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Renal

Systematic review and meta-analysis of renal replacement therapy modalities for acute kidney injury in the intensive care unit

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ABSTRACT

Purpose: To compare clinical outcomes among critically ill adults with acute kidney injury (AKI) treated with continuous renal replacement therapy (CRRT), intermittent hemodialysis (IHD) or sustained low efficiency dialysis (SLED).

Materials and methods: We completed a systematic review and meta-analysis of studies published in 2015 or earlier using MEDLINE®, EMBASE®, Cochrane databases and grey literature. Eligible studies included randomized clinical trials (RCTs) or prospective cohort studies comparing outcomes of mortality, dialysis dependence or length of stay among critically ill adults receiving CRRT, IHD or SLED to treat AKI. Mortality and dialysis dependence from RCTs were pooled using meta-analytic techniques. Length of stay from RCTs and results from prospective cohort studies were described qualitatively.

Results: Twenty-one studies were eligible. RRT modality was not associated with in-hospital mortality (CRRT *vs* IHD: RR 1.00 [95% CI, 0.92–1.09], CRRT *vs* SLED: RR 1.23 [95% CI, 1.00–1.51]) or dialysis dependence (CRRT *vs* IHD: RR 0.90 [95% CI, 0.59–1.38], CRRT *vs* SLED: RR 1.15 [95% CI, 0.67–1.99]).

Conclusions: We did not find a definitive advantage for any RRT modality on short-term patient or kidney survival. Well-designed, adequately-powered trials are needed to better define the role of RRT modalities for treatment of critically ill patients with AKI.

1. Introduction

Approximately 5% of patients admitted to the intensive care unit (ICU) receive renal replacement therapy (RRT) [1,2], and in-hospital mortality is generally above 50% [3-5]. Patients discharged after an episode of acute kidney injury (AKI) with RRT are at greater risk of long-term dialysis dependence and mortality compared to individuals without AKI [6,7].

RRT replaces some vital kidney functions by correcting fluid balance and removing toxins. Traditionally, there have been two RRT modalities for patients in the ICU: continuous renal replacement therapy (CRRT) and intermittent hemodialysis (IHD). IHD is typically administered over 3–4 h and mimics maintenance dialysis for end-stage renal disease. CRRT permits slow but continuous removal of solutes and water thereby conferring better hemodynamic tolerability. Though intuitively appealing, CRRT is associated with higher costs than IHD and studies have not shown a definitive benefit of patient survival and kidney recovery

Abbreviations: AKI, acute kidney injury; APACHE II, Acute Physiology and Chronic Health Evaluation II; CI, confidence interval; CRRT, continuous renal replacement therapy; ICU, intensive care unit; IHD, intermittent hemodialysis; LOS, length of stay; NR, not reported; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses; SAPS II, Simplified Acute Physiology Score; SD, standard deviation; SLED, sustained low efficiency dialysis; RCT, randomized clinical trials; RR, relative risks; RRT, renal replacement therapy; IQR, interquartile range.

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[8-11]. Sustained low efficiency dialysis (SLED, or extended daily dialysis/prolonged intermittent renal replacement therapy) represents the application of conventional hemodialysis technology with a modification of the typical IHD prescription to provide better hemodynamic tolerability. SLED is typically administered for 8 h with slower blood flows than IHD. Though SLED combines the putative benefits of CRRT and IHD, there is limited evidence on patient-relevant clinical outcomes.

Previous systematic reviews have summarized the clinical efficacy of RRT modalities for AKI – but many of these reviews are now outdated [8,9,12-15]. A recent systematic review by Schneider et al. [10] focused only on dialysis dependence and considered all intermittent modalities collectively, without distinguishing between SLED and IHD. Zhang et al. [11] also performed a systematic review and meta-analysis of CRRT and SLED, but not IHD. We followed a similar protocol to the systematic review by Tonelli et al. [14] to provide an updated comprehensive systematic review and meta-analysis of all three RRT modalities used for the management of AKI. The objective of this study was to compare outcomes of mortality, dialysis dependence and length of stay (LOS) among adult patients with AKI in the ICU treated with CRRT, IHD or SLED.

2. Material and methods

This systematic review followed reporting standards outlined in PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses; Additional File 1) [16].

2.1. Eligibility criteria

Eligible studies compared the clinical efficacy of SLED, IHD or CRRT for adult patients in the ICU receiving treatment for AKI. We sought randomized clinical trials (RCT) with any number of participants or prospective cohort studies comprising 100 or more participants. At least one outcome of interest had to be reported, specifically mortality, dialysis dependence or LOS. Studies in all languages were eligible.

2.2. Information sources

We reviewed studies published in 2006 or earlier from the Tonelli et al. [14] systematic review. We then searched the following sources from 2006 onwards: MEDLINE® (OVID), EMBASE® (OVID), Cochrane Database of Systematic Reviews (OVID), Cochrane Central Register of Controlled Trials (OVID), Cochrane Health Technology Assessment Database, Cochrane National Health Service Economic Evaluation Database, and Cochrane Database of Abstracts of Reviews of Effects. The following grey literature was also searched: Canadian Agencies for Drugs and Technologies in Health, Health Economic Evaluations Database, and ProQuest Dissertation and Theses.

2.3. Search strategy

Our search strategy was adapted from Tonelli et al. [14] and reviewed by a librarian. We included search terms for each RRT modality, AKI, RCTs, and prospective cohort studies (Additional File 2). The search was initially executed on November 8, 2014 and updated on May 21 and 22, 2015. We imported references into Reference Manager for screening.

2.4. Study selection

Study selection was completed by two reviewers (DN and SP) who independently screened references based on title and abstract. After initial screening, DN and SP independently retrieved relevant full-text articles for further review. Articles were compared and discrepancies resolved. Studies in the review by Tonelli et al. [14] were included if they reported at least one eligible outcome.

2.5. Data collection process

DN and SP independently extracted data using an abstraction form. The abstracted data included: study citation (authors, title, journal, publication year), study characteristics (country, design, sample size, study setting and dates, follow-up time), participant demographics and illness severity (mean age, sex, presence of sepsis, baseline serum creatinine, severity of illness measured by APACHE II [Acute Physiology and Chronic Health Evaluation II] or SAPS II [Simplified Acute Physiology Score], mechanical ventilation or vasopressors), RRT details (modalities, device and manufacturer, membrane material, dose, schedule, buffer, anticoagulants), and results (mortality in ICU, mortality in-hospital, other mortality, ICU LOS, hospital LOS, dialysis dependence). We planned to report other outcomes (treatment duration, RRT dose, complications) but decided not to since too few studies reported these results. DN and SP compared extracted information and resolved discrepancies.

2.6. Risk of bias assessment in individual studies

We assessed risk of bias for RCTs using the Cochrane Collaboration's tool for assessing bias [17]. We assessed risk of bias for prospective cohort studies using the Newcastle Ottawa Scale [18]. Risk of bias was assessed at study rather than the outcome level.

2.7. Synthesis of results

We conducted meta-analyses of RCTs only using Review Manager 5.3. We considered studies comparing CRRT to SLED and CRRT to IHD separately using SLED and IHD as sub-groups in the meta-analyses. This allowed us to make indirect comparisons between SLED and IHD using a test for sub-group differences [19,20]. We calculated relative risks (RR) with 95% confidence intervals (CI) for binary outcomes, as well as combined estimates using Forest plots. For LOS, we described distributions from individual studies rather than pooling the data, since distributions were skewed and studies reported means or medians. We assessed statistical heterogeneity using I^2 for pooled results. If significant heterogeneity was discovered ($I^2 > 25\%$), we used a random effects model for the meta-analysis. Results from prospective cohort studies were not included in the meta-analyses but were described narratively.

2.8. Risk of bias across studies

We constructed funnel plots to examine the risk of publication bias by plotting the study effect size (RR) *versus* the study precision (standard error) [21].

3. Results

3.1. Study selection

Study selection is depicted in Fig. 1. After removal of duplicates there were 4264 unique studies. There were 54 records identified through other sources that we screened for eligibility (thirteen studies from Tonelli et al. [14] and 41 studies from previous systematic reviews). After the title and abstract review, 52 relevant studies were retained. In total, 21 unique studies were eligible [22-42]. Two of these studies had the same study population; Van Berendoncks et al. [32] performed a 2-year follow-up of patients described in the paper by Lins et al. [24].

3.2. Study characteristics

Overall, 21 eligible studies published from 1989 to 2014 were included with a total of 5015 participants (CRRT *vs* IHD: 16 studies, 4539 participants [24-27,29,30,32-37,39-42]; CRRT *vs* SLED: five studies, 476 participants [22,23,28,31,38]). See Additional Files 3–6 for