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Timing of Initiation of Renal Replacement Therapy in Acute Renal Failure

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Drs Kellum and Venkataraman review the evidence on timing of initiation of renal replacement therapy in Acute Renal Failure.

Acute renal failure (ARF) occurs in as many as 15% of critically ill patients and is associated with significant morbidity and mortality. Despite the common occurrence and high morbidity and mortality associated with ARF, no pharmacological interventions have been shown to be efficacious for treatment. Supportive care, including renal replacement therapy (RRT) remains the mainstay of management for critically ill patients with ARF. Although RRT is widely prescribed for ARF, controversy exists on the best time to initiate RRT in these patients.

There is currently no consensus on the indications for RRT in ARF. Like other aspects of RRT, the indications have generally been extrapolated from the end-stage renal disease (ESRD) experience. These indications have generally

included refractory hyperkalemia, fluid overload not responding to diuretic therapy, severe persistent metabolic acidosis and overt uremic symptoms (pericardial effusion, encephalopathy etc). While there is little dispute regarding the necessity of RRT for the above indications, there is neither consensus on the degree of azotemia nor on the duration of ARF warranting initiation of therapy in the absence of these “absolute” indications. Patients with ARF are generally sicker, and warrant tighter acid-base, electrolyte and fluid balance control compared to ESRD patients. Moreover, critically ill patients with ARF are also more catabolic and need increased nutritional protein and hence generally have higher urea generation rates than ESRD patients. Finally, volume intake in these patients cannot be limited, due to the obligate administration of intravenous medications such as antibiotics and continuous infusions of vasopressors. Hence, intuitively, many would argue that, waiting for “conventional” indications for initiation of RRT in patients with ARF may be inappropriate and that the earlier RRT is provided, the better the outcome will be. However, evidence in support of this notion in ARF is lacking. On the other hand, many patients with ARF recover renal function without requiring any RRT. Excessively early initiation therefore poses the risk of initiating therapy in patients who might never require RRT using a more conservative approach (Venkataraman et al. 2005). Finally, the modulation of inflammatory mediators, particularly in patients in whom ARF occurs in the setting of sepsis or multi-system organ failure, has been proposed as an additional indication for RRT. However, controversy exists as to whether conventional doses of dialysis can effectively clear inflammatory mediators and hence this indication currently remains limited to experimental protocols.

Only two clinical studies have tried to evaluate the effect of timing of initiation of RRT on clinical outcomes in ARF patients and have provided conflicting results. One retrospective study, which used serum BUN as a surrogate for “timing of initiation“ of RRT in ARF, showed that patients who were dialyzed earlier in their course of disease (mean BUN 42.6 mg/dl) had a better survival (39% vs. 20%) compared to those for whom RRT was initiated later (mean BUN 94.5 mg/dl) (Gettings et al. 1999). Although this study is limited in that it is retrospective and that the reasons for initiation of RRT in the two groups were likely to have been different, these data suggest that initiation of RRT earlier in the course of ARF may be of benefit.

However, a subsequent prospective randomized study by Bouman et al. (n =106) (2002), does not support this finding. In this study, patients were randomized to three groups: early high-volume haemofiltration (n= 35; 72-96 L per 24 hrs), early low-volume haemofiltration (n=35; 24-36 L per 24 hrs), and late low-volume haemofiltration (n=36; 24-36 L per 24 hrs). In this study, survival at 28 days and recovery of renal function were not improved using early initiation of haemofiltration. This study is limited in that it was clearly underpowered to detect any differences in outcome.

In summary, no definitive conclusions can be made with regards to whether early initiation of RRT improves outcome in patients with ARF. Larger RCTs are necessary to answer this question. Moreover, conventional markers used to define “early vs. late” initiation of RRT, such as BUN or creatinine, are extremely non-specific in the ICU setting. Hence consensus should be reached on the indications for RRT and what constitutes “early vs. late” initiation of RRT, prior to conducting larger trials.

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