

# Early renal replacement therapy in acute kidney injury: a piece in the puzzle

## Alexandre Braga Libório<sup>1</sup>, Candice Torres de Melo Bezerra Cavalcante<sup>2</sup>

<sup>1</sup>Medical Sciences Postgraduate Program, <sup>2</sup>Medical Course, Universidade de Fortaleza – UNIFOR, Fortaleza, Ceara, Brazil

Correspondence to: Alexandre Braga Libório. Avenida Abolição, 4043 Ap 1203. Fortaleza-Ceará, Brazil. Email: alexandreliborio@yahoo.com.br.

Provenance and Peer Review: This article was commissioned by the editorial office, Annals of Translational Medicine. The article did not undergo external peer review.

Comment on: Tu GW, Xu JR, Liu L, et al. Preemptive renal replacement therapy in post-cardiotomy cardiogenic shock patients: a historically controlled cohort study. Ann Transl Med 2019;7:534.

Submitted Mar 31, 2020. Accepted for publication Apr 10, 2020. doi: 10.21037/atm.2020.04.55 View this article at: http://dx.doi.org/10.21037/atm.2020.04.55

Since renal replacement therapy (RRT) begins to be used, there is no doubt it is a procedure that safe lives. In the last years, an intense debate emerged about the optimal timing of starting RRT in critically ill patients with acute kidney injury (AKI) (1).

Recently, 3 large randomized clinical trials had conflicting results. The Early Versus Late Initiation of Renal Replacement Therapy In Critically Ill Patients With Acute Kidney Injury (ELAIN) trial was a single-center trial comparing early RRT [starting within <8 hours of fulfilling Kidney Disease: Improving Global Outcomes (KDIGO) stage 2 AKI] with delayed RRT (starting within <12 hours of developing KDIGO stage 3 AKI or upon an absolute indication) (2). In this study, there was a significant 15.4% reduction in 90-day mortality in the early RRT group. However, in two other large multicenter trials (Artificial Kidney Initiation in Kidney Injury-AKIKI 1 and 2) no survival benefit was demonstrated (3,4). However, there is a significant difference between ELAIN and AKIKI trials: the early arm in AKIKI trials started RRT later than the delayed arm in the ELAIN trial. In this setting, AKIKI 2 trial arms delayed even more than RRT starting.

Besides timing of initiating early RRT, ELAIN trial has another significant difference when compared with the AKIKI trials: a low percentage of patients allocated to delayed arm that not received RRT—9.2% against up to 50% in the AKIKI trial. At this last point, it is the main contribution of the paper published by Tu *et al.* (5) in this journal. In this retrospective study, the authors evaluate an early *vs*. late strategy to initiate RRT in patients with cardiogenic shock after open heart surgery. When evaluating a group of patients with severe hemodynamic derangement, the authors had a significant advantage to compare two different strategies of starting RRT: although not being a randomized controlled study, the 2 patients within two distinct periods had similar percentage of patients needing RRT during ICU stay—66% in the first period vs. 61% in the second period. Even being RCT, AKIKI studies were not able to avoid this confounder. In fact, this cannot at the moment be considered a confounder because it is a consequence of the proposed treatment strategy.

The closer number of patients requiring RRT between different groups during study period is probably the explanation because early RRT was associated with better survival in Tu *et al.* study and ELAIN trial, but not In the AKIKI trials. So, the complete interpretation of the cited studies suggest early RRT is beneficial if we are able to identify those patients who will have metabolic or volemic indications during ICU stay and avoiding delayed initiation of RRT. In other words, the question can move from if early RRT is beneficial but how to identify patients who will need RRT and initiate early RRT in these patients, or as the title of the commented article suggest: "pre-emptive RRT can reduce mortality..." in those whom will need it.

#### Acknowledgments

Funding: None.

#### Page 2 of 2

### Footnote

*Conflicts of Interest:* Both authors have completed the ICMJE uniform disclosure form (available at http://dx.doi. org/10.21037/atm.2020.04.55). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

*Open Access Statement:* This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

**Cite this article as:** Libório AB, Torres de Melo Bezerra Cavalcante C. Early renal replacement therapy in acute kidney injury: a piece in the puzzle. Ann Transl Med 2020;8(15):915. doi: 10.21037/atm.2020.04.55

#### Libório and Torres de Melo Bezerra Cavalcante. Early RRT

#### References

- 1. Bouman CSC, Oudemans-van Straaten HM. Timing of renal replacement therapy in critically ill patients with acute kidney injury. Curr Opin Crit Care 2007;13:656-61.
- Zarbock A, Kellum JA, Schmidt C, et al. Effect of Early vs Delayed Initiation of Renal Replacement Therapy on Mortality in Critically Ill Patients With Acute Kidney Injury. JAMA 2016;315:2190-9.
- Gaudry S, Hajage D, Schortgen F, et al. Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit. N Engl J Med 2016;375:122-33.
- Barbar SD, Clere-Jehl R, Bourredjem A, et al. Timing of Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis. N Engl J Med 2018;379:1431-42.
- Tu GW, Xu JR, Liu L, et al. Preemptive renal replacement therapy in post-cardiotomy cardiogenic shock patients: a historically controlled cohort study. Ann Transl Med 2019;7:534.