Case Report

Pump-controlled retrograde trial off for weaning from venoarterial extracorporeal membrane oxygenation in an adult patient with pulmonary embolism

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Background: Although pump-controlled retrograde trial off (PCRTO) is a practical method for weaning from venoarterial extracorporeal membrane oxygenation (VA-ECMO), its advantages and safety for patients with pulmonary embolism are not yet reported.

Case Presentation: A 62-year-old man with coronavirus disease 2019 experienced sudden cardiac arrest, and VA-ECMO was introduced. After confirming a massive acute pulmonary embolism, unfractionated heparin treatment was initiated. On day 6, the patient was confirmed stable with a flow rate of 1.0 L/min. However, decannulation led to cardiac arrest and reintroduction of VA-ECMO. After further treatment, a residual thrombus was observed, and pulmonary arterial pressure remained high. On day 23, ECMO was decannulated successfully after a weaning test with PCRTO, which simulated ECMO withdrawal by generating a partial arteriovenous shunt.

Conclusion: PCRTO is a feasible weaning strategy and can be considered for patients with uncertain cardiorespiratory recovery.

Key words: COVID-19, extracorporeal membrane oxygenation, hemodynamics, pulmonary embolism, safety

INTRODUCTION

WEANING STRATEGIES FOR venoarterial extracorporeal membrane oxygenation (VA-ECMO) remain controversial.[1] Serial hemodynamic and echocardiographic assessments are implemented with step-by-step flow rate reduction until a minimum is achieved. However, this causes right ventricular (RV) preload reduction resulting in inadequate cardiac function evaluation.[1,2] A pump-controlled retrograde trial off (PCRTO) is a feasible, safe, and reproducible weaning strategy that reduces the pump speed until blood flow becomes retrograde from the arterial cannula through the ECMO console to the venous cannula.[2] As this creates a partial arteriovenous shunt without invasive procedures, PCRTO can simulate weaning off ECMO by providing adequate preload to assess accurate cardiac function.[3] However, no case reports on PCRTO use in pulmonary embolism (PE) exist. We describe a case of a massive acute pulmonary thromboembolism treated with VA-ECMO. Safe weaning off ECMO failed using the conventional flow weaning method but succeeded after PCRTO.

CASE PRESENTATION

A 62-year-old man with chronic kidney disease and hypertension was hospitalized due to coronavirus disease 2019 (COVID-19). After recuperating for 11 days at home, he developed hemoptysis and dyspnea for >2 days. He received two COVID-19 vaccine doses before the onset of symptoms. On admission, he was stable without sustained hemoptysis, not requiring oxygen administration; he was not administered deep vein thrombosis prophylaxis. On hospitalization day 2, he experienced sudden-onset epigastric pain, followed by decreased oxygenation and hemodynamic failure leading to pulseless electrical activity. Femoro-femoral VA-ECMO was introduced 54 min after cardiac arrest owing to poor response to advanced cardiopulmonary

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life support. The patient was transferred to our hospital for intensive care. The ECMO system was set using the CAPIOX Emergency Bypass System (CAPIOX EBS; Terumo, Tokyo, Japan), which includes a centrifugal pump (CAPIOX Centrifugal Pump SL; Terumo) and a membrane oxygenator (CAPIOX LX; Terumo).

On hospitalization day 2, PE and acute epidural hemorrhage (AEDH) were diagnosed using computed tomography (CT; Fig. 1A–C). Unfractionated heparin (UFH) administration continued after CT confirmed no AEDH progression between days 2 and 3, with activated partial thromboplastin time targeted at 45–60 s as the therapeutic range. Flow was reduced gradually unless the mean arterial pressure was <65 mmHg or pulmonary artery pressure (PAP) increased by 5–10 mmHg from the baseline. On day 6, we reduced the ECMO flow from 2.0 to 1.0 L/min as a weaning trial and monitored the hemodynamic parameters (Table 1), echocardiographic findings, and blood gas levels. With low catecholamine doses (norepinephrine: 0.1 mcg/kg/min and dobutamine: 3 mcg/kg/min), blood pressure and PAP remained unchanged (137/77 to 141/69 and 81/32 to 84/37 mmHg, respectively) and cardiac index increased (2.1 to 2.8 L/min/m^2). There were no relevant changes in the echocardiographic findings and blood gases during the weaning trial. PAP was high but there was no exacerbation; thus, we decided to decannulate ECMO. However, his circulation gradually collapsed, and he developed pulseless electrical activity 30 min after withdrawal. VA-ECMO was reintroduced within a low flow time of 35 min. Although PE was assessed as the cardiac arrest cause, continuous UFH administration was stopped because of AEDH exacerbation (Fig. 1D–F). As the patient was comatose, targeted temperature management at 36°C was maintained for 72 h. Catheter-directed aspiration thrombectomy was performed on day 7 without a significant change in PAP. Surgical pulmonary arterial thrombectomy was not performed because the use of large amounts of heparin to introduce a cardiopulmonary bypass was considered fatal in the presence of AEDH. Resolution AEDH trends were confirmed with regular CT follow-up, and UFH administration, aimed at an activated partial thromboplastin time of 35–40 s, was cautiously resumed on day 9. By day 22, PAP, although higher than normal, progressively decreased. In addition, most of the PE remained on repeated CT (Fig. 1G–I). Therefore, VA-ECMO weaning through PCRTO was scheduled with

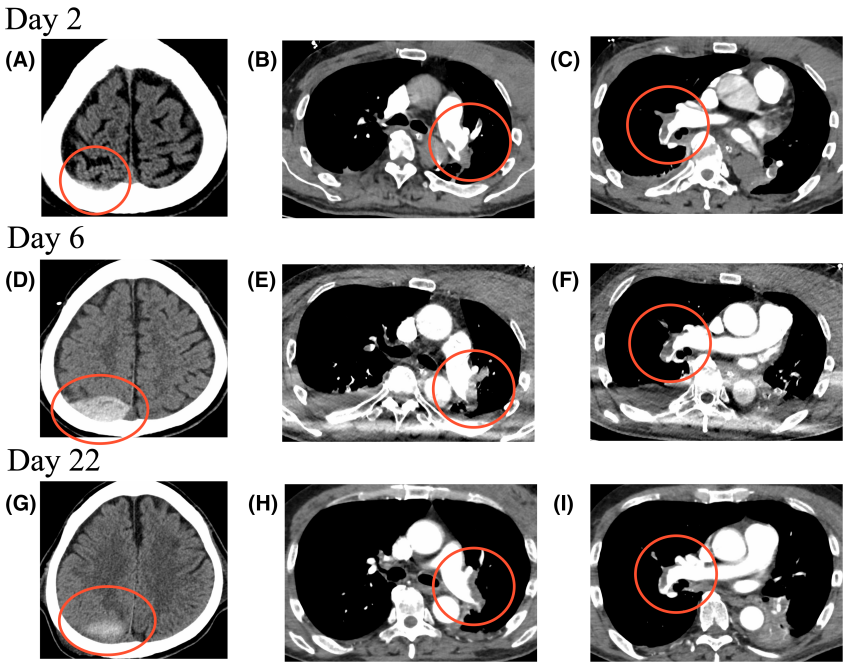

Fig. 1. Comparison of the head and chest CT scans between days (A–C) 2, (D–F) 6, and (G–I) 22. A mild AEDH and bilateral PE diagnosis were made on day 2. On day 6, after failure of decannulation and reintroduction of ECMO, AEDH showed an exacerbation, and the remaining bilateral PE was verified. On day 22, resolution of AEDH and the remaining PE were confirmed. AEDH, acute epidural hemorrhage; CT, computed tomography; PE, pulmonary embolism; ECMO, extracorporeal membrane oxygenation.

Table 1. The parameters of hemodynamic monitoring and the ECMO setting during the flow weaning trial on day 6

Parameters	Before flow weaning	15 min after flow weaning	1 h after flow weaning	2 h after flow weaning
ECMO pump speed (rpm)	1,712	1,249	1,249	1,249
ECMO flow (L/min)	2.02	0.97	0.97	1.04
Sweep gas flow (L/min)	2	2	2	2
Heart rate (/min)	100	99	102	104
Blood pressure, [MAP] (mmHg)	137/77 [97]	140/71 [94]	132/65 [87]	141/69 [93]
Pulmonary artery pressure, [MPAP] (mmHg)	81/37 [52]	85/39 [54]	83/40 [54]	84/37 [53]
Cardiac index (L/min/m^2)	2.1	2.6	2.5	2.8
Stroke volume index (L/min/m^2)	22	26	25	27
SVRI (DS m^2/cm^5)	3,610	2,835	2,707	2,597
RCWI (kg·m/m^2)	1.57	2.02	1.94	2.14
LCWI (kg·m/m^2)	2.93	3.52	3.13	3.75
Medications	0.1 mcg/kg/min of norepinephrine and 3 mcg/kg/min of dobutamine	0.1 mcg/kg/min of norepinephrine and 3 mcg/kg/min of dobutamine	0.1 mcg/kg/min of norepinephrine and 3 mcg/kg/min of dobutamine	0.1 mcg/kg/min of norepinephrine and 3 mcg/kg/min of dobutamine

ECMO, extracorporeal membrane oxygenation; LCWI, left cardiac work index; MAP, mean arterial pressure; MPAP, mean pulmonary arterial pressure; RCWI, right cardiac work index; SVRI, systemic vascular resistance index.

20-ppm inhaled nitric oxide, as cautious evaluation of RV compensatory function was required. On day 23, a heparin bolus (16 units/kg) was administered for trial initiation. The sweep gas flow was stopped after reducing the pump speed to 355 rpm, and a retrograde flow of 0.83 L/min was achieved. Hemodynamic monitoring parameters and ECMO settings before, after, and during PCRTO are presented in Table 2. On PCRTO initiation, the cardiac index (from 2.0 to 2.9 L/min/m^2), right cardiac work index (RCWI; from 0.95 to 1.67 kg·m/m^2), and pulmonary artery pulsatility index (PAPi; from 1.71 to 4.10) gradually increased. After confirming the patient's stability *via* repeated hemodynamic and echocardiography assessments, ECMO was discontinued 1 h after PCRTO. Hemodynamic parameters between 1 h after PCRTO and after decannulation were similar: PAP (68/27 versus 68/25 mmHg), CI (2.9 versus 3.1 L/min/m^2), RCWI (1.67 versus 1.74 kg·m/m^2), and PAPi (4.10 versus 3.90). The patient was extubated on day 32 and transferred to the previous hospital on day 37, with a cerebral performance category of 1.

DISCUSSION

WE PRESENT THE case of a 62-year-old man who underwent extracorporeal cardiopulmonary resuscitation after PE. ECMO weaning using the conventional flow weaning method resulted in circulatory collapse; however, it succeeded after PCRTO. In retrospect, the first attempt at ECMO weaning was premature, although it was difficult to predict this because no weaning protocol of VA-ECMO was validated, especially for patients with PE. We focused on the fact that there was no exacerbation in the various parameters after the flow rate was lowered. However, this minimal flow reduction of RV preload led to an insufficient evaluation of RV function, leading to the failure of withdrawal. Hence, we decided to perform PCRTO to make an appropriate and careful assessment of RV function at the second weaning trial, as indicated in the Extracorporeal Life Support Organization guidelines, to be more prudent.[4] This is the first case reporting PCRTO use as a weaning method for PE in adults; it seems physiologically reasonable.

Table 2. Hemodynamic monitoring parameters and ECMO setting before, after, and during PCRTO on day 23

Parameters	Before PCRTO	10 min after PCRTO	After 1 h of PCRTO	After decannulation
ECMO pump speed (rpm)	1,914	355	355	—
ECMO flow (L/min)	2.35	−0.83	−0.98	—
Sweep gas flow (L/min)	3	0	0	—
Heart rate (/min)	81	85	84	88
Blood pressure, MAP (mmHg)	123/65 [78]	109/54 [66]	134/60 [77]	146/63 [82]
Pulmonary artery pressure, MPAP (mmHg)	50/26 [33]	62/27 [39]	68/27 [40]	68/25 [39]
Right atrium pressure (mmHg)	14	13	10	11
Cardiac index (L/min/m^2)	2.0	2.1	2.9	3.1
Stroke volume index (L/min/m^2)	25	27	34	32
SVRI (DS m^2/cm^5)	3,522	2,752	2,420	2,597
RCWI (kg·m/m^2)	0.95	1.18	1.67	1.74
LCWI (kg·m/m^2)	2.25	2.00	3.21	3.66
PAPi	1.71	2.70	4.10	3.90
Medications	10 mg/h of nicardipine hydrochloride and 4 mg/h of nitroglycerin	None	None	None

ECMO, extracorporeal membrane oxygenation; LCWI, left cardiac work index; MAP, mean arterial pressure; MPAP, mean pulmonary arterial pressure; PAPi, pulmonary artery pulsatility index; PCRTO, pump-controlled retrograde trial off; RCWI, right cardiac work index; SVRI, systemic vascular resistance index.

Weaning off VA-ECMO is controversial. Although no set standard exists, several weaning methods are proposed: flow reduction to a minimum, flow discontinuation, arteriovenous bridge creation, and PCRTO use.[1] In general, VA-ECMO withdrawal is performed after flow reduction to 1.0–1.5 L/min, with confirmation of hemodynamic, respiratory, and echocardiographic stability. However, this minimal flow reduces the RV preload; consequently, biventricular heart failure occurs if RV compensation is insufficient after decannulation.[2] The patient was stable during the flow-reduction weaning trial, although PAP was higher than normal. No consensus exists on the PAP cutoff for safe decannulation in PE treated with VA-ECMO. As our patient could not tolerate the rapid increase in RV preload after decannulation owing to residual PE, inefficient cardiac function evaluation due to inadequate preload is a limitation of this method.

PCRTO is relatively new for weaning trials and is considered a good adaptation for patients with uncertain cardiorespiratory recovery due to altered physiology. Based on the technique for neonates with respiratory failure reported by Westrope *et al.*,[5] we used Ling and Chan's[2] protocol as a standardized PCRTO protocol in adults. As PCRTO causes a decreased left ventricular afterload and an increased RV preload, an appropriate assessment of RV function can be made, especially in patients with right heart failure, such as that associated with PE.[4] PAPi or RCWI, known as indices of RV failure, are useful tools during ECMO weaning.[6,7] For example, patients with low PAPi, indicative of RV failure, might need additional approaches to achieve ECMO weaning. PAPi and RCWI were gradually increased with PCRTO initiation in our patient, suggesting preserved RV function. Each hemodynamic parameter between 1 h after PCRTO and after decannulation was similar, implying that PCRTO can precisely simulate ECMO withdrawal. Furthermore, PCRTO is considered as a "stress test," because it causes additional cardiac output to maintain adequate perfusion owing to the induced left to right shunt.[8] Moreover, the whole process can be performed simply by lowering the flow. The potential complication for undergoing PCRTO is the appearance of microemboli reaching the lung, although no previous reports mention it.[3,5] PCRTO seems physiologically appropriate for patients with RV failure, as in our patient with PE. As this is the first reported case of PCRTO use in a patient with PE, its usefulness and safety should be further studied.

CONCLUSION

THE PATIENT WITH PE was successfully decannulated after VA-ECMO with PCRTO. As PCRTO can effortlessly and precisely simulate ECMO withdrawal, it is an effective weaning strategy for patients with marginal cardiac recovery.

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DISCLOSURE

APPROVAL OF THE Research Protocol with Approval No. and Committee Name: N/A.

Informed Consent: Written informed consent for the publication of this case report was obtained from the patient.

Registry and the Registration No. of the Study/Trial: N/A.

Animal Studies: N/A.

Conflict of Interest: None declared.

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