A case series of slow continuous ultrafiltration for COVID-19 patients on extracorporeal membrane oxygenation

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Contributions: (I) Conception and design: L Kannan; (II) Administrative support: L Kannan; (III) Provision of study materials or patients: U Syeda; (IV) Collection and assembly of data: L Kannan; (V) Data analysis and interpretation: U Syeda; (VI) Manuscript writing: Both authors; (VII) Final approval of manuscript: Both authors.

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Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged as a pandemic, affected millions of people and continues to spread across the globe. While knowledge about the disease is evolving, there are still uncertainties surrounding pathophysiology of severe form of the disease and optimal management strategies. Severe pulmonary disease is characterized by sepsis, acute respiratory distress syndrome, and respiratory failure. In these hospitalized patients, acquired volume overload remains an obvious risk of aggressive fluid resuscitation and the impact of interstitial edema and congestion on the functioning of other organ systems like the kidney and the lungs are detrimental.

Case Description: In this case series, we have included six patients who were admitted to the intensive care unit (ICU) with coronavirus disease 2019 (COVID-19) pneumonia complicated by volume overload. All six patients had persistent hypoxemia requiring extracorporeal membrane oxygenation (ECMO) and volume overload. Slow continuous ultrafiltration (SCUF) was utilized for controlled volume management for both patients in positive volume status despite being on loop diuretics and patients who had robust urine output causing negative pressure on the ECMO. Out of the six, three patients had reduced length of stay in the ICU, shorter period of SCUF (7–8 days) with no major complications.

Conclusions: This case series is aimed to understand the magnanimity of volume overload in hospitalized COVID patients and approach to management by utilizing slow continuous ultrafiltration.

Keywords: Coronavirus disease 2019 (COVID-19); slow continuous ultrafiltration (SCUF); extracorporeal membrane oxygenation (ECMO); volume overload; case series

Received: 21 September 2022; Accepted: 15 February 2023; Published online: 15 September 2023.

doi: 10.21037/jeccm-22-95

View this article at: https://dx.doi.org/10.21037/jeccm-22-95

Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has resulted in 3–15% of acute kidney injury (AKI) and in patients with severe infection, about 15–50% (1). The nephrologists and the intensivists are facing immense challenges while providing care for patients with AKI in the inpatient setting. Current treatment of AKI includes supportive management and renal replacement therapy (RRT) when necessary. Some of these patients may have intact kidney function but can develop acquired volume overload from aggressive fluid resuscitation, medications, nutrition and/or body metabolism. In COVID-19 where the lung tissue is already disturbed by the rapidly expanding inflammatory process, volume overload (pulmonary edema) can worsen hypoxia in patients with acute respiratory distress syndrome (ARDS) (2). In addition to oxygenation via extracorporeal membrane oxygenation (ECMO), these patients need fluid removal with either diuretics or RRT.

Putting them on diuretics like furosemide or bumetanide gives an unpredictable response which can potentially cause problems in the ECMO machine—such as increased negative pressure with high urine volume in a short span, interruption in ECMO blood flow, and a positive fluid balance/volume overload with decreased urine output. In our hospital, we tried to put these patients on slow continuous ultrafiltration (SCUF) for volume removal while on ECMO to prevent chugging/filter clotting and other complications. In this case series of six patients, we found that the patients who recovered were in SCUF for a short period (7–8 days), had fewer days of admission to the intensive care unit (ICU) (23–29 days) and had no major complications. We present this article in accordance with the AME case series reporting checklist (available at https://jeccm.amegroups.com/article/view/10.21037/jeccm-22-95/rc).

Case presentation

Study design

This is a retrospective case series conducted in a single tertiary care center and the cases are non-consecutive.

Setting

The six patients were admitted to a tertiary care center at Pikeville, Kentucky from 08/10/2021 to 03/05/2022.

Highlight box

Key findings

- Patients requiring slow continuous ultrafiltration (SCUF) while on extracorporeal membrane oxygenation (ECMO) had better outcomes in terms of complications, length of stay in the intensive care unit (ICU), and prognosis.

What is known and what is new?

- Continuous renal replacement therapy (CRRT) is usually the modality of choice in hemodynamically unstable patients with anuric acute kidney injury with volume overload;
- Coronavirus disease 2019 (COVID-19) patients with volume overload without evidence of kidney injury or electrolyte abnormality, while being on ECMO, benefit from just SCUF.

What is the implication, and what should change now?

- More clinical trials on using SCUF in COVID-19 patients in the ICU is required to study the impact of controlled volume removal on the lifespan of ECMO, SCUF and prognosis.

Ethical statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients for publication of this case series. A copy of the written consent is available for review by the editorial office of this journal.

Case 1

A 54-year-old man with hypertension, hyperlipidemia, and hypothyroidism came to the emergency department (ED) for shortness of breath for 4 days. On examination, his temperature was 99.8 °F, heart rate was 99/min, blood pressure was 150/78 mmHg and respiratory rate was 20/min. His oxygen saturation was 96% on 2 L of nasal cannula oxygen. He tested positive for COVID-19 in the ED. He was started on remdesivir, ceftriaxone, and azithromycin. At the time of admission, his creatinine was 0.7 mg/dL. His hospitalization was complicated by worsening hypoxia that initially required 100% oxygen through vapotherm and then bilevel positive airway pressure ventilation (BiPAP), and eventually he was intubated and moved to the ICU. The patient developed ARDS; therefore, he was paralyzed and started peripheral venovenous (VV) ECMO. For diuresis, he was initially placed on bumetanide 3 mg intravenous (IV). The patient had a robust urine output of about 800 mL in 2 hours, causing an increase in negative pressure on the ECMO pump that caused chugging. Hence, he was started on SCUF for controlled fluid removal. The patient remained on SCUF for a total of 7 days and he did not have any complications. He was discharged from the hospital to a skilled nursing facility after 23 days of admission to the ICU (*Table 1*).

Case 2

A 46-year-old male with a history of IV drug abuse presented to our hospital as a transfer from a different facility with acute hypoxic respiratory failure (AHRF) in the setting of COVID-19 infection. He required intubation and mechanical ventilation and upon transfer he was very cyanotic, appeared to have vascular congestion in the face and neck and was dyssynchronized on the ventilator with the settings of 100% fraction of inspired oxygen (FiO_2) and 18 of positive end expiratory pressure (PEEP). The patient

Table 1 Clinical characteristics and pertinent findings of six patients

Variables	Patient					
	1	2	3	4	5	6
Age (years)	54	46	53	29	38	48
Sex	Male	Male	Male	Male	Male	Female
Reason for ICU admission	AHRF from COVID-19 pneumonia	AHRF from COVID-19 pneumonia	AHRF from COVID-19 pneumonia	AHRF from COVID-19 pneumonia	AHRF from COVID-19 pneumonia	AHRF from COVID-19 pneumonia
Admission creatinine (mg/dL)	0.7	0.9	0.8	0.4	0.8	0.8
Creatinine at the time of initiating SCUF (mg/dL)	0.8	0.9	0.8	0.4	1.0	0.9
Duration of ECMO (days)	10	20	17	14	20	26
Duration of SCUF (days)	7	11	8	8	11	6
Complications from SCUF/ECMO	Polyuria in addition to fluid removal with SCUF causing ECMO pump issues	Developed an oligo-anuric AKI from septic shock—switched to CRRT	None	Right-temp IJ dialysis catheter-related DVT	Persistent hypoxia and inadequate ECMO flow rate, blood clot in the right atrium and anuric AKI from worsening shock—switched to CRRT	Developed anuric AKI with hyperkalemia—switched to CRRT Blood clots in the ECMO and CRRT circuit
Length of stay in the ICU (days)	23	20	29	26	38	43
Outcome	Discharged to a nursing facility	Died	Discharged to LTAC with Trach and PEG	Discharged to LTAC with Trach and PEG	Died	Died

ICU, intensive care unit; AHRF, acute hypoxic respiratory failure; COVID-19, coronavirus disease 2019; SCUF, slow continuous ultrafiltration; ECMO, extracorporeal membrane oxygenation; AKI, acute kidney injury; CRRT, continuous renal replacement therapy; IJ, internal jugular; DVT, deep vein thrombosis; LTAC, long-term acute care; PEG, percutaneous endoscopic gastrostomy; Trach, tracheostomy.

was prone and then started VV ECMO for refractory hypoxemia. At the time of admission, his creatinine was 0.9 mg/dL. He had significant urine output with furosemide causing interruption in the ECMO pump flow, hence was started on SCUF. After day 11 of SCUF, he developed acute anuric kidney injury due to worsening septic shock and switched to continuous renal replacement therapy (CRRT). After 20 days of admission to the ICU, he died of multiorgan failure (*Table 1*).

Case 3

A 53-year-old male with medical history significant for hypertension, type II diabetes mellitus and hyperlipidemia who tested positive for COVID-19 as an outpatient presented with worsening shortness of breath, cough, nausea, vomiting and diarrhea. In the ED, it was found that he was hypoxic with an oxygen saturation of 60% on room air. He was placed on BiPAP with 1,005 FiO_2. He was started on IV dexamethasone and remdesivir. He was admitted to the ICU and switched to vapotherm but he went into atrial fibrillation with rapid ventricular response. So, the patient was intubated and started on peripheral VV ECMO for persistent hypoxemia. Since there was unpredictability in patient urine output (made 10 L urine with bumetanide drip at 1 mg/h) causing flow problems with the ECMO pump, SCUF was started. He stayed in the ICU for a total of 29 days and was discharged to a long-

term acute care (LTAC) hospital with a tracheostomy and a percutaneous endoscopic gastrostomy (PEG) tube (*Table 1*).

Case 4

A 29-year-old man with hypertension and systemic lupus erythematosus (SLE) on hydroxychloroquine presented to our hospital with shortness of breath after being tested positive for COVID-19 1 week ago. The patient remained hypoxic despite non-rebreather and BiPAP. He was put on mechanical ventilation and started on SCUF while on ECMO for controlled volume management. After 8 days on SCUF, the patient developed right temporary internal jugular hemodialysis catheter related deep vein thrombosis. Hence, dialysis catheter was removed but the patient recovered and was discharged to LTAC with a tracheostomy and a PEG tube (*Table 1*).

Case 5

A 38-year-old-male presented to hospital with fever, cough and shortness of breath. Prior to admission, he was exposed to a coworker with COVID-19 and he himself had tested positive 3 days prior to admission. In the ED, his oxygen saturation was 86% on room air. He was placed on 4 L nasal cannula oxygen initially and started on IV dexamethasone and remdesivir. Despite this, he continued to worsen and was placed on BiPAP. Because he had increased work of breathing, the patient was intubated and put on mechanical ventilation. He developed ARDS that did not improve with proning, so he was placed on VV ECMO, which was complicated by a right atrial blood clot. The patient was again taken to the operating room to reposition the ECMO cannula. By this time, he had developed a positive fluid balance despite ongoing diuresis, he was started on SCUF. Eleven days after being on SCUF, he developed anuric AKI from worsening shock, and he was switched to CRRT. The patient died after being in the ICU for 38 days (*Table 1*).

Case 6

A 48-year-old woman with hypertension and obesity was admitted to the ICU for AHRF secondary to COVID-19 pneumonia. The course of her hospitalization was complicated by septic shock from klebsiella urinary tract infection and bacteremia. She was intubated and given mechanical ventilation for persistent hypoxemia. Initially her creatinine was only 0.8 mg/dL. She started on SCUF after being placed on VV ECMO. The patient had recurrent clotting, despite anticoagulation, of the ECMO and SCUF circuit resulting in blood loss, anemia, and worsening shock. After 6 days of SCUF, she was switched to CRRT for AKI and hyperkalemia. She stayed in the ICU for 43 days and died of septic shock (*Table 1*).

The three patients who got discharged from the hospital had good kidney function and were just discharged on furosemide.

Discussion

Fluid resuscitation is an important aspect of management in patients with COVID-19 for various reasons—for intravascular volume depletion from fever, nausea, vomiting and diarrhea that a subset of patients' experience, prerenal AKI, and sepsis (2). However, there is no clear endpoint for fluid resuscitation and the consequence is fluid overload. Patients with fluid overload have worse oxygenation, prolonged stay in the ICU, and prolonged duration of mechanical ventilation and increased mortality (3).

In patients with COVID-19, in addition to fluid resuscitation, pulmonary edema occurs due to the rapidly evolving inflammatory storm in the lung parenchyma resulting in increased vascular permeability (pulmonary leak) (4). Also, imbalance in fluid metabolism, protein-rich fluid entrance and pulmonary fluid clearance plays a role in pulmonary edema. ECMO is a lifesaving technique in critically ill patients. American Society of Nephrology (ASN) has recommended CRRT as one of the recommended RRT modalities in COVID-19 patients given the critical illness and hemodynamic instability (5). While CRRT is for both metabolic clearance and AKI, SCUF, a form of CRRT is an efficient therapy for volume management.

The advantages of SCUF in COVID-19, in addition to fluid extraction and optimization of volume status, include the ability to do pre-dialysis preparation and troubleshooting outside the patient's room, thus minimizing exposure and limiting the use of personnel protective equipment (PPE) (6). Multiple studies have shown that for ECMO survivors who received CRRT, the overall fluid balance was less than that of non-CRRT patients (7-9). In the retrospective study by He *et al.* (9), the authors found that shorter ECMO to CRRT interval time is associated with early fluid overload reversal and improved cardiac function.

In our patient series, three patients who were on ECMO-SCUF survived with a shorter duration on the SCUF and shorter ICU stay. The other three patients who died had

developed complications like septic shock, AKI, electrolyte derangements, recurrent clotting of the ECMO and SCUF circuits resulting in blood loss and anemia.

Major drawbacks of using SCUF in critically ill patients are that it is not useful in patients with metabolic abnormalities as solute removal is very minimal, increased risk of intracranial hemorrhage and gastrointestinal bleeding, and enhanced hemolysis from shear stress, positive pressure, wall impact forces and properties of non-endothelialized surfaces during combined ECMO and CRRT (8). Acute prerenal insufficiency with excessive ultrafiltration is a complication as well.

The major limitation of our study is the small patient population. However, combination of ECMO and SCUF might be a safe and effective technique to improve and maintain fluid balance, reduce ECMO weaning time, reduce mortality and improve patient outcome.

Conclusions

The reporting of this case series is an attempt by the authors to highlight the impact of SCUF in the ICU in patients with COVID-19 on ECMO. Further studies involving larger patient population and multi-center studies need to be conducted to analyze the usefulness of SCUF in patients on ECMO with volume overload without any metabolic derangements as it enables controlled fluid removal, lesser complications, and better prognosis.

Acknowledgments

Funding: The authors would like to acknowledge the education department at Pikeville Medical Center, KY for providing financial support for the publication of this manuscript.

Footnote

Reporting Checklist: The authors have completed the AME Case Series reporting checklist. Available at https://jeccm.amegroups.com/article/view/10.21037/jeccm-22-95/rc

Peer Review File: Available at https://jeccm.amegroups.com/article/view/10.21037/jeccm-22-95/prf

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://jeccm.amegroups.com/article/view/10.21037/jeccm-22-95/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients for publication of this case series. A copy of the written consent is available for review by the editorial office of this journal.

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doi: 10.21037/jeccm-22-95
Cite this article as: Kannan L, Syeda U. A case series of slow continuous ultrafiltration for COVID-19 patients on extracorporeal membrane oxygenation. J Emerg Crit Care Med 2023;7:2.