

# Renal Replacement Therapy



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## KEYWORDS

• Continuous renal replacement therapy • Timing • Dose • Citrate • Heparin

## KEY POINTS

- Early renal support therapy may be more effective than late renal replacement therapy (RRT) to improve the outcomes of patients with acute kidney injury (AKI).
- Continuous RRTs should be preferred to intermittent therapies, mainly for hemodynamically unstable patients with AKI.
- The prescribed dose should be carefully evaluated for each patient and the delivered dose continuously monitored during the treatment.
- Citrate anticoagulation may be used for all patients without contraindications, particularly in high-expertise centers: heparin as a first choice is still feasible in nonbleeding patients, especially for units using RRT less frequently.

## INTRODUCTION

Acute kidney injury (AKI) is a clinical syndrome characterized by a sudden decrease in kidney function resulting in accumulation of fluids, creatinine, urea, and other waste products.<sup>1</sup> The incidence of AKI widely ranges depending on the studied population and on the definition used. Through integration of the previous risk, injury, failure, loss, and end stage classification (RIFLE) and acute kidney injury network (AKIN) classifications, in 2012 the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines defined AKI as an increase in the serum creatinine level of 0.3 mg/dL (26.5  $\mu$ mol/L) or more within 48 hours, a serum creatinine level that has increased by at least 1.5 times the baseline value within the previous 7 days, or a urine volume of less than 0.5 mL/kg of body weight per hour for 6 hours.<sup>2</sup>

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The authors declare no disclosures.

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Crit Care Clin 31 (2015) 839–848

<http://dx.doi.org/10.1016/j.ccc.2015.06.015>

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Approximately 5% to 7% of hospitalized patients develop AKI during their hospital length of stay; this incidence is further increased to 25% among critically ill patients in the intensive care unit (ICU).<sup>1,3</sup> A mortality rate more than 50% has been reported for patients with AKI and multiorgan failure.<sup>3</sup> In the absence of any effective pharmacologic therapies, AKI is usually managed through supportive treatments focused on optimization of fluid balance, prevention or treatment of electrolyte and acid-base disturbances, adjustment of the dosing of medications that are excreted by the kidney, and avoidance of secondary hemodynamic and nephrotoxic renal injuries. Beyond these conservative therapies, renal replacement therapy (RRT) is essentially the only effective method for the management of the critically ill patients with severe AKI.<sup>1,3</sup>

Even if it is currently a matter of debate if RRT optimization may reduce the mortality of patients with AKI,<sup>4</sup> it is reasonable to remark that avoidance of renal support in an oligo-anuric critically ill patient is not acceptable. Furthermore, an accurate evaluation of the most important issues on RRT, such as timing, modality, and dose of treatment, may be quintessential to improve renal and nonrenal outcomes in these patients.

### TIMING OF INITIATION

The adequate timing for the RRT initiation in patients with AKI has not been exactly defined, so far. In current practice, the decision to initiate an RRT is often based on clinical or biochemical features of fluid overload and/or solutes imbalances (azotemia, hyperkalemia, severe acidosis).<sup>2</sup> However, these emergency indications characterize a rescue therapy for renal substitution in which the initiation of the treatment forestalls an imminent death. More reasonably, current practice should be based on the pre-emptive initiation of RRT, well before the development of these advanced complications; the aim is to early support the renal function during early phases of organ dysfunction instead of completely replacing kidney function in the late phases of organ insufficiency (**Table 1**).

An early onset of RRT is usually considered to be associated with an improved outcome in patients with AKI, even if no significant evidence supports this notion in current literature; however, indications of RRT and timing of RRT initiation are currently 2 of the fundamental questions listed among the top priorities in research in this field.<sup>4</sup> The levels of evidence that guide current practice primarily derive from retrospective and observational cohort studies and small, underpowered prospective trials.<sup>5</sup> With not-graded recommendations, the KDIGO guidelines currently suggest to emergently initiate an RRT when life-threatening changes in fluid, electrolyte, and acid-base

**Table 1**

**Examples of possible indications for a late RRT aimed to completely substitute the kidney function and for an early renal support therapy aimed to promptly maintain homeostasis, to reduce organs dysfunction, and the further renal insult**

<b>RRT</b>	<b>Renal Support Therapy</b>
<b>Absolute Indications (Life-Treating Conditions)</b>	<b>Relative Indications</b>
Acid-base control	Volume removal in patients with fluid overload
Ions alterations	Immunomodulation in sepsis
Solutes control	Allowing to reach an adequate nutrition support
	Blood purification during cancer chemotherapy

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