

ISN Trial-List

November 2018



Once a month, the ISN-ACT (Advancing Clinical Trials) team collects and publishes a list of important nephrology trials from the latest medical literature. Each trial is reviewed in context and their risk of bias in seven key areas assessed.

Key to risk of bias assessment

- | | |
|---|-------------------------------|
| (R) Random sequence generation | ● High risk |
| (A) Allocation concealment | ● Uncertain risk / not stated |
| (BP) Blinding of participants/personnel | ● Low risk |
| (BO) Blinding of outcome assessment | |
| (CD) Complete outcome data | |
| (CR) Complete outcome reporting | |
| (B) No other sources of bias | |

ISN Academy: [Acute Kidney Injury, Hemodialysis](#)

What's the hurry? No benefit to early RRT in sepsis

Timing of Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis

[Barbar, et al. N Eng J Med. 2018;379\(15\):1431-1442](#)

With conflicting results in previous trials of early vs. late initiation of renal replacement therapy (RRT), it remains unclear if early initiation of RRT is superior. Barbar, et al. hypothesized that the pathophysiology of sepsis-associated acute kidney injury might affect the relationship between timing of RRT and outcomes. The IDEAL-ICU trial randomized participants with septic shock requiring vasopressor support to receive RRT within 12 hours of the diagnosis of renal 'failure' (according to the RIFLE criteria) – the early RRT group – or to delay RRT until 48 hours after this diagnosis, provided no criteria for emergent dialysis was met or if renal function spontaneously recovered – the late RRT group. After randomizing 488 participants, the 90-day mortality was 58% in the early RRT group and 54% in the late RRT group ($P=0.38$). The trial was stopped at interim analysis as a significant difference between the two groups was deemed unlikely to emerge. In the late RRT group, 62% eventually received RRT. No differences were observed in overall survival at 28 or 180-days or length of ICU stay. This trial provides an important addition to the growing body of evidence addressing the issue of timing of RRT and, in particular, suggests that early initiation of RRT in sepsis-associated AKI may not provide benefit.



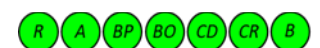
ISN Academy: [Acute Kidney Injury, Hemodialysis](#)

High cut off membranes no better than standard membranes in patients requiring hemofiltration for AKI and shock

A Double-Blind Randomized Controlled Trial of High Cutoff Versus Standard Hemofiltration in Critically Ill Patients With Acute Kidney Injury

[Atan, et al. Crit Care Med. 2018 Oct;46\(10\):e988-e994. doi: 10.1097/CCM.0000000000003350](#)

Reduction in pro-inflammatory cytokines may reduce the duration of the shock state associated with sepsis and critical illness. Previous studies using a variety of targeted cytokine reducing therapies have failed to improve outcomes. High-cut off membranes may result in greater clearance of cytokines from critically ill patients and may be beneficial. Atan, et al. randomized 76 critically ill patients on vasopressor support with concurrent acute kidney injury (AKI) requiring renal replacement therapy to receive continuous veno-venous hemofiltration with a high-cut off membrane (up to 100kDa) or standard membrane (up to 30kDa). Both participants and treating clinicians were blinded to treatment allocation. There were no differences in the primary outcome of vasopressor-free time (median 32 vs. 56 hours; $P=0.52$) between high-cut off and standard hemofiltration, nor in secondary outcomes of in-hospital mortality (55.6 vs. 34.2% $P=0.19$) or time to cessation of hemofiltration ($P=0.56$). There were no differences in serum albumin or volume of albumin replacement. These findings were robust in multivariable analysis. Although small and single centre, this study suggests that high-cut off hemofiltration does not improve outcomes in critical illness and AKI.



Alkali therapy may affect vascular function in CKD

Effect of treatment of metabolic acidosis on vascular endothelial function in patients with CKD

[Kendrick, et al. Clin J Am Soc Nephrol. 2018;13\(10\):1463-1470](#)

Metabolic acidosis is common in the later stages of CKD and a number of small trials suggest that bicarbonate therapy may slow the progression of CKD. However, the impact of bicarbonate therapy on vascular function and cardiovascular outcomes is unknown. For this pilot crossover study, Kendrick, et al. recruited 20 participants with stage 3b-4 CKD and serum bicarbonate levels of 16-21mmol/l. Each participant received 6 weeks of bicarbonate therapy targeting serum bicarbonate \geq 23mmol/l followed by a two-week washout period and a further 6-week control period (or vice-versa). Brachial artery flow-mediated dilation (a measure of vascular endothelial function that has been associated with cardiovascular mortality) improved while receiving oral bicarbonate (mean increase 1.8% [95%CI 0.3, 3.3]; $P=0.02$). This small study has a number of important limitations including a lack of blinding and its small size, however it may encourage further studies investigating this simple and inexpensive therapy.



Novel locking cocktail of trimethoprim, EDTA and ethanol may reduce dialysis catheter related infections

Locking hemodialysis catheters with Trimethoprim-Ethanol-Ca-EDTA to prevent bloodstream infections. A randomized, evaluator blinded clinical trial

[Rijnders, et al. Clin Infect Dis. 2018 Oct 3. doi: 10.1093/cid/ciy840](#)

Dialysis catheter associated bacteraemia (CAB) is a major source of morbidity and cost. A variety of antibacterial and antibiotic locks have been shown to reduce the rates of CAB, but debate as to the optimal formulation ongoing. Rijnders, et al. randomized 270 participants on maintenance hemodialysis to receive a lock containing trimethoprim, ethanol 25% and calcium-EDTA 3% or standard heparin locking (5,000 U/ml). Over a median follow up of almost 6 months, the intervention arm had significantly fewer CAB (0.09 per 1000 catheter days) than the standard arm (0.41 per 1000 catheter days) ($P<0.03$). However, catheter dysfunction requiring thrombolytic instillation was more common in the intervention arm (40% vs. 12%; $P<0.001$). The main limitation of this study was size, with only 11 primary outcomes being observed. However, it still clearly highlights the need for longer-term comparative efficacy studies of the various antimicrobial locks available. Differences in the rate of catheter patency complications, cost effectiveness and the potential for bacterial resistance remain poorly understood, but are essential for clinicians attempting to choose the most appropriate agent for their patient population.

