Editorial

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Timing or Modality of Renal Replacement Therapies in Critically Ill Patients

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Editorial

The use of renal replacement therapies (RRT) in critically ill patients has changed the prognosis of acute kidney injury in these patients over the last 30 years. However, many questions remain unanswered especially those concerning when to start RRT (timing) and which modality should be selected. Early strategies referred to timing have been encouraged in critically ill patients in the last two decades based on clinical experiences but not randomized controlled trials (RCT). Two recent RCT seem to support a delayed strategy in patients with AKI who do not present a life-threatening fluid overload condition.

Different RRT modalities have been also studied in the last years trying to demonstrate clinical improvement in critically ill patients specially those who presented septic AKI. Those modalities with increased renal dose did not improve survival whereas adverse effects related to the technique (dialytrauma) where more common. Sustained low efficacy dialysis (SLED) has been extensively used in critical care units although continuous renal replacement therapies (CRRT) still represent the main tool when RRT is required in these critically ill patients. Among CRRT, diffusion techniques have progressively acquired importance respect to convective modalities as diffusion seems to increase circuit life and could potentially present clinical advantages. Adsorptive properties of last generation membranes contribute to this diffusive current as inflammatory mediator can be also removed from circulation with pure diffusion modalities (CVVHD).

Delayed RRT strategies and the use of CVVHD should be encouraged in critically ill patients with no severe fluid overload.

Timing remains the big question concerning the use of RRT in critically ill patients. Early strategies have been encouraged in the last decade especially in septic patients in whom RRT immunomodulation capacity could play a role in the pathophysiology potentially modifying the clinical course of sepsis. The use of RRT was tested in patients with early stages of acute kidney injury (AKI) or even in patients with no AKI. Despite initial promising results in experimental models and small observational series no randomized controlled trials (RCT) have been able to demonstrate any benefit with the use of RRT in early stages of AKI. Furthermore, one of this RCT had to be stopped as patients in the early group seemed to present higher mortality compared to the control group.

Once AKI is established urine output and fluid overload constitute the main problem in critically ill patients and the first reason to initiate RRT. Two recent RCT studied patients with advanced AKI (stages 2 & 3 of AKIN classification) in two different settings. First published trial was a multicenter French study that recruited more than 600 critically ill patients with advanced AKI (AKIN3) but no immediate RRT initiation criteria (electrolytic disorders and respiratory failure due to fluid overload). These patients were either assigned to an early RRT strategy or to a delayed RRT strategy. Patients assigned to the early strategy were immediately started on RRT after randomization whether patients in the delayed group were only started on RRT when immediate RRT initiation criteria appeared. No differences in mortality were observed between both groups but more 50% of patients in the delayed arm did not require RRT. These patients who were not started on RRT had lower mortality when compared to the early group although after adjusting for severity scores no differences were found. Most of the patients who required RRT in the delayed group where initiated because of fluid overload criteria (respiratory failure) and these RRT “delayed” patients had the worst outcome of all patients although differences could not be demonstrated after adjusting for severity scores. One week later a single center study was published this time evaluating an early vs delayed CRRT strategy in more than 200 critically ill patients presenting stage 2 AKI. Most of these patients had cardiovascular compromise as the main group was recruited in a post cardiac surgery critical care department. Patients in the early group were immediately started on CRRT whether delayed patients were only started when fulfilling AKIN 3 criteria or immediate CRRT where present (basically the same electrolytic and fluid overload criteria as in the previous study). Interestingly nearly all patients in the delayed group finally required CRRT and this time statistically significant survival differences were observed with a 60-days better outcome in those patients assigned to an early CRRT strategy. Once again most of patients assigned to the delayed group were started when achieving respiratory failure criteria revealing a fluid overload scenario that was also present when patients were initially randomized (mean positive fluid balance in both groups was nearly 7 liters).

Both studies seem complementary as fluid overload in patients with cardiovascular disease (or cardiovascular impairment to manage such volume condition) and advanced AKI (AKIN 2 and 3 stages) should be an immediate initiation criterion for RRT. When life threatening electrolytic disorders is not present and fluid overload is clinically tolerated (from a respiratory point of view) critically ill patients with advanced AKI should not be started on RRT.

Sustained low efficacy dialysis (SLED) has been extensively used in critical care units although continuous renal replacement therapies (CRRT) still represent the main tool when RRT is required in these critically ill patients. Different CRRT modalities have been also studied in the last years trying to demonstrate clinical improvement in critically ill patients specially on those patients with sepsis associated AKI (SA-AKI). Modalities with increased renal dose (HVHF) did not improve survival whereas adverse effects related to the technique (dialytrauma) where more frequently observed. Recent studies suggest that renal dose should be daily adjusted to the patient clinical situation starting with 20-25 mL/kg/h but rapidly descending even to less than 15 mL/kg/h if clinical condition improves as this “low doses” present lower electrolytic disorders related to technique and increase filter life.

CRRT modalities employing convection (CVVH) were initially recommended respect to modalities with diffusion (CVVHDF and CVVHD) as convection seemed to have more immunomodulatory capacity. However, some studies began to show that adding a diffusion dose to the technique could have beneficial effects. Diffusion could increase circuit life and could potentially present clinical advantages (lower transfusion rates for example). Furthermore, last generation membranes development with increased adsorption properties contribute to this diffusive current as inflammatory mediator can be also removed from circulation with pure diffusion modalities (CVVHD). A recent RCT (not published yet) seems to demonstrate this clinical benefit of CVVHD respect to CVVH with no differences in terms of immunomodulation capacity.

Critically ill patients with advanced AKI meeting immediate initiation criteria should be preferably started on SLED or CRRT where a mostly diffusive modality should be prescribed (CVVHD or CVVHDF) with an initial dose of 20-25 mL/kg/h rapidly descending to 15 mL/kg/h when clinical condition improves. Last generation membranes with an increased adsorption capacity could potentially improve diffusion immunomodulatory capacity.