Kidney Medicine

The Promise of Continuous Kidney Replacement Therapy Optimization to Improve Patient Outcomes and Reduce Resource Utilization

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Acute kidney injury requiring continuous kidney replacement therapy (CKRT) is one of the deadliest conditions regularly encountered in the intensive care unit (ICU). Approximately 4%-6% of patients in the ICU in the United States are treated with CKRT,[1] with associated mortality rates of 50%-60%; these are significantly higher than the mortality rates among patients in the ICU who experience myocardial infarction (20%),[2] sepsis (30%),[3] or acute respiratory distress syndrome (ARDS) (35%).[4] Despite the combination of high incidence and high mortality seen in acute kidney injury-CKRT, large-scale randomized controlled trials (RCTs) looking at CKRT delivery are relatively rare, and much of the existing literature comes from single-center analyses. Hence, there is an enormous variability in the CKRT prescribing practices worldwide. As described in this issue of *Kidney Medicine*,[5] CRRTnet begins to step into this void providing initial prospective epidemiologic data from 6 centers, such as demographic data; comorbid conditions; and illness acuity and CKRT prescription characteristics.

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The CRRTnet name subtly evokes the previous work done through the Acute Respiratory Distress Syndrome Network (ARDSNet), and the comparison is fitting. ARDSNet and ARDSNet 2 were collaborations of approximately 40 hospital sites that, over nearly 2 decades, combined to enroll more than 5,500 patients across 10 RCTs.[6] Notably, many of these studies did not focus on novel pharmacologic agents, but rather on the optimization of supportive care.[7] A key example is the ARMA study that demonstrated the use of low tidal volumes in ARDS.[8] The findings from these trials were credited in part with a ~10% reduction in absolute mortality among patients with ARDS,[9] thus, demonstrating a stunning success. Similarly, CRRTnet plans to develop a collaborative network of centers, which will conduct comparative studies to determine the optimal CKRT prescription, with a goal of improving patient outcomes and reducing use of resources. Planned projects, such as evaluation of the effect of fluid overload (FO) status, volume removal strategies, and CKRT filter patency strategies, including citrate anticoagulation, with potential for more in the future.

The epidemiologic findings presented in this analysis are a foretaste of this promising collaboration. There is a wealth of data presented within this manuscript, and no shortage of intriguing findings that demonstrate CRRTnet's potential while also highlighting some of challenges that lie ahead. First, it is quickly apparent that there is substantial patient heterogeneity, particularly with regard to the underlying comorbid conditions, admission diagnoses, and indications for CKRT. This is a definite challenge and may require expansion of the network over time to ensure sufficient patient enrollment to overcome this barrier.

Second, it is striking that, even among the 5 highly respected academic centers included in this initial analysis, there are sizable variations in practice patterns, and some notable departures from the existing Kidney Disease Improving Global Outcomes (KDIGO) guidelines in the areas of dose, catheter placement, and anticoagulation. These differences may not be merely incidental because the standardized mortality ratios ranging from just under 1.0 to just over 1.5 suggest that even at these leading institutions, there may be differences in outcomes related to institution-specific CKRT practices.

The appropriate dose of CKRT was addressed in 2 major RCTs. The Acute Renal Failure Trial Network compared doses of 20 mL/kg/h with 35 mL/kg/h,[10] and the Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients trial compared a dose of 25mL/kg/h with 40 mL/kg/h.[11] Neither trial showed a difference in mortality between the groups, and hence, KDIGO guidelines now recommend a dose of 20-25 mL/kg/h (grade 1A) to reduce unnecessary dialysate use during CKRT.[12] The KDIGO guidelines state that "in clinical practice, in order to achieve a delivered dose of 20-25 mL/kg/h, it is generally necessary to prescribe in the range of 25-30 mL/kg/hour, and to minimize interruptions in CRRT." Most of the patients in the CRRTnet registry were prescribed doses >30 mL/kg/h, and only one-fifths were prescribed a dose of 25-30 mL/kg/h. The median prescription dose ranged at each institution from 25.3-36.8 mL/kg/h, and the number of patients prescribed a dose >30 mL/kg/h ranged from 17%-79%, showing the degree of practice heterogeneity even among top CKRT institutions. KDIGO also recommends regional citrate anticoagulation (RCA) if not contraindicated (grade 2B). However, in this observational data, the use of RCA was highly institution dependent and split nearly evenly between those using RCA and those using no anticoagulation. The discrepancy between mortality rates in citrate use versus no anticoagulation (50% vs 69%) is a tantalizing finding that has been hinted at in recent studies,[13] and warrants further investigation. Finally, KDIGO recommends that dialysis catheters be placed preferentially in the right internal jugular (IJ) vein, with the

femoral vein recommended as the second site (recommendation not graded). In this study, only 50% of patients had a right IJ catheter, and the left IJ was the second-most probable location, again with strong institutional effects. The associations of the catheter location and outcomes, such as filter life, are not presented here, but are a probable future area of exploration.

There are other findings presented here that will directly inform the development of future studies. One such area is FO%, an emerging concept that has gained traction particularly in the pediatric population.[14] Of note, FO was noted to be the second-most common reason for CKRT initiation after the related problem of oliguria/anuria. However, the median FO% was 5.2%, and, interestingly, there was essentially no difference in FO% between the full cohort and those specifically noted to have FO listed as a CKRT indication. This lack of correlation between degree of FO% and the CKRT indication noted by providers could potentially suggest an issue with the way FO% is determined and used in adults. Furthermore, although FO% has been strongly related to mortality in the pediatric ICU, there was no clear signal for FO% and mortality in this study.

Finally, another potential benefit of the CRRTnet registry, particularly as it continues to grow, is the possibility of evaluating changes in practice over time. The data presented here were collected from 2013-2021, and multiple RCTs related to timing of CKRT initiation were published after or at the end of the enrollment period.[15] Whether and how quickly time to CKRT initiation changed after these articles were published could provide important insights into rates of practice change related to new published research.

In conclusion, this initial salvo from CRRTnet should be seen both as reason for optimism and a sober-minded acknowledgement of the difficulties facing CKRT research. These challenges are formidable, but just as ARDSNet was able to make major advances through optimization of supportive measures, there is reason to hope that evidence-based standardization of CKRT can improve the patient outcomes and use of resources in this most deadly of conditions.

ARTICLE INFORMATION

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