Duration of sweep gas off trial for weaning from venovenous extracorporeal membrane oxygenation

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Soo Jin Na, Hee Jung Choi, Chi Ryang Chung, Yang Hyun Cho, Kiick Sung, Jeong Hoon Yang, Gee Young Suh, Joong Hyun Ahn, Keumhee C. Carriere and Kyeongman Jeon

Abstract

Background: No data are available on the duration of time needed to assess the adequacy of lung function after stopping sweep gas for weaning of venovenous extracorporeal membrane oxygenation (ECMO). The objective of this study was to investigate changes in arterial blood gases (ABGs) during sweep gas off trials in patients receiving venovenous ECMO.

Methods: Data on patients receiving venovenous ECMO, with a weaning trial at least once, were collected prospectively from January 2012 through December 2017. Serial changes in ABGs during sweep gas off trial and clinical outcomes after weaning from venovenous ECMO were evaluated.

Results: Over the study period, 192 sweep gas off trials occurred in 93 patients: 115 (60%) failed and 77 (40%) were successful. During the trial, significant changes in blood gases were observed within 1 h in all patients. When serial ABGs were compared according to trial off results, there were no significant differences in the pH, $PaCO_2$, and HCO_3^- trends across time points between successful and failed trials. However, PaO_2 (70.6 *versus* 93.4 mmHg), SaO_2 (91.9 *versus* 95.2%), and PaO_2/FiO_2 ratio (164.0 *versus* 233.4) were significantly lower in failed trials than successful trials within 1 h after stopping sweep gas. After 2 h of trial off, no significant change in blood gases was observed until the end of the trial.

Conclusions: No change in blood gases was observed 2 h after stopping sweep gas in patients receiving venovenous ECMO. Based on our institutional experience, however, we suggest monitoring for 2 h or more after stopping sweep gas flow to assess if patients are ready for decannulation.

The reviews of this paper are available via the supplemental material section.

Keywords: extracorporeal membrane oxygenation, respiratory insufficiency, standards, trends, weaning

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Correspondence to:
Kyeongman Jeon
Department of Critical Care Medicine and Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Republic of Korea
kjeon@skku.edu

Soo Jin Na
Chi Ryang Chung
Department of Critical Care Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Hee Jung Choi
Intensive Care Unit Nursing Department, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Yang Hyun Cho
Kiick Sung
Department of Thoracic and Cardiovascular Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Jeong Hoon Yang
Department of Critical Care Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Division of Cardiology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Gee Young Suh
Department of Critical Care Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Introduction

Extracorporeal membrane oxygenation (ECMO) is an artificial means of maintaining adequate oxygenation and carbon dioxide elimination in patients who have severe acute respiratory failure.[1,2] Although the role and proper use of ECMO for patients with respiratory failure have not been definitely established,[3,4] advances in technology have made ECMO safer and easier to use, allowing more widespread applications in patients with severe acute respiratory failure.[4] Nevertheless, ECMO can have several, sometimes serious and fatal, complications while providing respiratory support to maintain life.[5] Therefore, deciding when to start ECMO support, as well as assessing and determining if patients are ready to be weaned from ECMO, is important.

Weaning patients with acute respiratory failure from ECMO is relatively simple, and should be considered when the reason for starting ECMO is substantially improved or resolved.[2] However,

Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Joong Hyun Ahn
Biostatistics and Clinical Epidemiology Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Keumhee C. Carriere
Biostatistics and Clinical Epidemiology Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Department of Mathematical and Statistical Sciences, University of Alberta, Edmonton, Alberta, Canada

the most appropriate strategy for weaning from ECMO has not been established.[1] The Extracorporeal Life Support Organization (ELSO) and some centers suggest that patients could be ready for decannulation when lung function is adequate for an hour or more after stopping sweep gas flow.[6] However, no data are available on the amount of time needed to assess the adequacy of lung function after stopping sweep gas flow. Therefore, we investigated changes in arterial blood gases (ABGs) over time after stopping sweep gas flow in patients treated with venovenous ECMO for severe acute respiratory failure.

Material and methods

Study design

This observational study involving adult patients aged 18 years or older treated with ECMO for severe acute respiratory failure was conducted at Samsung Medical Center (a 1989-bed, university-affiliated, tertiary referral hospital in Seoul, South Korea) between January 2012 and December 2017. Because our interests were serial changes in ABGs after stopping sweep gas in patients treated with venovenous ECMO for severe acute respiratory failure, we only analyzed patients who had weaning trials from venovenous ECMO at least once. We excluded patients who died on ECMO or were withdrawn for futility, who were transferred to another hospital, were switched from venovenous ECMO to venoarterial ECMO, or whose cannula were removed without trial off.

The Institutional Review Board of the Samsung Medical Center approved this study (Approval No: 2017-07-075-001), and waived the requirement for informed consent because of the observational nature of the study. Patient information was anonymized and de-identified prior to analysis.

Weaning from ECMO

Patient selection, medical management, and settings of the mechanical ventilation (MV) and ECMO circuits followed institutional protocols that have been described previously.[7] All patients included in the analysis were in venovenous mode before weaning from ECMO. After ECMO initiation, we controlled pump blood flow and sweep gas flow rate with a blender setting of 100% oxygen without change until the end, to maintain target arterial saturation and carbon dioxide removal. The possibility of weaning from ECMO was assessed daily, and trial off was performed to determine decannulation when arterial blood gas was maintained within the target range with a sweep gas flow of 1 l/min or less regardless of pump blood flow at acceptable ventilator settings or supplemental oxygen. Trial off procedures were: sweep gas flow to the oxygenator was turned off and disconnected to prevent oxygen leaking around the flow meter, even when it appeared to be off. Pump blood flow did not need to be reduced for the off trial, and, if needed, ventilator setting was re-established within the range of the fraction of inspired oxygen (FiO_2) ≤ 0.6 and peak inspiratory pressure <30 cm H_2O on pressure-limited ventilation applied to all patients, in which the peak pressure can be used as a surrogate for plateau pressure,[8] but not titrated during the trial. In cases that were not mechanically ventilated (extubated in 23 and tracheostomized in 15) at the time of the sweep gas off trial, supplemental oxygen was considered, with conventional oxygen supplement devices including high-flow nasal cannula based on the adequacy of gas exchange while receiving ECMO prior to the trial,[9] but not titrated during the trial. ABG analysis was obtained 30 min after trial off. For arterial pH less than 7.35 or oxygen partial pressure in arterial blood per FiO_2 (PaO_2/FiO_2) ratio less than 150 mmHg, we stopped the weaning trial and turned on sweep gas flow. Patients who maintained adequate gas exchange without sweep gas flow were closely monitored for at least 2 h, and decannulation was considered for patients who were stable during this period. The decision about total duration of weaning trial and decannulation were made by treating intensivists and an ECMO team. Weaning trials were stopped for respiratory distress (respiratory rate ≥ 30 breaths/min or using accessory muscles for respiration), desaturation identified by pulse oximetry (SpO_2 $<90\%$ more than 5 min), or hemodynamic instability at any time during the off trial. In patients for whom decannulation was decided, sweep gas flow remained at 0 l/min until pumps were stopped. Thus, regardless of the time to determine decannulation, the duration of trial off was defined as the time from stopping sweep gas to decannulation.

Data collection and clinical outcomes

In our hospital, clinical and laboratory data from patients receiving ECMO were prospectively

registered in an ECMO database. Data on respiratory measurements and ABG from trial off to 24 h after decannulation were collected retrospectively for this study through medical record review. Respiratory measurements were recorded in an electronic medical record system automatically every minute, and at the moment mechanical ventilator settings changed. Timing of ABG analysis during weaning trials, except for 30 min after the trial, was at the individual physician's discretion.

The primary outcome was the change in gas exchange during weaning trial at the following time points: ABG obtained before trial off (H0), within 1 h (H1) and at 1-h intervals (H1–H5) until 5 h after trial off. The secondary outcome was successful weaning defined as weaning from ECMO followed by survival without reinsertion beyond 24 h.

Statistical analysis

Categorical variables were compared with Chi-square test or Fisher's exact tests, when applicable, and presented as numbers and percentages. Continuous variables were reported as medians with interquartile range and differences between groups were analyzed with Mann–Whitney *U* tests. A generalized estimating equations model was used to analyze the changes in ABG between time points after trial off, and to test for interaction between time points and successful/failed weaning. For all analyses, statistical significance was set at $p < 0.05$. SAS 9.2 (SAS Institute Inc., Cary, NC, USA) and SigmaPlot (SyStat Software, San Jose, CA, USA) were used for statistical analyses.

Results

During the study period, 171 consecutive patients received venovenous ECMO for severe acute respiratory failure. Of these, 78 were excluded because ABG data on weaning were not available ($n = 2$), or the patient was withdrawn or died on ECMO before trial off ($n = 63$), transferred to another hospital ($n = 4$), switched from venovenous ECMO to venoarterial ECMO ($n = 1$), or had cannulae removed without trial off ($n = 8$). A total of 93 patients who had a weaning trial from venovenous ECMO at least once were included (Table 1).

Over the study period, 192 sweep gas off trials occurred in 93 patients: 115 (60%) failed and 77 (40%) were successful. Changes in ABG during trial off are presented in Figure 1. When all trials were analyzed, PaO_2 and arterial oxygen saturation (SaO_2) were significantly decreased at H1, increased at H2, and then remained the same from H3 to H5. pH, partial pressure of carbon dioxide in arterial blood ($PaCO_2$), and PaO_2/FiO_2 ratio were significantly altered at H1, but there were no differences during later time points. No significant differences were observed in HCO_3^- from H0 to H5.

When serial ABGs were compared according to trial off results (Figure 2), there were no significant differences in the pH, $PaCO_2$, and HCO_3^- trends across time points between successful and failed trials. However, there were different trends in PaO_2, SaO_2, and PaO_2/FiO_2 ratio between successful and failed trials. PaO_2 at H1 was significantly decreased from H0 in both successful (111.3 mmHg *versus* 93.4 mmHg, $p < 0.001$) and failed (96.4 mmHg *versus* 70.6 mmHg, $p < 0.001$) trials. PaO_2 was significantly lower than H0 at subsequent time points in failed trials (H0 *versus* H2, 96.4 mmHg *versus* 83.6 mmHg, $p = 0.049$; H0 *versus* H3, 96.4 mmHg *versus* 84.8 mmHg, $p = 0.053$; H0 *versus* H4, 96.4 mmHg *versus* 66.4 mmHg, $p < 0.001$; H0 *versus* H5, 96.4 mmHg *versus* 58.8 mmHg, $p < 0.001$), while differences between PaO_2 at H0 and H2–H5 were not significantly different in successful trials (H0 *versus* H2, 111.3 mmHg *versus* 100.5 mmHg, $p = 0.079$; H0 *versus* H3, 111.3 mmHg *versus* 105.1 mmHg, $p = 0.293$; H0 *versus* H4, 111.3 mmHg *versus* 112.1 mmHg, $p = 0.919$; H0 *versus* H5, 111.3 mmHg *versus* 101.3 mmHg, $p = 0.184$). Changes in SaO_2 and PaO_2/FiO_2 ratio were similar to those of PaO_2.

Discussion

In this study, we investigated changes in ABG over time after trial off, and the association between duration of trial off and clinical outcomes in patients requiring ECMO support for severe acute respiratory failure. Our results demonstrated the following: no significant change in ABG from 2 h after stopping sweep gas until trial off end; different trends in ABG including PaO_2, SaO_2, and PaO_2/FiO_2 ratio between failed and successful trials were identified at subsequent time points of trial off.

Table 1. Characteristics of patients who had weaning trial from venovenous ECMO.

Patients who did trial off (*N* = 93)	
Demographics	
Age, years	57 (47–65)
Male	70 (75.3)
Cardiovascular disease	9 (9.7)
Chronic renal disease	3 (3.2)
Chronic obstructive lung disease	9 (9.7)
Primary diagnosis	
Bacterial pneumonia	38 (40.9)
Viral pneumonia	14 (15.1)
Chronic obstructive lung disease	1 (1.1)
Trauma/burn	3 (3.2)
Asphyxia	1 (1.1)
Acute exacerbation of ILD	13 (14.0)
Others	23 (24.7)
RESP score	1 (−1–2)
PRESERVE score	5 (4–6)
Airway management prior to sweep gas off trial	
Extubated	23 (12.0)
Tracheostomized	89 (46.4)
Intubated	80 (41.7)
MV during ECMO support prior to sweep gas off trial[a]	154 (80.2)
Adverse event during ECMO	
ECMO-related complications	
Cannula	21 (22.6)
Others	22 (23.7)
Patient complications[b]	
Hematological	23 (24.7)
Neurological	11 (11.8)
Cardiovascular	63 (67.7)
Pulmonary	23 (24.7)
Renal	40 (43.0)
Infection	42 (45.2)
Clinical outcomes	
ECMO outcomes	
Decannulation	79 (84.9)[c]
Bridging to lung transplantation	3 (3.2)
Died on ECMO or withdrawal	11 (11.8)
Duration of ECMO support, days	10 (5–22)
Weaning of mechanical ventilation	66 (71.0)
Duration of mechanical ventilation, days	21 (11–32)
Mortality	
Hospital	31 (33.3)
Intensive care unit	28 (30.1)
Length of stay, days	
Hospital	43 (29–74)
Intensive care unit	29 (17–42)

Values are median with interquartile range or *n* (%).
ECMO, extracorporeal membrane oxygenation; ILD, interstitial lung disease; RESP, respiratory extracorporeal membrane oxygenation survival prediction; PRESERVE, predicting death for severe ARDS on VV-ECMO.
[a]Among the tracheostomized patients, 74 (83.1%) patients were mechanically ventilated.
[b]Hematological complications include gastrointestinal bleeding, cannula site bleeding, surgical site bleeding, plasma hemoglobin >50 mg/dL or disseminated intravascular coagulation, neurological complications include brain death, seizure, cerebral infarction or brain hemorrhage, cardiovascular complications include inotrope or vasopressor use, myocardial stunning, arrhythmia, cardiac tamponade, or cardiac arrest, pulmonary complications include pneumothorax or pulmonary hemorrhage, renal complications include serum creatinine >1.5 mg/dl or continuous renal replacement therapy, and infection include white blood cell $<1500 \times 10^3/mm^3$, culture confirmed new infection, or ECMO-associated wound infection.
[c]Two cases in which the cannula was accidentally withdrawn after failed sweep gas off trial are included.

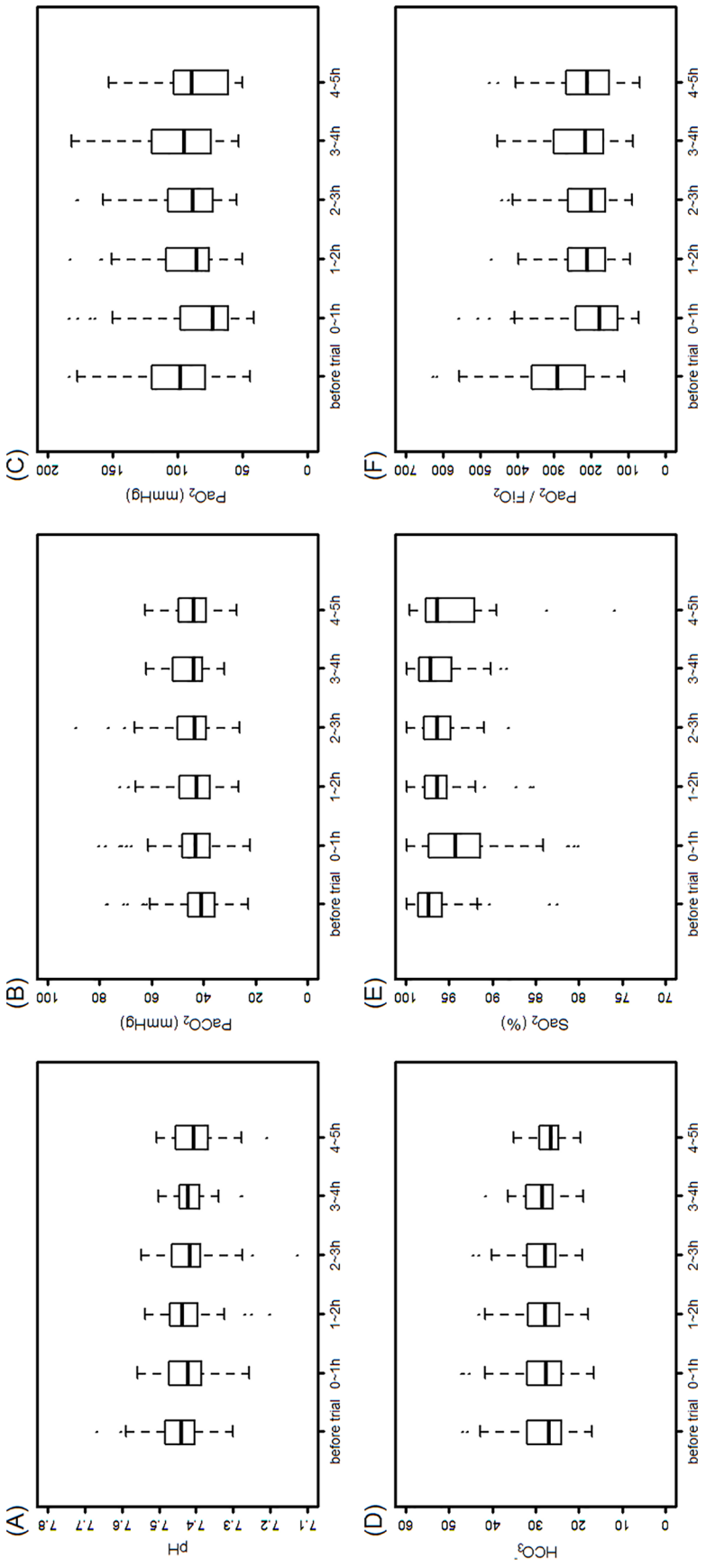

Figure 1. Changes of arterial blood gas over the time during overall weaning trial.
(A) pH, (B) $PaCO_2$, (C) PaO_2, (D) HCO_3^-, (D) SaO_2, and (F) PaO_2/FiO_2 ratio values are presented as box and whisker plots, where boxes encompass values between the 25th and 75th percentiles, horizontal lines indicate the median values, and the lines above and below the boxes indicate the 90th and 10th percentiles, respectively.

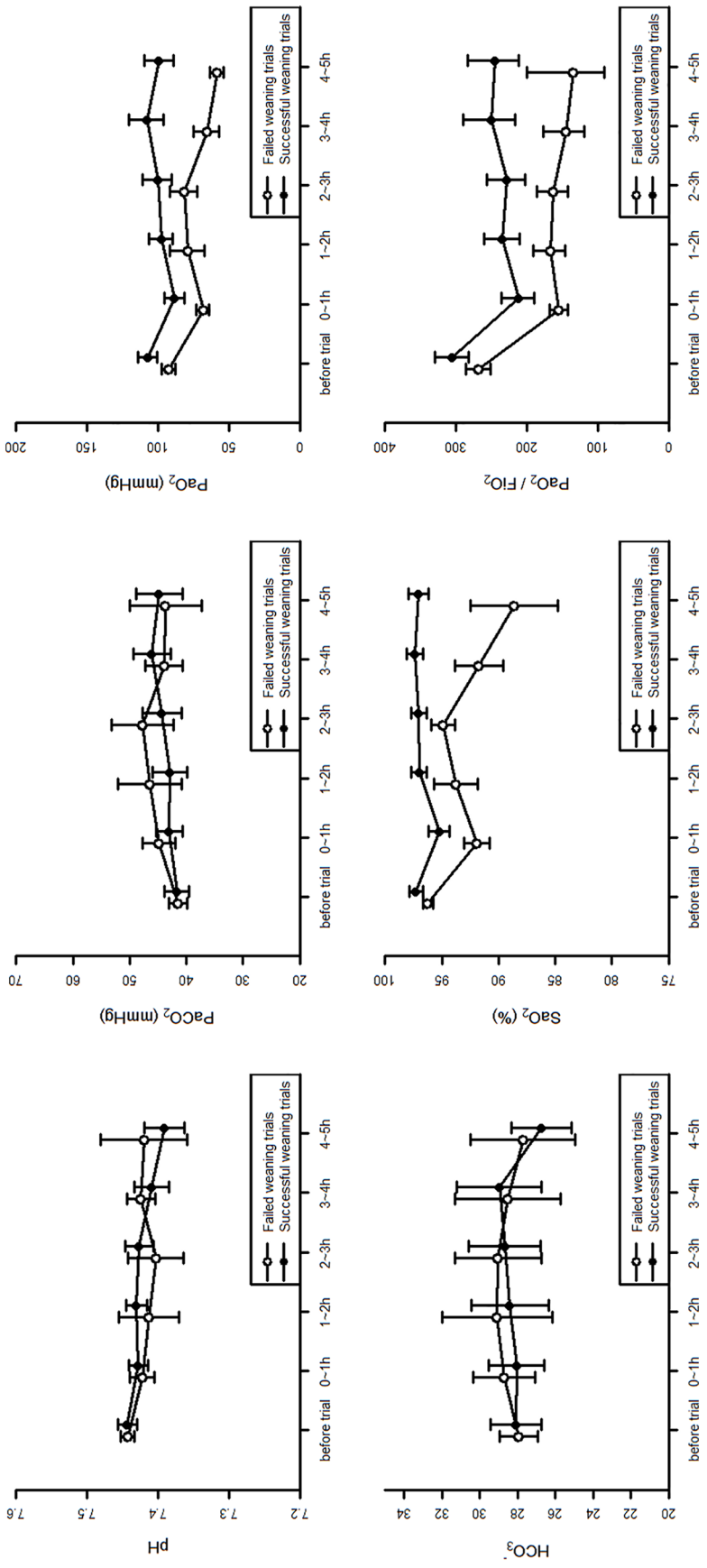

Figure 2. Comparison arterial blood gas over the time during weaning trial.
ABG analysis obtained before trial off ($n = 115$ *versus* 77) and within 1 h ($n = 57$ *versus* 63), 1–2 h ($n = 17$ *versus* 32), 2–3 h ($n = 20$ *versus* 34), 3–4 h ($n = 6$ *versus* 23) and 4–5 h ($n = 8$ *versus* 16) after trial off according to failure or success for trial. Open and black circle plots represent failed and successful trials, respectively.

The risk of various complications exists while maintaining ECMO.[5] Therefore, when signs of pulmonary function recovery appear, physicians assess a patient's condition, including symptoms, hemodynamics, and gas exchange at the minimum ECMO setting, to determine whether ECMO can be discontinued. Although no data are available on the time needed to assess gas exchange status using ABG analysis during a weaning trial for venovenous ECMO, previous studies showed the time courses of oxygenation-related parameters after changes in respiratory mechanics in mechanically ventilated patients. The time to reach 90% final equilibrated PaO_2 after FiO_2 alteration is less than 10 min.[10–13] In a study in which patients were divided into groups by PaO_2/FiO_2 ratio, similar results were obtained regardless of PaO_2/FiO_2 ratio.[12] Although patients with chronic obstructive lung disease take longer to reach oxygenation equilibration than patients without the disease, 30 min is considered reasonable for PaO_2 to reflect patient condition after changes in supplemental oxygen, even in patients with chronic obstructive lung disease.[10]

Weaning trials in patients treated with ECMO for respiratory failure, however, are not simply stopping oxygenation of circulating blood by ECMO. They are a process to assess if the patient can maintain adequate gas exchange under sufficient ventilator support in the absence of ECMO support. In this study, we demonstrated a significant change in PaO_2 and SaO_2 within 2 h after stopping sweep gas. PaO_2 and SaO_2 increased to a level similar to pretrial values, and remained stable until the end of successful trials. Such improvements in oxygenation were not observed in failed trials.

In patients with acute respiratory failure, ECMO is also a means of supporting ventilation, not just oxygenation. $PaCO_2$ could be increased during the period of stopping sweep gas because the removal of carbon dioxide is affected by sweep gas flow through the oxygenator.[14] $PaCO_2$ changes slowly and reaches steady state when the minute volume is altered, unlike changes in PaO_2. Therefore, more time is needed than the time for PaO_2 to reflect adequate gas exchange to determine if patients can maintain adequate carbon dioxide removal with mechanical ventilation after weaning from ECMO.[15,16] However, in our study, a significant change in $PaCO_2$ was identified only within the first hour after trial off, while changes in PaO_2 were also observed at 2 h.

This study provides new information on the duration of sweep gas off trials in patients receiving venovenous ECMO but has some limitations. First, given its observational nature, selection bias influencing the significance of our findings is a possibility. Although we used a protocol for sweep gas off trials, specific timing and tests during trials except for ABG at 30 min were not clarified. Compliance with the protocol was not monitored during the study period. The small sample size limited the power of these findings. In addition, our study was based at a single institution with a multidisciplinary ECMO team,[7] which could limit the generalizability of our findings to other hospitals. Second, we could not evaluate which patients needed longer to properly assess readiness to wean from ECMO. Further study with a large number of patients with various pulmonary diseases should be conducted.

In summary, ABG were not changed from 2 h after stopping sweep gas in patients receiving venovenous ECMO. Explaining the time course and unique equilibrium time of ABG measurements during venovenous ECMO weaning trials in this study is difficult. Based on our institutional experience, however, we suggest 2 h or more of monitoring after stopping sweep gas flow to assess if patients are ready for decannulation.

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Conflict of interest statement

The authors declare that there are no conflicts of interest.

ORCID iD

Kyeongman Jeon https://orcid.org/0000-0002-4822-1772

Supplemental material

The reviews of this paper are available via the supplemental material section.

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