

# Is SLED Efficient in Sepsis Associated Acute Kidney Injury: Hope but Hold!!

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Acute kidney injury (AKI) is a common clinical syndrome with diverse etiology. It may complicate around 30% of intensive care unit (ICU) admissions.<sup>1</sup> Acute kidney injury with sepsis is a lethal combination effectively responsible for 50–70% of mortality.<sup>2,3</sup> This mortality range differs in literature because of a lack of standard definitions and ambiguous reference benchmarks. It is not very sure whether patients die because of renal failure or with renal failure.

Multiple definitions of AKI led to a great disparity in the reported occurrence of AKI. This inconsistency added complexity to compare the studies focusing on AKI.

Large differences are observed in AKI defining criteria between developing and developed countries. As acute kidney injury network (AKIN) defines AKI by two creatinine measurements within 48 hours, some patients may have been missed before hospitalizations as every patient doesn't undergo a creatinine test every day. So, community-acquired or outside-hospital AKI may have excluded if judged by AKIN criteria. Additionally, patients with slow reduction in renal function also got skipped.

A few times baseline creatinine is unknown in clinical practice which is required in RIFLE criteria. The etiology of AKI, RRT requirement, and biomarkers to identify the AKI in earliest stage are also missing in a few AKI definitions.

Renal replacement therapy (RRT) is an integral part of its management in the ICU. Optimal renal replacement intervention for these patients remains a matter of debate. Initially, RRT was performed as intermittent hemodialysis (IHD). In 1977 Peter Kramer performed the first continuous arteriovenous hemofiltration (CAVH) treatment in Gottingen, Germany. The limitations of CAVH propelled new research and the discovery of novel treatments such as continuous veno venous hemofiltration (CVVH).

Also, there is a lack of data about deserving hemodynamically unstable patients who would have undergone sustained low-efficiency dialysis (SLED) before the continuous renal replacement therapy (CRRT) era and were otherwise deprived of RRT because of the unavailability of CRRT.

Each of these modalities has its specific advantages and limitations. The amalgamation of intermittent hemodialysis (IHD) and CRRT is SLED.

It is a slower form of dialysis that maintains better hemodynamic stability as compared to IHD, and since it is intermittent, it also allows time for patient transport and procedures which is not possible with CRRT.

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It has most of the advantages of IHD and CRRT.

Sustained low-efficiency dialysis has been proposed as an alternative to other forms of RRT and is used in many centers worldwide for logistical reasons. Because of the requirement of expertise, limited availability, the need for circuit anticoagulation, watchful monitoring, patient immobility, intensive nursing requirements, and higher overall costs of replacement fluid, CRRT is less preferred in resource-limited settings. However, this is determined by the nature of the illness rather than only the mode of renal replacement therapy and renal failure.

A recent survey including 60 centers from the USA and 48 from the Indian subcontinent and Latin America revealed a marked geographical variation in RRT practices. Sustained low-efficiency dialysis, however, was used in 25% of centers in developing countries as compared to 20% in developed countries.<sup>4</sup>

There are very few independent studies to compare the performance of SLED and CRRT. Clinicians and researchers tried to reach some consensus by using varying methodologies of RCTs and cohort study designs. However, due to small sample sizes, different methodologies, subject selection, and outcome assessment, it became very difficult to reach any firm conclusions on the performance of these two modalities.

In addition to classical indications of renal replacement therapy CRRT and SLED are preferred in hemodynamically unstable patients.

In 2007, meta-analysis and Cochrane Review showed significant improvement in hemodynamic parameters in patients receiving CRRT compared to IHD whereas hemodynamic stability was similar between CRRT and SLED. Whereas another meta-analysis indicates that CRRT and SLED are preferable to IHD in hemodynamically unstable patients with AKI.<sup>5,6</sup>

Though there are specific preferences for the mode of Renal replacement therapy, CRRT is recommended in patients with acute brain injury or increased intracranial tension as per ISCCM guidelines.<sup>7</sup>

The Kidney Disease Improving Global Outcomes (KDIGO) also suggests using CRRT, rather than intermittent RRT, for AKI patients with acute brain injury or other causes of increased ICP or generalized brain edema.

The definition of hemodynamic instability in literature is very vague and puzzling. Several definitions have been used in studies comparing IHD or SLED with CRRT. Defining hemodynamic instability by a decrease in mean arterial pressure (MAP) is not enlightening when the practice is to achieve a target MAP by titrating the dose of vasopressor drugs. The recent meta-analysis comparing SLED and CRRT also commented that no relevant data could be extracted about hemodynamic management of septic shock when patients were already on vasopressors and the MAPs were maintained.<sup>6</sup>

Acute disease quality initiative (ADQI) 16 consensus statement fails to lay down a specific target number for hypotension at which CRRT, SLED, and IHD become preferred treatment modalities but leaves the ultimate decision to the clinician.<sup>8</sup>

Marshall et al.<sup>9</sup> at the University of Arkansas Medical Sciences (UAMS) found a higher MAP post-CRRT compared with SLED but also noted that those patients who could not tolerate SLED also could not undergo CRRT.

Most RCTs and systematic reviews comparing CRRT and intermittent therapies such as IHD and SLED have failed to show any survival benefit or significant difference in recovery of renal function with either modality of RRT in ICU.<sup>10,11</sup>

There is not enough literature available comparing SLED and CRRT in sepsis-associated kidney injury.

A Pilot randomized controlled trial done in Indian septic patients by Mishra SB and group concluded similar hemodynamic effects of CRRT and SLED in patients with septic shock. Sustained low-efficiency dialysis was cost-effective compared to CRRT.<sup>12</sup>

In this edition of the journal, the prospective study done by Abdalla KA Tahain Sudan (Low-income Country) effectively compared the use of SLED and CRRT in sepsis-associated acute kidney injury of hemodynamically unstable patients.

The risk of death remained the same in both groups of patients; 15 (48.4%) in SLED vs 13 (59.1%) in the CRRT group. Also rates of renal recovery, length of ICU stays, and dialysis recovery were similar in both arms. Though it was not statistically significant, patients undergoing SLED were more likely to be on intermittent hemodialysis.

It was open labelled single-center study with a small sample size.

The author's findings are identical with few other studies with similar outcomes. The prospective study by Schwenger in the surgical intensive care unit showed no difference in the 90-day mortality, ICU, or in-hospital mortality when compared SLED vs CRRT. In fact, the SLED group was associated with reduced nursing time and lower cost.<sup>13</sup>

In an academic medical Centre, Kitchlu et al. in a nonrandomized study showed no difference in the 30-day mortality were 158 patients received CRRT and 74 were on SLED.<sup>14</sup>

Kovacs<sup>15</sup> reviewed 1,564 patients and 18 studies in critically ill patients with AKI. This meta-analysis concluded that both modalities are safe and effective means of treating AKI in the critically ill adult.

There is no clear advantage of continuous renal replacement in the hemodynamically unstable patient. No statistically significant difference was observed in the primary outcome, renal recovery [risk ratio (RR) 0.87, 95% confidence interval (CI) from 0.63 to 1.20].

A recent meta-analysis compared SLED with CRRT in critically ill patients with AKI and revealed no difference in outcome between the two modalities.<sup>10</sup> The authors found mortality benefits in the observational trial in favor of SLED, but this finding could be attributed to possible allocation bias.

To extrapolate the results of this study in an Indian scenario will be interesting to know as tropical diseases contribute significantly to Sepsis-induced AKI in the Indian subcontinent, whereas Pneumonia and urinary tract infections were common in the study done in Sudan.<sup>16</sup>

Abdalla KA Taha et al. also mentioned that neither the government nor private medical insurance companies in Sudan support the cost of CRRT, but readily available cost-effective SLED was covered by medical insurance. This therapeutic option of SLED compared with CRRT may be explored in Indian settings, where only 17% of India's population is insured; but obviously in a clinically appropriate framework.<sup>17</sup>

It is essential and crucial to establish a consensual definition of AKI that may be accurate/near accurate so that can be used worldwide.

Sustained low-efficiency dialysis is less labor-intensive and less expensive compared to CRRT and hence can be a suitable alternative in resource and expertise-limited settings. We hope this study becomes the basis of the starting point for future research in this critical area of AKI and sepsis. This research should focus on well-planned RCTs or cohort studies with longer duration follow-up addressing key outcomes like death, renal recovery and cost.

More studies not only from developing or low-income countries but also from developed and high-income countries would enable policymakers to better plan RRT in sepsis. Albeit, CRRT can be replaced by SLED not only for cost but also for similar efficiency, we are optimistic to hold on to this hope till enough data is available.

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