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Other Articles

Timing of renal replacement therapy and clinical outcomes in critically ill patients with severe acute kidney injury☆

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Abstract

Purpose: The aim of this study is to evaluate the relationship between timing of renal replacement therapy (RRT) in severe acute kidney injury and clinical outcomes.

Methods: This was a prospective multicenter observational study conducted at 54 intensive care units (ICUs) in 23 countries enrolling 1238 patients.

Results: Timing of RRT was stratified into "early" and "late" by median urea and creatinine at the time RRT was started. Timing was also categorized temporally from ICU admission into early (<2 days), delayed (2-5 days), and late (>5 days). Renal replacement therapy timing by serum urea showed no significant difference in crude (63.4% for urea ≤24.2 mmol/L vs 61.4% for urea >24.2 mmol/L; odds ratio [OR], 0.92; 95% confidence interval [CI], 0.73-1.15; $P = .48$) or covariate-adjusted mortality (OR, 1.25; 95% CI, 0.91-1.70; $P = .16$). When stratified by creatinine, late RRT was associated with lower crude (53.4% for creatinine >309 μmol/L vs 71.4% for creatinine ≤309 μmol/L; OR, 0.46; 95% CI, 0.36-0.58; $P < .0001$) and covariate-adjusted mortality (OR, 0.51; 95% CI, 0.37-0.69; $P < .001$).

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However, for timing relative to ICU admission, late RRT was associated with greater crude (72.8% vs 62.3% vs 59%, $P < .001$) and covariate-adjusted mortality (OR, 1.95; 95% CI, 1.30-2.92; $P = .001$). Overall, late RRT was associated with a longer duration of RRT and stay in hospital and greater dialysis dependence.

Conclusion: Timing of RRT, a potentially modifiable factor, might exert an important influence on patient survival. However, this largely depended on its definition. Late RRT (days from admission) was associated with a longer duration of RRT, longer hospital stay, and higher dialysis dependence.

1. Introduction

Severe acute kidney injury (AKI) is a well-recognized complication of critical illness with an important impact on morbidity, mortality, and health resource utilization [1-7]. Renal replacement therapy (RRT) represents a considerable escalation in the complexity and cost of care for those with severe AKI yet is eventually applied in most such patients [2].

Despite its widespread use, there are several controversies about the optimal delivery of RRT, especially with respect to dose prescription and modality. Accordingly, these aspects of RRT have been explored in many studies [8,9]. On the other hand, the question of timing of implementation of RRT (ie, early vs late) has seldom been the focus of investigation [10-24]. This is unfortunate because, theoretically, earlier application of RRT might affect control of uremia, acid-base homeostasis, electrolyte balance, temperature regulation, and volume status and thereby affect clinical outcome.

To explore the issue of timing of RRT in critically ill patients with severe AKI, we obtained data on the timing of initiation of RRT as part of a prospective multicenter study of AKI [2]. We sought to study the relationship between the timing of RRT and clinically important outcomes.

2. Methods

2.1. Study protocol

This was a prospective, multinational, multicenter observational cohort study of critically ill patients with severe AKI. The study was conducted at 54 centers across 23 countries [2]. The research ethics board at each participating center reviewed the study protocol before commencement.

2.2. Study population

All patients aged more than 12 years with evidence of AKI who were admitted to a participating intensive care unit (ICU) were considered eligible for study inclusion. Acute kidney injury was defined by the presence of marked azotemia (serum urea >30 mmol/L) and/or urine output less than 200 mL in 12 hours, as previously described [2]. From this population, only patients with severe AKI who were treated with RRT (71.8%) were included. Patients with preexisting end-stage renal disease receiving chronic RRT and those treated with RRT before ICU admission or for drug toxicity not associated with AKI were excluded.

The timing of RRT was assessed using several approaches. First, timing was categorized by serum biomarker values into "early" or "late" RRT. Specifically, we stratified patients according to the median values of serum urea and serum creatinine (SCr) at the time of initiation of RRT, where early represented initiation at values below the median and late at values above the median [18,24].

Second, we assessed timing based on acute changes to kidney function. For this, patients were stratified into early or late RRT according to the median change (Δ) in urea from ICU admission to start of RRT. Similarly, patients were stratified into early or late RRT according to the median ΔSCr from baseline to start of RRT for patients with available prehospital values (n = 977, 78.9%).

Finally, we assessed the temporal relationship between the start of RRT relative to the date of ICU admission. We evaluated both the time from ICU admission to start of RRT as a continuous variable and also stratified patients into 3 categories: (1) RRT at admission or within 2 days (early RRT), (2) RRT from 2 to 5 days inclusive (delayed RRT), and (3) RRT later than 5 days after ICU admission (late RRT) as was similarly performed previously [25].

2.3. Data collection

All data were prospectively collected on standardized data forms. Data variables collected included age, sex, body weight, presence of premorbid chronic kidney disease (any evidence of abnormal SCr or creatinine clearance before hospital admission), and type of admission. Numerous clinical and physiologic details were also collected including components of the Simplified Acute Physiology (SAPS II) score and Sequential Organ Failure Assessment (SOFA) score [26,27]. Several a priori contributing factors for AKI were also ascertained as described elsewhere [2]. Sepsis was diagnosed using published consensus criteria [28]. Measures of kidney function (ie, SCr, urea) were