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Delaying Renal Replacement Therapy Could Be Harmful in Patients with Acute Brain Injury

To the Editor:

We read with interest the article by Gaudry and colleagues on the recent advances regarding the timing of the initiation of renal replacement therapy (RRT) for acute kidney injury (AKI) in critically ill patients (1). The authors conducted the two most recent large-scale studies in this area (2, 3) with concordant results, and propose a potential algorithm for RRT indication and timing. Schematically, their proposal is that unless severe complications related to AKI occur (e.g., hyperkalemia, severe metabolic acidosis, severe fluid overload with pulmonary edema, or neurological symptoms associated with uremic encephalopathy), RRT should be postponed. The use of this strategy did not change the mortality rate of general critically ill patients or those with severe septic shock, and was associated with reduced use of RRT, suggesting a benefit for the "delayed" initiation strategy. The authors should be commended for conducting these studies, which will surely impact the daily practice of ICU physicians. However, we would like to draw attention to a subset of patients who may not benefit from such a delay. Patients with acute brain injury and at risk for cerebral edema and elevated intracranial pressure (e.g., patients with brain trauma, severe stroke, subarachnoid hemorrhage, post–cardiac arrest, meningitis, hepatic encephalopathy, encephalitis, or other brain infections) frequently present with an increased brain volume and reduced brain compliance. The slow increase in serum osmolality related to increased concentrations of metabolites as a result of failing kidney function will have little impact. In addition to variations in cerebral blow flow and arterial pressure, initiation of RRT will induce a rapid osmotic shift due to a drop in serum osmolality, and the extent of this shift is mostly driven by initial urea levels. The osmotic shift will then cause an increase in brain volume secondary to the osmolar gradient, with potential catastrophic consequences such as severe intracranial hypertension and brain death. According to the Monro-Kellie doctrine, the intracranial space is a fixed volume inside the skull and the cerebral pressure–volume correlation is initially linear (compensation), becoming exponential (compliance is reduced after compensatory mechanisms have reached their limits), meaning that a small increase in volume will induce a major increase in intracranial pressure (the so-called Langfitt curve). Therefore, patients with brain injury are at high risk of reaching the right inflection point of the curve and developing severe intracranial hypertension. Several case reports and reviews have described these complications (4, 5). Even the use of recommended "soft" RRT methods, such as sustained or continuous low-efficiency dialysis for patients with AKI and brain injury (6) will hardly moderate this shift, which occurs within the first minutes of RRT. We suggest not using the delayed RRT initiation strategy in patients at risk for elevated intracranial pressure. We believe that the best strategy for RRT modalities and initiation in this subset of patients remains to be determined. ■

Author Contributions: All of the authors approved the content of the letter.

Originally Published in Press as DOI: 10.1164/rccm.201903-0527LE on May 15, 2019

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Reply to Chousterman *et al.*

From the Authors:

We thank Chousterman and colleagues for their positive appreciation of our work (1). However, we believe that their contention is mainly speculative, as it is based on anecdotal reports that provide no or little detail on the renal replacement therapy (RRT) modalities that were supposed to be responsible for neurological deterioration.

More important, we feel that the authors miss several points. They reason as if RRT were not associated with any risk except the increase in intracranial pressure. They fail to incorporate in their thinking process the different regulators of cerebral blood flow: arterial blood pressure, intracranial pressure, and cerebrovascular resistance (2). The first component, the cardiovascular component, has been highlighted for over a century (3). Hemodynamic instability is a frequent issue in brain-injured patients, and even more so in cases involving multiple trauma. Thus, RRT-associated hemodynamic instability, which occurs frequently and within the first minute of RRT (unlike disorders linked to osmolal changes, which are rare and have a delayed onset) may have catastrophic consequences on an injured brain. Starting RRT in a patient with recent head injury (especially in the context of polytrauma) may likely affect hemodynamics. In addition, the authors fail to consider that a delayed strategy has been shown to allow the avoidance of RRT in one-third to one-half of patients (4, 5). Obviously, the best way to avoid RRT-associated osmolal brain changes is to avoid RRT. The application of an early RRT strategy potentially increases the risk of hemodynamic fluctuation (which may decrease cerebral perfusion and contribute to acute brain injury) for all patients. In this regard, the remedy they propose (starting RRT early in all acute kidney injury patients with brain injury) may be worse than the disease. Finally, a careful reading of case reports and case series cited by Chousterman and colleagues (6) shows that in most cases, patients received "aggressive" intermittent RRT. For instance, in one case blood urea nitrogen decreased from 141 to 54 mg/dl in one session, which is not desirable even in a patient without brain injury. Several ways to avoid acute osmotic shifts exist (7) but were not discussed: slow and gentle initial hemodialysis (time <2 h and low blood flow rate), increasing dialysate sodium level, or administration of osmotically active substances (e.g., intravenous manitol).

In our era of evidence-based medicine, we must point out that stating "we suggest not using the delayed RRT initiation strategy in patients at risk of elevated intracranial pressure" is not supported by data. Similarly, stating that "the best strategy for RRT modalities and initiation in this subset of patients remains to be determined" means that one has to carefully weigh the actual (and proven) risk of undue RRT against that of delaying RRT in brain-injured patients. We suggest that before issuing so strong a warning without firm evidence, it would be necessary to conduct a randomized clinical trial on this particular population. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Originally Published in Press as DOI: 10.1164/rccm.201904-0723LE on May 15, 2019