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Original Research Article

Continuous renal replacement therapy during extracorporeal membrane oxygenation run: a questionary-based survey

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ABSTRACT

Background: Extracorporeal membrane oxygenation is becoming a broadly available form of prolonged cardiopulmonary support. Given a higher risk of complications fluid overload and acute kidney injury with ECMO, its conjugation with renal replacement therapy is seems to be beneficial in correcting acid-base and electrolyte imbalance and fluid overload. ECMO with RRT is rarely used in Indian centers. This survey gathered expert's opinion for routinely faced clinical questions related to ECMO run during RRT/Continuous RRT.
Methods: This was a questionary-based survey wherein a structured questionnaire composed of seven questions about ECMO run during RRT/CRRT was mailed as Google form to randomly selected 23 physicians and their responses have been received within one month duration (November 2022 to December 2022).
Results: Fluid overload (65.2%) and AKI (47.8%) were found to be the most common indications to put a patient on RRT while ECMO. Almost responders (36.4%) stated that 20-40% patients required RRT while on ECMO. Continuous venovenous hemodiafiltration (47.8%) was the most preferred choice of RRT while on ECMO. Hypotension (38.1%), electrolyte disturbance (14.3%), and hemolysis (23.8%) were the three most common complications in patient on CRRT with ECMO. Majority of the experts feel that introducing CRRT with ECMO circuit was moderately challenging.
Conclusions: Clinicians should consider the early introduction of CRRT to address acute kidney injury and fluid overload in the ECMO population. With this survey, we would like to spread awareness among physicians about important aspect CRRT during ECMO.

Keywords: Extracorporeal membrane oxygenation, Renal replacement therapy, Fluid overload, Acute kidney injury

INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) has been employed for both circulatory and respiratory support in critical care over the past two decades, including for patients with cardiogenic shock, post-cardiotomy shock, acute respiratory distress syndrome, and trauma.[1-6] In ECMO, blood is pumped outside the body, after removing carbon dioxide and adding oxygen, blood is again pumped back into the body. Two main configurations of ECMO are: veno-arterial ECMO (VA-ECMO) (support the patients suffering from refractory cardiogenic shock or combined cardiorespiratory failure), and veno-venous ECMO (VV-ECMO) (support the patients with potentially reversible causes of respiratory failure). Extracorporeal Life Support Organization (ELSO) guidelines endorse ECMO as a rescue therapy, whenever there is an 80% or higher risk of mortality, if not applied.[7]

However, over the last few decades, patients utilizing ECMO are at a higher risk of developing other organ failures because of a considerable number of

pathophysiologic, hemodynamic, and inflammatory abnormalities (because of both the primary disease and exposure of blood to the non-endothelialized surface of the ECMO circuit).[8-10] Fluid overload is a frequent problem in patients receiving ECMO because of several reasons, including the volume related to blood product transfusions, medication infusions, and fluid boluses to maintain adequate intravascular volume.[9,11,12] Additionally, acute kidney injury (AKI) is the most frequently encountered complication in this patient population and may occur as part of multiple organ failure.[13,14] Nearly 32–85% of patients have developed AKI during ECMO.[11,15]

The addition of renal replacement therapy (RRT) to ECMO is beneficial to treat acid-base and electrolyte imbalance as well as fluid overload. Up to 70% of adult patients and 60% of children requiring ECMO require RRT.[16] In India, ECMO with RRT is rarely used modality and only few centres practiced it (i.e., ECMO centres in India: Apollo Children Hospital, Chennai; Apollo Hospital, New Delhi; Aster Medcity Hospital, Kochi; Blk-Max Superspeciality Hospital, New Delhi; Clio/SPS Hospital; Kanchi Kamakoti childs trust hospital Chennai (KKCTH); Manipal hospital, Bengaluru; Medanta Hospital, Delhi; Narayana health hospital, Kolkata; Narayana institute of cardiac science, Bengaluru; Rainbow children's hospital, Hyderabad; rainbow children's hospital, Bengaluru; Rainbow children's hospital, Chennai; and Ridhhi Vinayak Multispeciality Hospital, Mumbai). The knowledge pertaining to ECMO with RRT are still suppressed; hence, the present survey was conducted to gather expert's opinion for routinely faced clinical questions related to ECMO run during RRT/Continuous RRT (CRRT).

METHODS

This was a questionary-based survey wherein a questionnaire about ECMO run during RRT/CRRT was mailed as Google form to 23 doctors in November 2022. The randomly selected physicians from different areas like pediatric critical care, adult critical care, cardiothoracic surgery, cardiac anesthesia and cardiology having good experience and are successfully running ECMO in their respective institutes were considered as responders. The responses have been received from dedicated professionals' physicians within in one month duration (November 2022 to December 2022).

A structured questionnaire composed of seven questions (Table 1) was designed to assess expert's opinion for routinely faced clinical questions related to ECMO run during RRT/CRRT. Doctors from departments of cardiology anesthesia, cardiothoracic, critical care (Adults and Pediatrics), and Riddhi Vinayak ECMO support were chosen for this survey.

Table 1: Questionaries.

Questions
What is the commonest indication to put a patient on RRT while on ECMO?
Fluid overload
Prevention of fluid overload
Electrolyte disturbance
AKI
Toxins/cytokine removal
Other
What percentages of patients required RRT while on ECMO?
10-20
20-40
40-60
60-80
>80
Other
What is the preferred choice of RRT while on ECMO?
CVVH
CVVHD
CVVHDF
SLED
Hemofilter
Other
What way your unit prefer to institute RRT in a patient on ECMO?
Continuous venovenous hemodiafiltration (CVVHD)
Continuous venovenous hemodiafiltration (CVVHDF)
Sustained low efficiency dialysis (SLED)
Hemofilter
Other
What way you prefer to introduce CRRT device in ECMO circuit
Draining line to pre-pump and return line between pump and oxygenator
Both draining and return line to pre pump
Draining line at post oxygenator and return to pre pump
Other
Commonest complication your unit encounter in patient on CRRT with ECMO
Hypotension
Electrolyte disturbance
Hemolysis
Clotting
Frequent change of CRRT filter
Other
Amount of difficulty you experience while introducing CRRT with ECMO circuit?
Easy
Moderately challenging
Hard
Other

RESULTS

Responses achieved

In this survey, we have sent questionaries to 23 respondents. Number of responses achieved for each question were summarized in (Table 2).

Table 2: Responses achieved for each question of questionaries.

Questions	N
What is the commonest indication to put a patient on RRT while on ECMO?	23
What percentages of patients required RRT while on ECMO?	22
What is the preferred choice of RRT while on ECMO?	23
What way your unit prefer to institute RRT in a patient on ECMO?	23
What way you prefer to introduce CRRT device in ECMO circuit	20
Commonest complication your unit encountered in patient on CRRT with ECMO	21
Amount of difficulty you experience while introducing CRRT with ECMO circuit	23

Indications for RRT during ECMO

The commonest indications to put a patient on RRT while ECMO were fluid overload (65.2%) followed by AKI (47.8%). The least common indications included prevention of toxins/cytokine removal (17.4%), electrolyte disturbance (13%), and prevention of fluid overload (4.3%) (Figure 1).

Need for RRT while on ECMO

Majority of responders (36.4%) reported that 20-40% patients required RRT while on ECMO. Five responders (22.7%) stated that 10-20% and 40-60% patients required RRT while on ECMO (Figure 2).

Preferred modalities of RRT during ECMO

As demonstrated in (Figure 3), CVVHDF (47.8%) was found to be the most preferred choice of RRT while on ECMO. The least preferred choice included CVVH (8.7%), CVVHD (13%), SLED (8.7%), hemofilter (17.4%), and CRRT (8.7%).

Introduction of CRRT device to ECMO circuit in a patient on ECMO

Introduction of CRRT device to ECMO circuit (73.9%) followed by introduction of hemofilter to ECMO circuit (17.4%) was the most commonly preferred unit to institute RRT in a patient on ECMO. Less preferred unit included independent CRRT access, which achieved response rate of 8.7% (Figure 4).

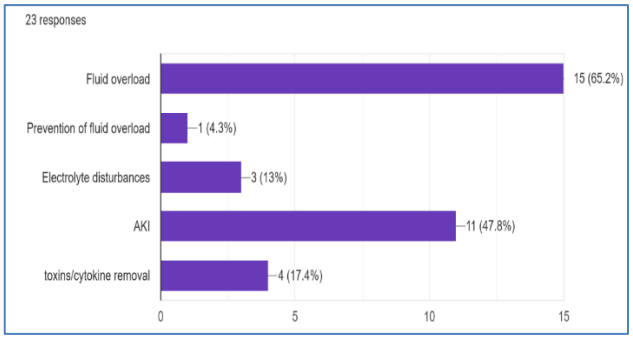

Figure 1: Responses rate for commonest indications to put a patient on RRT while ECM.

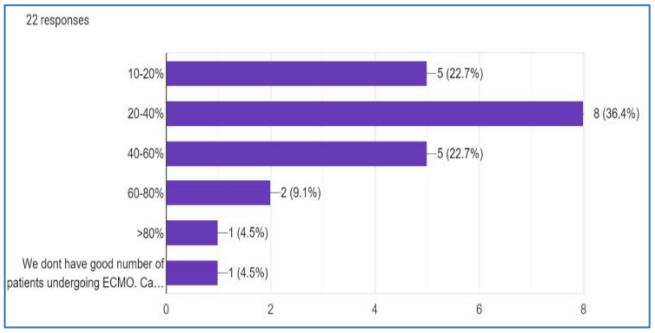

Figure 2: Response rate for need for RRT while on ECMO.

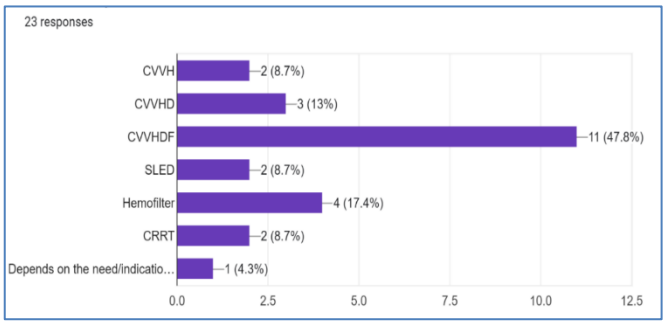

Figure 3: Response rate for preferred modalities of RRT while on ECMO.

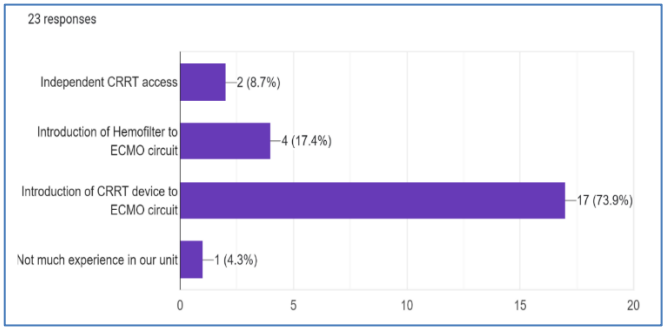

Figure 4: Response rate for unit preference to institute RRT in a patient on ECMO.

Preferred way to introduce CRRT device in ECMO circuit

As depicted in (Figure 5), response rate for draining line at post oxygenator and return to pre pump (35%) was higher as most preferred way to introduce CRRT device in ECMO circuit.

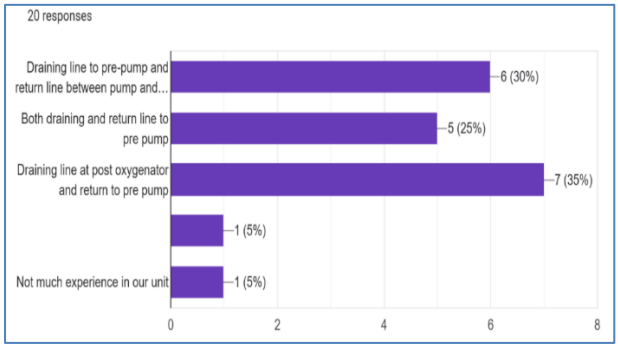

Figure 5: Response rate for the most preferred way to introduce CRRT device in ECMO circuit.

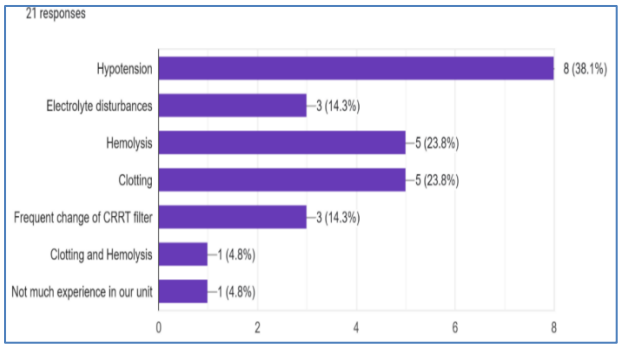

Figure 6: Response rate for complications that unit encounter in patient on CRRT with ECMO.

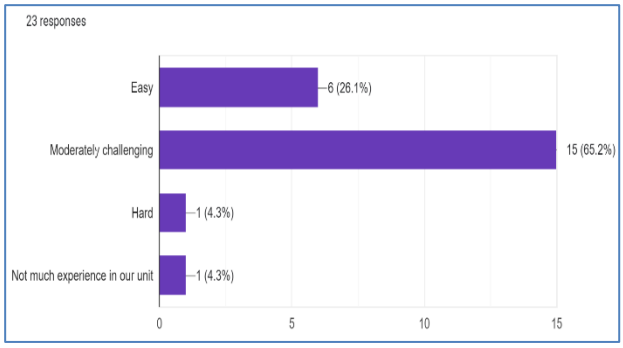

Figure 7: Response rate for amount of difficulty you experience while introducing CRRT with ECMO circuit.

Complications encountered in patient on CRRT with ECMO

Probability of complications encountered in patient on CRRT with ECMO were as follows: hypotension (38.1%), electrolytre disturbance (14.3%), hemolysis (23.8%), clotting (23.8%), frequent change of CRRT filters (14.3%), clotting and hemolysis (4.8%) (Figure 6).

Amount of difficulty you experience while introducing CRRT with ECMO circuit

More than half of responders (65.2%) stated that introducing CRRT with ECMO circuit was moderately challenging (Figure 7).

DISCUSSION

ECMO has been exceedingly utilized in emergency departments, critical care units, operating rooms, interhospital transfers, and during cardiopulmonary resuscitation. The present survey aims to gather expert's opinion for routinely faced clinical questions related to ECMO run during RRT/CRRT. The key findings of the survey were: a) Two most common indications to put a patient on RRT while ECMO were fluid overload and AKI, b) most of responders (36.4%) reported that 20-40% patients required RRT while on ECMO, c) CVVHDF (47.8%) was found to be the most preferred choice of RRT while on ECMO, d) Introduction of CRRT device to ECMO circuit was the most preferred unit to institute RRT in a patients on ECMO, e) draining line at post oxygenator and return to pre pump (35%) was the most preferred way to introduce CRRT device in ECMO circuit, f) the most frequent complications seen in patient on CRRT with ECMO were: hypotension (38.1%), electrolyte disturbance (14.3%), hemolysis (23.8%), clotting (23.8%), frequent change of CRRT filters (14.3%), clotting and hemolysis (4.8%), and g) many of the experts (65.2%) believe that introducing CRRT with ECMO circuit was moderately challenging.

In this survey, we found that fluid overload (65.2%) followed by AKI (47.8%) was most common indications to put patient on RRT while ECMO. These findings were in agreement with the Kidney intervention during ECMO study group (KIDMO) classification who reported fluid overload (43%), prevention of fluid overload (16%), AKI (35%) and electrolyte disturbances (4%) as the most common indications for RRT in patients on ECMO. Other indications include shock, sepsis, liver dysfunction, poisonings, optimizing nutrition, and improved protein delivery and cytokine removal in coronavirus disease (COVID-19)/sepsis. Fluid overload is not be tolerated in some patients such as patients with severe lung disease and respiratory failure. Fluid removal undoubtedly remains a common reason for RRT during ECMO, followed by correction of metabolic derangements being the second reason.[17] Both continuous and intermittent RRT modalities are efficient treatment strategies for removing excess fluid and achieving metabolic control. There isn't any solid proof that either one of the modalities is better than the other for survival.[18] Another common RRT indications is AKI. Based on the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, a current statistic showed that AKI is prevalent in 60–74% of neonatal-paediatric patients

supported on ECMO.[17] Earlier studies demonstrated a good relationship between fluid overload/AKI and increased morbidity and mortality in critically ill patients.[19-23] AKI during ECMO is independently associated with both increase duration of ECMO as well as mortality in neonatal and paediatric patients.[24] One multicentre study performed by the KIDMO demonstrates that AKI of any stage is associated with increased mortality at decannulation, with unadjusted odd's ratio of 2.55 when compared to no AKI, which was 1.75.[17] Most of the responders (36.4%) reported that 20-40% patients required RRT while on ECMO. The rate for usage of RRT in adult patients is varied among various reported studies, which are summarized in (Table 3).

Table 3: Previous studies reporting the usage of renal replacement therapy in adult patients on ECMO.

Study	ECMO patient population	Treatment with renal replacement therapy (%)
Brogan et al[25]	1473 (ELSO registry)	44
Yap et al[26]	10	50
Wu et al[27]	102	100
Chen et al[28]	102	41
Yan et al[29]	67	45
Luo et al[30]	45	20
Luo et al[31]	11	27
Lee et al[32]	185	41
Kielstein et al[33]	200	59
Aubron et al[34]	158	56

There are three means to provide RRT with ECMO: using an in-line hemofilter, connecting an RRT device to the ECMO circuit (integrated system), or using a separate RRT access.[35] Regardless of whether the RRT circuit is integrated into the ECMO or a separate circuit, it is possible to deliver all RRT modalities, including CVVH, CVVHD, CVVHDF, and SCUF. To deliver RRT safely, however, specialized knowledge of the intra-circuit pressures is required. In this survey, CVVHDF (47.8%) was found to be the most preferred choice of RRT while on ECMO. Introduction of CRRT device to ECMO circuit was the most preferred unit to institute RRT in a patient on ECMO. Draining line at post oxygenator and return to pre pump (35%) was higher is the most preferred way to introduce CRRT device in ECMO circuit. ECMO does come with a wide range of potential complications, including, blood clots (oxygenator, pump, tubing, hemofilter), bleeding (surgical site, cannulation site, gastrointestinal, intracranial, tracheostomy, hemolysis, disseminated intravascular coagulation); pump failure; oxygenator failure; neurologic and musculoskeletal complications (intracranial bleed, stroke, seizure, encephalopathy); limb ischemia; infection; renal failure; multiple organ dysfunction syndrome; problems during cannulation, and hyperbilirubinaemia.[36] In our cohort, we observed hypotension (38.1%), electrolyte disturbance (14.3%), hemolysis (23.8%), clotting (23.8%), frequent change of CRRT filters (14.3%), clotting and hemolysis (4.8%) as the most common complications in patient on CRRT with ECMO. This study is subject to limitations related to respondent bias. People who voluntarily choose to participate in the survey may possess distinct characteristics or hold differing opinions compared to those who opt not to participate. This bias can affect the generalizability of study findings. Additionally, it's important to recognize that questionnaires rely on self-reported data, which may not always reflect actual behavior or attitudes accurately.

CONCLUSION

The use of ECMO is exceedingly increasing in the recent era. Patients on ECMO are more likely to develop AKI and thus need RRT. Aggressive fluid management is a critical aspect of ECMO care. The concept of Multiple Organ Support Therapy (MOST), which includes the combination of CRRT and ECMO, is an extracorporeal strategy that is increasingly used in the ICU. Next-generation machines are required to achieve harmonization of components, methods, and operations of MOST. Meticulous attention should be given to every aspect of CRRT on ECMO, since these patients have been shown higher mortality. Given that each ECMO center has its own tools, expertise persons, and practices, the international ECMO community must continue to work together in a collaborative approach. Notably, the United States food and drug administration has not granted the combination of any of these circuits together, and such use is off-label. It is suggested that individual institutions create site-specific protocols based on experience, equipment accessibility, and target patient population.

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REFERENCES

1. Wu MY, Huang CC, Wu TI, Wang CL, Lin PJ. Venovenous extracorporeal membrane oxygenation for acute respiratory distress syndrome in adults: prognostic factors for outcomes. Medicine. 2016; 95(8):e2870.
2. Chen SW, Tsai FC, Lin YS, Chang CH, Chen DY, Chou AH, et al. Long-term outcomes of extracorporeal membrane oxygenation support for postcardiotomy shock. J Thorac Cardiovasc Surg. 2017;154(2):469-77.
3. Lin CY, Tsai FC, Lee HA, Tseng YH. Extracorporeal membrane oxygenation support in post-traumatic

cardiopulmonary failure: a 10-year single institutional experience. Medicine. 2017;96(6):6067.
4. Wu SC, Chen WT-L, Lin HH, Fu CY, Wang YC, Lo HC, et al. Use of extracorporeal membrane oxygenation in severe traumatic lung injury with respiratory failure. Am J Emerg Med. 2015;33(5):658-62.
5. Diddle JW, Almodovar MC, Rajagopal SK, Rycus PT, Thiagarajan RR. Extracorporeal membrane oxygenation for the support of adults with acute myocarditis. Crit Care Med. 2015;43(5):1016-25.
6. Burrell AJ, Pellegrino VA, Wolfe R, Wong WK, Cooper DJ, Kaye DM, et al. Long-term survival of adults with cardiogenic shock after venoarterial extracorporeal membrane oxygenation. J Crit Care. 2015;30(5):949-56.
7. Organization ELS. ELSO Guidelines for cardiopulmonary extracorporeal life support. ELSO Ann Arbor. 2013.
8. Selewski DT, Askenazi DJ, Bridges BC, Cooper DS, Fleming GM, Paden ML, et al. The impact of fluid overload on outcomes in children treated with extracorporeal membrane oxygenation: A multicenter retrospective cohort study. Pediatr Crit Care Med. 2017;18(12):1126-35.
9. Jenks CL, Raman L, Dalton HJ. Pediatric extracorporeal membrane oxygenation. Crit Care Clin. 2017;33(4):825-41.
10. Foland JA, Fortenberry JD, Warshaw BL, Pettignano R, Merritt RK, Heard ML, et al. Fluid overload before continuous hemofiltration and survival in critically ill children: a retrospective analysis. Crit Care Med. 2004; 32(8):1771-6.
11. Foti L, Villa G, Romagnoli S, Ricci Z. Acute kidney injury and extracorporeal membrane oxygenation: review on multiple organ support options. Int J Nephrol Renovasc Dis. 2021;14:321-9.
12. Foland JA, Fortenberry JD, Warshaw BL, Pettignano R, Merritt RK, Heard ML, et al. Fluid overload before continuous hemofiltration and survival in critically ill children: A retrospective analysis. Crit Care Med. 2004;32(8):1771-6.
13. Jetton JG, Askenazi DJ. Acute kidney injury in the neonate. Clin Perinatol. 2014;41(3):487-502.
14. Prowle JR, Echeverri JE, Ligabo EV, Ronco C, Bellomo R. Fluid balance and acute kidney injury. Nat Rev Nephrol. 2010;6(2):107-15.
15. Selewski DT, Wille KM, editors. Continuous renal replacement therapy in patients treated with extracorporeal membrane oxygenation. Semin Dial. 2021;34(6):537-49.
16. Hansrivijit P, Lertjitbanjong P, Thongprayoon C, Cheungpasitporn W, Aeddula NR, Salim SA, et al. Acute kidney injury in pediatric patients on extracorporeal membrane oxygenation: A systematic review and meta-analysis. Medicines. 2019;6(4):32-8.
17. Fleming GM, Askenazi DJ, Bridges BC, Cooper DS, Paden ML, Selewski DT, et al. A multicenter international survey of renal supportive therapy during ECMO: the Kidney Intervention during Extracorporeal Membrane Oxygenation (KIDMO) group. Asaio J. 2012;58(4):407-14.
18. Yan X, Jia S, Meng X, Dong P, Jia M, Wan J. Acute kidney injury in adult postcardiotomy patients with extracorporeal membrane oxygenation: evaluation of the RIFLE classification and the Acute Kidney Injury Network criteria. Eur J Cardiothorac Surg. 2010;37(2): 334-8.
19. Alobaidi R, Morgan C, Basu RK, Stenson E, Featherstone R, Majumdar SR, et al. Association between fluid balance and outcomes in critically ill children: A systematic review and meta-analysis. JAMA Pediatr. 2018;172(3):257-68.
20. Goldstein SL. Fluid management in acute kidney injury. J Intensive Care Med. 2014;29(4):183-9.
21. Kwiatkowski DM, Sutherland SM. Acute kidney injury in pediatric patients. Best Pract Res Clin Anaesthesiol. 2017;31(3):427-39.
22. Modem V, Thompson M, Gollhofer D, Dhar AV, Quigley R. Timing of continuous renal replacement therapy and mortality in critically ill children. Crit Care Med. 2014;42(4):943-53.
23. Sethi SK, Raghunathan V, Shah S, Dhaliwal M, Jha P, Kumar M, et al. Fluid overload and renal angina index at admission are associated with worse outcomes in critically ill children. Front Pediatr. 2018;6:118.
24. Lin CY, Chen YC, Tsai FC, Tian YC, Jenq CC, Fang JT, et al. RIFLE classification is predictive of short-term prognosis in critically ill patients with acute renal failure supported by extracorporeal membrane oxygenation. Nephrol Dial Transplant. 2006;21(10): 2867-73.
25. Brogan TV, Thiagarajan RR, Rycus PT, Bartlett RH, Bratton SL. Extracorporeal membrane oxygenation in adults with severe respiratory failure: a multi-center database. Intensive Care Med. 2009;35(12):2105-14.
26. Yap HJ, Chen YC, Fang JT, Huang CC. Combination of continuous renal replacement therapies (CRRT) and extracorporeal membrane oxygenation (ECMO) for advanced cardiac patients. Ren Fail. 2003;25(2):183-93.
27. Wu VC, Tsai HB, Yeh YC, Huang TM, Lin YF, Chou NK, et al. Patients supported by extracorporeal membrane oxygenation and acute dialysis: acute physiology and chronic health evaluation score in predicting hospital mortality. Artif Organs. 2010; 34(10):828-35.
28. Chen YC, Tsai FC, Chang CH, Lin CY, Jenq CC, Juan KC, et al. Prognosis of patients on extracorporeal membrane oxygenation: the impact of acute kidney injury on mortality. Ann Thorac Surg. 2011;91(1):137-42.
29. Yan X, Jia S, Meng X, Dong P, Jia M, Wan J. Acute kidney injury in adult postcardiotomy patients with extracorporeal membrane oxygenation: evaluation of the RIFLE classification and the Acute Kidney Injury Network criteria. Eur J Cardiothorac Surg. 2010; 37(2):334-8.
30. Luo XJ, Wang W, Sun HS, Hu SS, Long C, Xu JP, et al. Extracorporeal membrane oxygenation for

treatment of cardiorespiratory function failure in adult patients. Zhonghua Wai Ke Za Zhi Chin J Surg. 2009; 47(20):1563-5.
31. Ostermann M, Connor Jr M, Kashani K. Continuous renal replacement therapy during extracorporeal membrane oxygenation: why, when and how? Curr Opin Crit Care. 2018;24(6):493-503.
32. Lee SH, Chung CH, Lee JW, Jung SH, Choo SJ. Factors predicting early- and long-term survival in patients undergoing extracorporeal membrane oxygenation (ECMO). J Card Surg. 2012;27(2):255-63.
33. Kielstein JT, Heiden AM, Beutel G, Gottlieb J, Wiesner O, Hafer C, et al. Renal function and survival in 200 patients undergoing ECMO therapy. Nephrol Dial Transplant. 2013;28(1):86-90.
34. Aubron C, Cheng AC, Pilcher D, Leong T, Magrin G, Cooper DJ, et al. Factors associated with outcomes of patients on extracorporeal membrane oxygenation support: a 5-year cohort study. Crit Care. 2013;17(2): 73.
35. Chen H, Yu RG, Yin NN, Zhou JX. Combination of extracorporeal membrane oxygenation and continuous renal replacement therapy in critically ill patients: a systematic review. Crit Care. 2014;18(6):675.
36. Bartlett RH. Extracorporeal life support registry report 1995. Asaio J. 1997;43(1):104-7.

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