 0.18 | 2.08 (0.44–9.75) | 0.35 |
| Thromboembolic | Not calculable | | | |
| Bleeding | Not calculable | | | |
| Cerebrovascular complications | 2.18 (0.66–7.19) | 0.20 | NA | NA |

BMI, body mass index; CPCR, cardiopulmonary cerebral resuscitation; CVA, cerebrovascular accident; CKD, chronic kidney disease; CI, confidence interval; CRRT, continuous renal replacement therapy; CAD, coronary artery disease; ECMO, extracorporeal membrane oxygenation; Hb, hemoglobin; NA, not applicable; OR, odds ratio; PAOD, peripheral arterial occlusive disease; PLT, platelet; ref., reference range; VV, venovenous.

**SUPPLEMENTAL TABLE 1. In-hospital Mortality Rates According ECMO Indications**

| | No. of ECMOs | VA ECMO | VV ECMO |
|---|---|---|---|
| Indications | | | |
| Cardiac failure | 285/489 (58.3) | 285/487 (53.0) | 0/2 |
| Post-cardiotomy shock | 66/148 (44.6) | 66/144 (45.8) | 0/4 |
| Respiratory failure | 77/184 (41.8) | 36/57 (63.2) | 41/127 (32.3) |
| PTE | 7/13 (53.8) | 7/13 (53.8) | 0/0 |
| Septic shock | 7/9 (77.8) | 7/8 (87.5) | 0/1 |
| Others | 2/13 (29.3) | 0/0 | 2/13 (29.3) |

Values in parentheses are percentages.
ECMO, extracorporeal membrane oxygenation; PTE, pulmonary thromboembolism; VA, venoarterial; VV, venovenous.

**SUPPLEMENTAL TABLE 2. Factors Associated With ECMO-related Thromboembolic Complications in VA ECMOs**

| | Univariable Analysis | | Multivariable Analysis | |
|---|---|---|---|---|
| | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value |
| Age | 0.97 (0.95–0.99) | <0.01 | 0.98 (0.95–1.00) | 0.02 |
| Female sex | 1.63 (0.85–3.11) | 0.14 | NA | NA |
| BMI | 0.95 (0.87–1.03) | 0.22 | NA | NA |
| Hypertension | 0.64 (0.33–1.23) | 0.18 | NA | NA |
| Diabetes mellitus | 1.02 (0.52–2.02) | 0.95 | NA | NA |
| Smoking | 1.64 (0.84–3.21) | 0.15 | NA | NA |
| PAOD | 0.97 (0.12–7.53) | 0.98 | NA | NA |
| History of CAD | 0.70 (0.32–1.55) | 0.38 | NA | NA |
| History of CVA | 1.08 (0.36–3.24) | 0.89 | NA | NA |
| History of CKD | 1.51 (0.68–3.38) | 0.31 | NA | NA |
| CPCR | 0.54 (0.22–1.33) | 0.12 | NA | NA |
| CRRT | 5.74 (1.95–16.87) | <0.01 | 5.27 (1.66–16.77) | <0.01 |
| ECMO running time (10 hours) | 1.01 (1.00–1.01) | 0.09 | 1.00 (0.99–1.01) | 0.46 |
| Arterial cannula size | 0.99 (0.77–1.27) | 0.92 | NA | NA |
| Initial Hb (ref. ≥ 10.0 g/dL) | | 0.26 | | |
| <8.0 g/dL | 3.10 (0.74–13.04) | 0.12 | NA | NA |
| 8.0–10.0 g/dL | 1.73 (0.55–5.48) | 0.35 | NA | NA |
| Initial PLT (ref. ≥100 × $10^3$/μL) | | 0.04 | | 0.25 |
| <50 × $10^3$/μL | 3.46 (1.35–8.89) | 0.01 | 2.27 (0.81–6.38) | 0.12 |
| 50–100 × $10^3$/μL | 1.07 (0.32–3.63) | 0.91 | 0.58 (0.09–3.84) | 0.57 |

BMI, body mass index; CPCR, cardiopulmonary cerebral resuscitation; CVA, cerebrovascular accident; CKD, chronic kidney disease; CI, confidence interval; CRRT, continuous renal replacement therapy; CAD, coronary artery disease; ECMO, extracorporeal membrane oxygenation; Hb, hemoglobin; NA, not applicable; OR, odds ratio; PAOD, peripheral arterial occlusive disease; PLT, platelet; ref., reference range; VA, venoarterial.

**SUPPLEMENTAL TABLE 3. Factors Associated With ECMO-related Bleeding Complications in VA ECMOs**

| | Univariable Analysis | | Multivariable Analysis | |
|---|---|---|---|---|
| | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value |
| Age | 1.00 (0.99–1.02) | 0.83 | NA | NA |
| Female sex | 1.25 (0.72–2.16) | 0.43 | NA | NA |
| BMI | 0.95 (0.89–1.00) | 0.054 | NA | NA |
| Hypertension | 0.68 (0.40–1.17) | 0.16 | NA | NA |
| Diabetes mellitus | 0.73 (0.40–1.35) | 0.32 | NA | NA |
| Smoking | 0.74 (0.39–1.39) | 0.35 | NA | NA |
| PAOD | 1.21 (0.27–5.44) | 0.80 | NA | NA |
| History of CAD | 0.73 (0.37–1.41) | 0.34 | NA | NA |
| History of CVA | 1.19 (0.44–3.19) | 0.73 | NA | NA |
| History of CKD | 1.51 (0.78–2.90) | 0.22 | NA | NA |
| CPCR | 1.19 (0.72–1.98) | 0.50 | NA | NA |
| CRRT | 1.74 (0.94–3.22) | 0.08 | NA | NA |
| ECMO running time (10 hours) | 1.01 (1.00–1.02) | <0.01 | 1.01 (1.00–1.02) | <0.01 |
| Arterial cannula size | 0.79 (0.64–0.96) | 0.02 | 0.79 (0.63–0.99) | 0.04 |
| Initial Hb (ref. ≥10.0 g/dL) | | <0.01 | | <0.01 |
| <8.0 g/dL | 5.29 (2.84–9.86) | <0.01 | 4.19 (2.21–7.96) | <0.01 |
| 8.0–10.0 g/dL | 1.15 (0.62–2.13) | 0.66 | 0.90 (0.46–1.74) | 0.75 |
| Initial PLT (ref. ≥100 × $10^3$/μL) | | <0.01 | | 0.06 |
| <50 × $10^3$/μL | 2.21 (1.03–4.74) | 0.04 | 1.45 (0.66–3.19) | 0.35 |
| 50–100 × $10^3$/μL | 2.61 (1.50–4.55) | <0.01 | 2.07 (1.13–3.79) | 0.02 |

BMI, body mass index; CPCR, cardiopulmonary cerebral resuscitation; CVA, cerebrovascular accident; CKD, chronic kidney disease; CI, confidence interval; CRRT, continuous renal replacement therapy; CAD, coronary artery disease; ECMO, extracorporeal membrane oxygenation; Hb, hemoglobin; NA, not applicable; OR, odds ratio; PAOD, peripheral arterial occlusive disease; PLT, platelet; ref., reference range; VA, venoarterial.

**SUPPLEMENTAL TABLE 4. Factors Associated With ECMO-related Vascular Complications in VV ECMOs**

| | Univariable Analysis | |
|---|---|---|
| | OR (95% CI) | *P* Value |
| Age | 1.02 (0.97–1.07) | 0.37 |
| Female sex | 2.99 (1.01–8.86) | 0.048 |
| BMI | 0.98 (0.90–1.07) | 0.64 |
| Hypertension | 2.39 (0.80–7.14) | 0.12 |
| Diabetes mellitus | 0.84 (0.20–3.51) | 0.81 |
| Smoking | 0.25 (0.03–1.96) | 0.19 |
| PAOD | 9.36 (0.55–158.04) | 0.12 |
| History of CAD | 1.49 (0.17–13.30) | 0.72 |
| History of CVA | 4.64 (0.40–54.48) | 0.22 |
| History of CKD | 0.00 (0.00–0.00) | <0.01 |
| CPCR | 0.67 (0.10–4.71) | 0.69 |
| CRRT | 1.81 (0.62–5.25) | 0.28 |
| ECMO running time (10 hours) | 1.02 (1.01–1.04) | <0.01 |
| Initial Hb (ref. ≥10.0 g/dL) | | 0.048 |
| <8.0 g/dL | 4.93 (1.21–20.07) | 0.03 |
| 8.0–10.0 g/dL | 0.89 (0.23–3.47) | 0.87 |
| Initial PLT (ref. ≥100 × $10^3$/μL) | Not calculable | |
| <50 × $10^3$/μL | | |
| 50–100 × $10^3$/μL | | |

BMI, body mass index; CPCR, cardiopulmonary cerebral resuscitation; CVA, cerebrovascular accident; CKD, chronic kidney disease; CI, confidence interval; CRRT, continuous renal replacement therapy; CAD, coronary artery disease; ECMO, extracorporeal membrane oxygenation; Hb, hemoglobin; NA, not applicable; OR, odds ratio; PAOD, peripheral arterial occlusive disease; PLT, platelet; ref., reference range; VV, venovenous.

**SUPPLEMENTAL TABLE 5. Factors Associated With Cerebrovascular Complications in VV ECMOs**

| | Univariable Analysis | |
|---|---|---|
| | OR (95% CI) | *P* Value |
| Age | 1.01 (0.95–1.08) | 0.73 |
| Female sex | 0.51 (0.13–2.01) | 0.34 |
| BMI | 0.93 (0.78–1.10) | 0.37 |
| Hypertension | 2.03 (0.62–6.68) | 0.24 |
| Diabetes mellitus | 3.80 (1.10–13.15) | 0.04 |
| Smoking | 0.31 (0.04–2.49) | 0.27 |
| PAOD | 0.00 (0.00–0.00) | <0.01 |
| History of CAD | 4.93 (0.85–28.70) | 0.08 |
| History of CVA | 5.72 (0.48–68.20) | 0.17 |
| History of CKD | 7.59 (1.87–30.75)) | <0.01 |
| CPCR | 0.00 (0.00–0.00) | <0.01 |
| CRRT | 2.94 (0.86–9.89) | 0.08 |
| ECMO running time (10 hours) | 1.00 (0.99–1.02) | 0.74 |
| Initial Hb (ref. ≥10.0 g/dL) | Not calculable | |
| <8.0 g/dL | | |
| 8.0–10.0 g/dL | | |
| Initial PLT (ref. ≥100 × $10^3$/μL) | | 0.13 |
| <50 × $10^3$/μL | 4.51 (0.71–28.73) | 0.11 |
| 50–100 × $10^3$/μL | 3.43 (0.75–15.80) | 0.11 |

BMI, body mass index; CPCR, cardiopulmonary cerebral resuscitation; CVA, cerebrovascular accident; CKD, chronic kidney disease; CI, confidence interval; CRRT, continuous renal replacement therapy; CAD, coronary artery disease; ECMO, extracorporeal membrane oxygenation; Hb, hemoglobin; NA, not applicable; OR, odds ratio; PAOD, peripheral arterial occlusive disease; PLT, platelet; ref., reference range; VA, venoarterial.

## 국문요약

### 배경

체외 막 산소공급장치(ECMO)를 시행 받는 환자에서 치명률과 이환률은 지속적으로 높은 상태이다. ECMO 연관 혈관, 뇌혈관 합병증의 위험인자를 알아내고, 교정한다면, 치료의 질을 올리고, 연관 사망률을 줄일 수 있을 것이다.

### 목적

ECMO를 시행 받은 환자에서, ECMO와 연관된 혈관, 뇌혈관 합병증의 예측인자를 평가하고, ECMO 연관 합병증이 해당 환자들의 병원내 사망률의 증가와 연관이 있는지 확인하기 위해 본 연구를 진행하게 되었다.

### 방법

2015년 1월부터 2019년 12월까지, 769명의 환자에서 856건의 대퇴동맥을 통한 ECMO가 시행되었고, 정맥-동맥간 체외 막 산소화요법 (VA ECMO), 정맥-정맥간 체외 막 산소화요법 (VV ECMO)으로 분류하여 후향적으로 분석하였다. 결과로 병원내 사망률, ECMO연관 혈관 합병증의 발생률, 뇌혈관 합병증의 발생률을 조사하였고, 이러한 합병증 발생률과 병원내 사망률과의 연관 관계를 분석하였다.

### 결과

ECMO 연관 혈관/뇌혈관 합병증의 발생률은 각각 20.2%, 13.6%였다. 전체 연구대상자에서 사망률은 48.7%였고, VA ECMO를 시행한 환자에서 52.8%, VV ECMO를 시행한 환자에서 29.3% 였다. 다변량분석 결과, 고령의 나이 ($p<0.01$), 심폐소생술 시행 ($p<0.01$), 지속적 신대체요법 시행 ($p<0.01$), 낮은 초기 혈소판 수치 [$< 50 \times 10^3/\mu L$ ($P=0.02$), $50–100 \times 10^3/\mu L$ ($P<0.01$)] 가 병원 내 사망률을 높이는 것으로 나타났다. ECMO 연관 혈관/뇌혈관 합병증은 VA ECMO, VV ECMO 모두에서 병원 내 사망률과 연관이 없었다.

### 결론

ECMO를 시행한 환자에서, ECMO관련 혈관/뇌혈관 합병증은 병원내 사망률 증가와 연관이 없다.