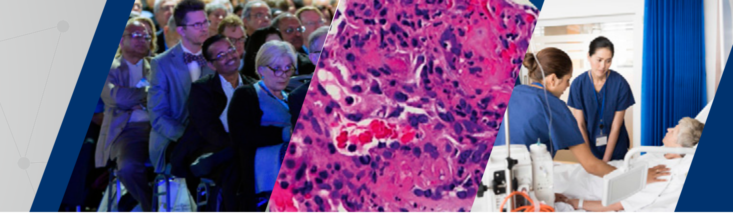
Kidney Case Conference:
How I Treat



Providing Continuous Renal Replacement Therapy in Patients on Extracorporeal Membrane Oxygenation

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Case Presentation

A 34-year-old male was admitted for respiratory failure due to H1N1 influenza. His hypoxia worsened despite maximal ventilator support and thus initiated on venovenous extracorporeal membrane oxygenation (VV-ECMO). Whereas this stabilized his respiratory and hemodynamic status, his creatinine increased (from 1.2 to 2.4 mg/dl), urine output declined (despite furosemide), and his weight had increased from 79 to 92 kg. Ultrasound assessment revealed a noncollapsing vena cava and B-lines in his lungs. Nephrology was consulted for management of AKI and volume overload.

Introduction to Extracorporeal Membrane Oxygenation

ECMO is being increasingly used to manage severe respiratory or cardiopulmonary failure (1). The key components of ECMO circuits are a large-bore access cannula(s), blood pump, and gas and heat exchangers, connected *via* circuit tubing (Figure 1). Centrifugal pumps, which have largely replaced roller pumps, produce a negative prepump pressure that draws blood from the patient. The positive postpump pressure drives the blood through the ECMO circuit and back to the patient. Circuit blood flow is determined by pump speed, access/tubing characteristics, and intravascular volume status. The gas-exchange membrane oxygenates and removes carbon dioxide from the blood *via* an exchange between the patient's blood and the sweep gas (the oxygen gas flowing through the membrane). The blood is warmed *via* a heat exchanger before returning to the patient. Sensors, strategically placed along the circuit, measure various pressures, blood flow, oxygen saturation, and air in the blood (2).

There are two types of ECMO: venoarterial (VA-ECMO) and VV-ECMO. In VA- ECMO, the collection catheter is placed into a major vein (reaching near the right atrial inlet) and the infusion catheter into a major artery. VA-ECMO provides full cardiopulmonary support, and is used to manage cardiac and cardiopulmonary failure. Conversely, VV- ECMO is restricted to the venous circulation *via* either a double lumen catheter placed into the right internal jugular vein or by using two catheters; one in the internal jugular and one in the femoral vein. VV-ECMO is used in refractory hypoxemia (2).

AKI and Extracorporeal Membrane Oxygenation

Patients on ECMO are severely ill and frequently develop AKI; its incidence is >50% in adults, more than one-half of whom require KRT (3). The etiology of AKI in these patients is comparable to that in critically ill patients not on ECMO, except that ECMO-related variables (*e.g.*, hemorheological variations, systemic inflammation, hemolysis, *etc.*) can also promote AKI (2). Despite its potentially adverse effects on the kidney, ECMO can improve systemic hemodynamics, which may improve kidney function, presumably by increasing kidney perfusion. Regardless of the cause, AKI, and in particular the initiation of KRT, heralds a large increase in mortality (4). Notwithstanding, it is important to remember that these patients are getting aggressive care and many will survive. Because of our inability to consistently predict who will survive, provision of KRT is frequently warranted. Consequently, nephrologists should be familiar with the nuances of KRT on ECMO.

Technical Aspects of Kidney Replacement Therapy on Extracorporeal Membrane Oxygenation

When to Initiate

Definitive studies establishing the ideal time to initiate KRT in critically ill AKI patients, especially ECMO patients, are lacking. In the absence of a validated indicator to initiate KRT, we have adopted the demand/capacity imbalance concept (5). Thus, we take into consideration the patients' severity of illness, and the balance between the demands on the kidney (solute and fluid load) and function in deciding when to start. We most commonly initiate KRT for fluid management, which is similar to a published survey (6); fluid overload prompted KRT initiation in 60% of patients. Indeed, because fluid overload is an independent risk factor for mortality (7) and preventing it has been associated with better survival (8), we strive to prevent it, but we most often find

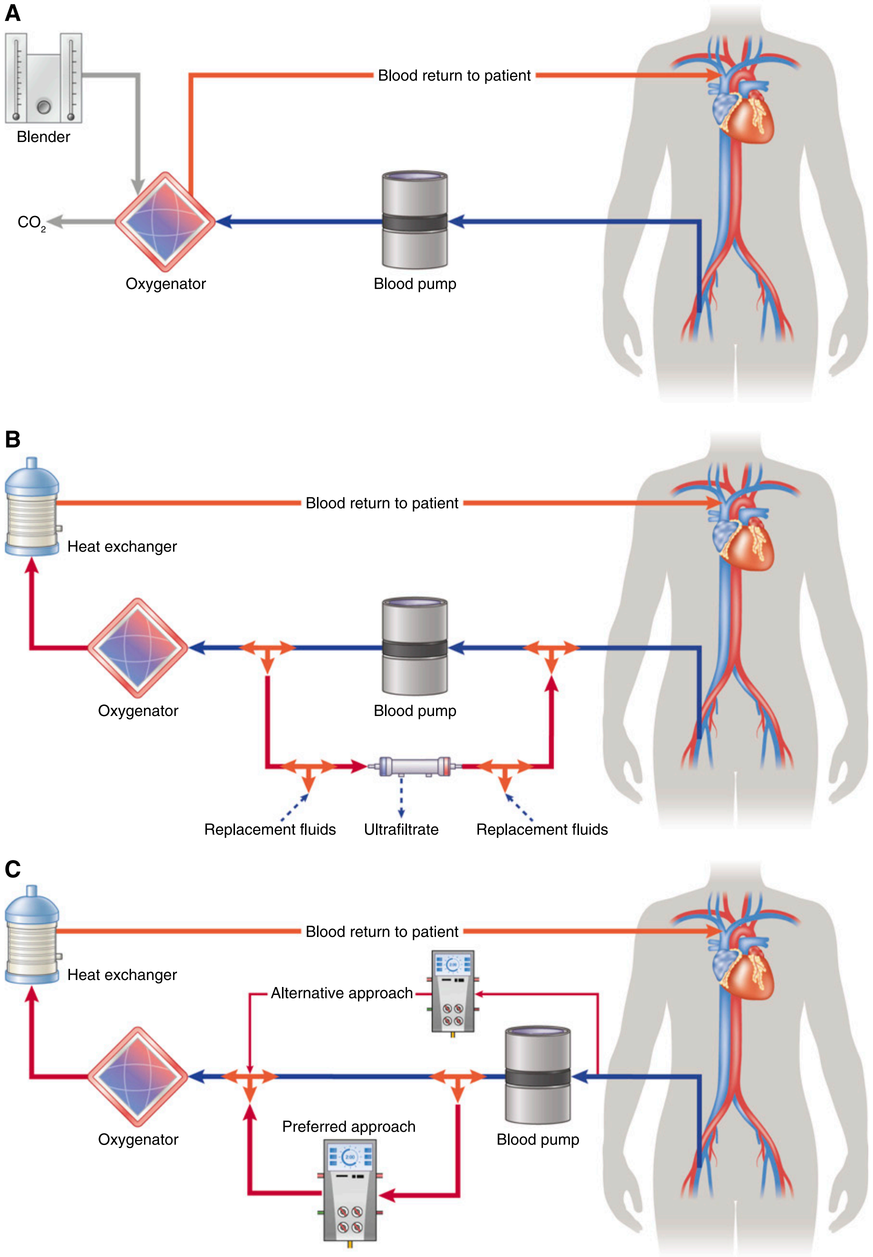

Figure 1. | **Schematic of an ECMO circuit.** Schematic of an ECMO circuit (A) incorporating either in-line hemofiltration (B) or a CRRT device integrated into the ECMO circuit, showing our preferred and alternative connections (C). CRRT, continuous RRT; ECMO, extracorporeal membrane oxygenation.

ourselves treating it. Along these lines, a meta-analysis (21,624 patients) found an association between earlier initiation of KRT and survival (9). Whereas the authors did not study potential mechanisms behind this association, it is tempting to speculate that it was related to enhanced fluid management.

Modality of Kidney Replacement Therapy

KRT options during ECMO include peritoneal dialysis, intermittent hemodialysis, prolonged intermittent RRT, and continuous renal replacement therapy (CRRT). Whereas each has advantages and disadvantages, CRRT is most commonly used because it facilitates continuous volume management (with less hemodynamic compromise) and ample solute clearance (2,4).

CRRT in ECMO patients was originally provided *via* an in-line filter placed directly into the ECMO circuit by creating a shunt from a postpump to a prepump segment of the ECMO circuit (Figure 1) (10). The pressure gradient between these segments drives blood flow through a hemofilter placed along this shunt. Blood flow is controlled through the use of resistive tubing, whereas infusion pumps deliver replacement fluid and/or dialysate, and regulate effluent flow. Urometers are used to accurately measure effluent rates. Advantages of this system include its simple setup; specialized equipment is not needed. Disadvantages include limitations in accuracy and CRRT dosing (due to infusion pump constraints).

Modern CRRT machines provide precise dialysate/replacement fluid delivery and fluid removal rates; consequently, they have become the preferred method for providing KRT. They can be operated either entirely independent of the ECMO circuit *via* a standard dialysis catheter, as in any patient not on ECMO. This approach is less complex and many nephrologists may be more comfortable with this familiar setup. Moreover, interruptions in ECMO have fewer effects on the CRRT treatment. The main limitations are related to the extravascular access.

We prefer the alternative option of integrating a CRRT device into the ECMO circuit *via* a shunt (Figure 1). In this case, we hook up both ports to the positive pressure segments of the circuits before the oxygenator (to prevent embolic events). Depending on the CRRT device being used, the access alarm pressure limits will either have to be reset to a positive pressure range or disabled. Resistors may be placed at the inlet and outlet ports to maintain access pressures within favorable ranges. CRRT is then performed as usual. This approach has the advantage of not requiring another access point, drawing from a high-flow circuit, and better filter life. However, standardizing the setup and sustaining appropriate training and monitoring are essential.

Other Technical Considerations

As with initiation, dosing of CRRT is extrapolated from data in non-ECMO patients and ultimately depends on physician discretion. We target a minimum of 20 ml/kg per minute, but adjust the CRRT dose on the basis of the patients' metabolic parameters. Nephrologists should be particularly attentive to changes in the patient's volume status, because abrupt or excessive changes can affect ECMO flow/function. Electrolyte levels, medication dosing, and delivery of nutrition, vitamins, and essential elements should be carefully monitored. Finally, most patients on ECMO are anticoagulated, obviating the need for CRRT anticoagulation. However, either regional citrate anticoagulation or heparin are used when needed.

Acknowledgments

Nephrologists are being increasingly called upon to provide KRT to ECMO patients. This is most commonly achieved *via* CRRT devices that are either integrated into the ECMO circuit or operate *via* a standard dialysis catheter (independent from the circuit). It is essential to develop a standardized setup protocol to ensure the safety and efficacy of CCRT initiation and delivery. Once connected, CRRT delivery is largely provided as in non-ECMO patients with particular attention being paid to volume management.

Disclosures

Dr. Juncos reports that he has been a member of a speakers' bureau for Baxter to speak about RRT in the Intensive Care Unit; this role is unrelated to this article and did not influence the content of the manuscript. The manuscript does not contain any recommendations of a brand of RRT machine or anything directly related to the perceived conflict of interest. Dr. Karakala has nothing to disclose.

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