COVID-19–Associated Acute Kidney Injury: Learning from the First Wave

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As the coronavirus disease 2019 (COVID-19) pandemic swept through American hospitals in the early part of 2020, the multisystem nature of the disease quickly became apparent, with AKI featuring as a prominent complication of severe acute respiratory syndrome coronavirus 2 infection.1 Severe infection likely drives an immunologic storm, leading to tubular, vascular, and in some cases, glomerular injury. A direct viral cytopathic effect on the kidney is a subject of debate.2,3 It is unclear if this relates to differences in ascertainment, respiratory syndrome coronavirus 2 infection.1 Severe infection likely drives an immunologic storm, leading to tubular, vascular, and in some cases, glomerular injury. A direct viral cytopathic effect on the kidney is a subject of debate.2,3

In this issue of JASN, two investigative groups provide a comprehensive description of their experience with COVID-19–associated AKI.4,5 Chan et al.4 report on the epidemiology of COVID-19–associated AKI among nearly 4000 patients admitted at a five-hospital health system in New York City. As part of the Study of the Treatment and Outcomes in Critically Ill Patients With COVID-19 project that recruited patients from 67 United States hospitals, Gupta et al.5 followed 3099 critically ill patients with COVID-19 and focused on those who received RRT in the context of AKI.

Collectively, these timely studies deliver three crucial messages: (1) AKI afflicted nearly half of all patients hospitalized with COVID-19 and the majority of those admitted to the intensive care unit (ICU), (2) 20% of critically ill patients with COVID-19 received RRT, and (3) survivors of COVID-19–associated AKI often have incomplete recovery of kidney function at hospital discharge, with one-third of patients who received acute RRT having a persistent requirement for dialysis at the time of hospital discharge.

The high frequency of AKI among patients hospitalized with COVID-19 in United States hospitals contrasts with reports from China, where AKI tended to be less frequent.6,7 It is unclear if this relates to differences in ascertainment, thresholds for hospitalization, ICU care (e.g., concomitant use of mechanical ventilation and fluid management), or the prevalence of AKI risk factors. The proportion of critically ill patients initiating RRT was especially high, which is consistent with reports from patients with COVID-19 in the United Kingdom8 but higher than what was observed in patients with influenza A subtype H1N1.9,10 The receipt of RRT correlates with both severity of AKI and overall illness acuity, but the ultimate decision to commence RRT is complex and guided by a variety of clinical and logistic factors as well as clinician judgement. Neither of the two papers described the specific triggers for RRT. Recent trials have shown that the preemptive initiation of RRT, specifically before a metabolic or fluid-related emergency of AKI supervenes, does not confer improved survival but may portend a higher risk of persistent dialysis dependence and iatrogenic complications.11

With the procurement of ventilators dominating pandemic preparedness efforts in early 2020, dialysis capacity emerged as a “blind spot” as patients with COVID-19–associated AKI overwhelmed health care systems in New York City and other regions.12 Well-established acute RRT programs struggled due to a lack of machines, supplies, and personnel. Scarcity prompted centers to rapidly alter their usual RRT strategies; novel approaches included “sharing” continuous RRT (CRRT) machines between two patients, each receiving a daily 10- to 12-hour session, and the utilization of peritoneal dialysis,13 which is not traditionally used in North American ICUs for the treatment of AKI. The unexpected deluge of patients with AKI forced rapid adaptation and creative problem-solving. Kidney programs preparing for future COVID-19 surges must proactively prepare for scenarios in which their RRT resources may again become stressed, necessitating the development of well-conceived backup plans. It is also hoped that future surges will see enhanced coordination between health systems and manufacturers to ensure an adequate supply of dialysis hardware and disposables across modalities, with flexible plans to rapidly shift supplies and staff to sites facing the greatest needs.

The dialysis prescription in COVID-19–associated AKI presents unique considerations. Irrespective of RRT modality, the optimal ultrafiltration target for patients with COVID-19 is uncertain. Hypoxemic respiratory failure and acute respiratory distress syndrome, central features of severe COVID-19, may be exacerbated by fluid accumulation, which is worsened by AKI. Whether and how fast to remove fluid with ultrafiltration are uncertain. On one hand, more rapid fluid removal may improve oxygenation and accelerate liberation from mechanical ventilation. However, ultrafiltration may predispose patients to hypotension and secondary organ injury.

COVID-19 is associated with a syndrome of hypercoagulability with implications for RRT-related anticoagulation.14 Clinicians should consider using anticoagulation for all

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therapies unless an unequivocal contraindication exists. For CRRT in particular, our experience and that of others have highlighted the challenges in maintaining circuit patency with standard anticoagulation regimens,15 A combination of systemic heparin and regional citrate anticoagulation may be an effective way of maximizing circuit patency, although more information on the safety and efficacy of this approach is needed. Peritoneal dialysis may represent a viable alternative for patients with recalcitrant clotting on CRRT or conventional hemodialysis.

Although the long-term outcomes of COVID-19–associated AKI have yet to be described, the studies by Chan et al.,4 and Gupta et al.,5 remind us that AKI survivors often have incomplete recovery of kidney function at discharge and may benefit from follow-up after their acute hospitalization. Virtual care and telemedicine, which have rapidly gained traction during the pandemic, may prove to be especially valuable in the care of this vulnerable population. Follow-up should include serial assessments of kidney function and albuminuria, attention to BP and cardiovascular risk factors, and a thorough review of medications. The latter would include tailoring drugs and doses to the patients’ evolving kidney function as well as the reintroduction of key drugs that may have been appropriately stopped during the hospitalization. Patients still receiving dialysis at hospital discharge require close surveillance for kidney recovery and when appropriate, the thoughtful weaning of dialysis.

The papers in this issue of JASN have provided us with a vivid understanding of the effect of COVID-19–associated AKI in hospitalized patients while highlighting issues that are relevant to the wider population of patients with AKI. Future research will hopefully provide insights on AKI prevention and mitigation strategies in patients with COVID-19, inform optimal RRT prescriptions for this population, and describe the long-term prognosis of AKI survivors. Most importantly, clinicians and hospital administrators must internalize the lessons of spring 2020 to ensure that health systems will have adequate resources and capacity to deliver safe and effective RRT during the next wave of illness.

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REFERENCES


See related articles, “AKI Treated with Renal Replacement Therapy in Critically Ill Patients with COVID-19,” and “AKI in Hospitalized Patients with COVID-19,” on pages xxx–xxx and xxx–xxx, respectively.