Systematic Review and Meta-Analysis

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Sustained low efficiency dialysis is non-inferior to continuous renal replacement therapy in critically ill patients with acute kidney injury

A comparative meta-analysis

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Abstract

Background: Critically ill adults with acute kidney injury (AKI) experience considerable morbidity and mortality. This systematic review aimed to compare the effectiveness of continuous renal replacement therapy (CCRT) versus sustained low efficiency dialysis (SLED) for individuals with AKI.

Methods: We carried out a systematic search of existing databases according to standard methods and random effects models were used to generate the overall estimate. Heterogeneity coefficient was also calculated for each outcome measure.

Results: Eleven studies having 1160 patients with AKI were included in the analyses. Meta-analysis results indicated that there was no statistically significant difference between SLED versus continuous renal replacement therapy (CRRT) in our primary outcomes, like mortality rate (rate ratio [RR] 0.67, 95% confidence interval [CI] 0.44–1.00; $P=.05$), renal recovery (RR 1.08, 95% CI 0.83–1.42; $P=.56$), and dialysis dependence (RR = 1.03, 95% CI 0.69–1.53; $P=.89$). Also, no statistically significant difference was observed for between SLED versus CRRT in the secondary outcomes: that is, length of intensive care unit stay (mean difference –0.16, 95% CI – 0.56–0.22; $P=.41$) and fluid removal rate (mean difference –0.24, 95% CI –0.72–0.24; $P=.32$). The summary mean difference indicated that there was a significant difference in the serum phosphate clearance among patients treated with SLED and CRRT (mean difference –1.17, 95% CI –1.90 to –0.44, $P=.002$).

Conclusions: The analysis indicate that there was no major advantage of using continuous renal replacement compared with sustained low efficiency dialysis in hemodynamically unstable AKI patients. Both modalities are equally safe and effective in treating AKI among critically ill patients.

Abbreviations: AKI = acute kidney injury, CCRT = continuous renal replacement therapy, EDD = extended daily dialysis, GFR = glomerular filtration rate, ICU = intensive care unit, IHD = intermittent hemodialysis, MOOSE = meta-analysis of observational studies in epidemiology guideline, RCTs = randomized controlled trials, RR = rate ratio, RRT = renal replacement therapy, SLED = sustained low efficiency dialysis, SLEDD = sustained low efficiency daily dialysis.

Keywords: acute kidney injury, continuous renal replacement therapy, hemodynamic instability, intensive care, meta-analysis, sustained low efficiency dialysis

1. Introduction

Acute kidney injury (AKI) is a new term for acute renal failure which is defined as a sudden, sustained decline in glomerular filtration rate (GFR), which is usually associated with uremia and a decline in urine output. Renal replacement therapy (RRT) is required for patients having severe AKI. It has been estimated that the mortality rate among AKI patients requiring RRT who were admitted in the intensive care unit (ICU) is 50% to 70%.[1] Continuous renal replacement therapy (CRRT) was introduced

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in 1977 with the intention of improving homeostasis among hemodynamically unstable patients having resistance to anti-diuretics. This treatment modality has been suggested to provide superior hemodynamic and cardiovascular stability owing to hypothermia, which increased venous return and blood pressure when compared with intermittent hemodialysis.[2–4] Another variant of CRRT is pump-driven continuous veno-venous hemofiltration which provides for higher ultrafiltration rates and thereby, higher doses can be achieved by supplementing it with typical CRRT. However, owing to cost issues related with CRRT as it required sterilized solution bags for substitution fluids or dialysates, the concept of extended daily dialysis (EDD) was developed.[5–7]

EDD uses conventional dialysis machine, and the treatment time lasts for about 8 hours allowing for slower fluid and toxin removal.[8,9] Furthermore, the introduction of sustained low-efficiency dialysis (SLED) has been considered as a major breakthrough in renal replacement therapy. SLED utilizes a single-batch dialysis system with on line dialysate production, which enables it to replace expensive and complex dialysis processes requiring operation by dialysis nurses.[8,9] It has been reported that SLED provide similar outcomes in terms of urea removal when compared with CRRT. This technology is also known as prolonged intermittent renal replacement therapy as technologically, it is a hybrid of CRRT and intermittent hemodialysis (IHD). There are various synonyms for this technology like sustained low efficiency daily dialysis (SLEDD), sustained low efficiency daily dia-filtration, EDD, slow continuous dialysis, go slow dialysis, and accelerated veno-venous hemofiltration.[10]

It has been documented in the literature that although CRRT is a conventional and more preferred treatment modality, its high costs makes it unavailable and inaccessible to the patients who need them.[7–9] This motivated the development of hybrid techniques like SLEDD which is both cost effective as well as have similar efficacy to that of CRRT. Individual studies, both observational as well as randomized controlled trials have been conducted among ICU patients to compare these 2 treatment modalities.[6,11–23] But owing to small sample sizes of individual studies, and different methodologies utilized by them for measuring outcome variables, none of these studies have adequate power to provide concrete evidence as to which of the treatment modalities is better.

Hence, the question remains regarding the effectiveness of the 2 RRT techniques, that is, CRRT versus SLED. A number of systematic reviews and meta-analysis of studies on intermittent RRT modalities have been carried out, but they did not adequately compare the effectiveness of CRRT versus SLED. Schneider et al[19] reviewed the rate of dialysis dependence among patients on intermittent RRT modalities collectively. Zhang et al[24] review compared CRRT and SLED in 2015, but in their analysis they separated the results of randomized controlled trials (RCTs) and observational studies resulting in inconclusive findings. Also, there was evidence of publication bias from the selected studies as many of the included studies were not available online and were from China.[24] Furthermore, the review by Nash et al[25] in 2017 compared all the existing 3 modalities of RRT but they limited their study selection to RCTs only and very few outcome parameters were assessed.

Therefore, we carried out the present review to compare the efficacy of CRRT versus SLED by including both RCTs and prospective observational studies, and by considering all the outcome measures pertaining to survival, and various clinical and biochemical parameters among critically ill patients suffering from acute kidney injury and hemodynamic instability.

2. Aim

To compare clinical (renal and survival) and biochemical outcomes among critically ill patients with acute kidney injury and hemodynamic instability treated with CRRT and SLED.

3. Objectives

3.1. Primary objective

1. To compare in-hospital and ICU mortality rates among critically ill patients with acute kidney injury and hemodynamic instability treated with CRRT and SLED.
2. To compare renal outcomes (dialysis dependence and renal recovery posttreatment) for the above stated treatment modalities among critically ill patients with acute kidney injury and hemodynamic instability.

3.2. Secondary objective

1. To compare secondary outcomes like ICU length of stay, solutes clearance rate, and fluid removal rate among the same group of patients.

4. Null hypothesis

1. There is no difference in the renal and mortality outcome among critically ill-patients having acute kidney injury and hemodynamic instability treated with CRRT and SLED.
2. There are no differences for the secondary outcomes among these patients treated with CRRT as compared with SLED.

5. Methodology

We have done this meta-analysis as per the standard guidelines of Cochrane Collaboration. We used the preferred reporting items for systematic reviews and meta-analyses and meta-analysis of observational studies in epidemiology (MOOSE) to report a systematic review and meta-analysis of RCTs and observational studies (235, 26).

5.1. Study population/Exposure Group

Critically ill patients having acute kidney injury and hemodynamic instability.

5.2. Interventions to be compared

CRRT versus SLED.

5.3. Outcome measures

1. In-hospital and ICU mortality rates.
2. Renal outcome: kidney recovery, and dialysis dependence.
3. Secondary outcomes like ICU length of stay, solutes clearance rate, and fluid removal rate (L/24 h).

5.4. Operational definitions

CRRT: It included all synonymous terms like continuous hemofiltration or continuous hemodiafiltration or continuous hemodialysis, being done 24 hours a day.

SLED: Similarly, we planned to include all studies which described extended session of >6 hours but <24 hours of hemodialysis or hemodiafiltration. It included all synonyms that is, prolonged intermittent renal replacement therapy, SLED, SLED-f, SLEDD, EDD, slow continuous dialysis, go slow dialysis, and accelerated veno-venous hemofiltration which have been described in the introduction section.[7]

5.5. Study selection

5.5.1. Types of study. We decided to include all randomized controlled trials as well as prospective cohort studies which compared the outcomes of CRRT and SLED among critically ill-patients of AKI and hemodynamic instability from January 1995 up to December 2018.

5.5.2. Study selection. The following data sources were searched for all RCTs and prospective cohort-control studies:

a. PubMed,
b. EMBASE/ Excerpta Medica,
c. Cochrane Central Register of Controlled Trials,
d. Google Scholar,
e. Reference lists.

Search strategies were independently designed and performed by 2 separate investigators. We used the following MeSH terms or keywords in different combinations and permutations for searching studies from year January 1995 to December 2018 in advanced PubMed search:

"Acute kidney injury," "Acute kidney failure," "hemodialysis," "hemodiafiltration," "dialysis," "Continuous renal replacement therapy," and "slow low efficiency dialysis and its synonyms."

The search strategies described above provided a list of studies. The titles and abstracts of all the retrieved studies were screened independently by 2 authors. The irrelevant studies were discarded in the first attempt. Later on, the full-text version of the shortlisted studies was analyzed for the presence of a measurable outcome variable in terms of:

a. ICU or in-hospital mortality rates among two treatment groups.
b. Renal recovery rates.
c. Dialysis dependence rates among 2 groups.
d. Fluid removal rates.
e. Solutes clearance rate (serum uric acid, serum creatinine and serum phosphate)
f. Length of hospital/ICU stay.

We did not pose any restrictions on the language of the articles as most of the articles could be translated by the google translate tool; which most of the journals supported for language conversion. But at the end, we chose only full text articles where detailed data were available for extraction and analysis.

5.6. Data extraction

We extracted the following study features: first author, publication year, country, number of participants in each group, RRT modalities, number of deaths in each group, number of patients who had 100% kidney recovery, number of patients who were dependent on dialysis after treatment, fluid removal rates in L/24 h in both treatment group, length of stay in ICU (days), and clearance rates of serum uric acid, serum creatinine, and serum phosphate among 2 groups. Outcomes reported in ≥2 articles were extracted for meta-analysis.

5.7. Quality assessment of studies

Internal validity of randomized controlled trials (RCTs) was assessed using the Cochrane Risk of Bias Tool while the quality of prospective cohort studies was assessed using the Newcastle–Ottawa scale.

5.8. Data analysis

Extracted data were entered and analyzed using Revman 5.3. Before the analysis, data were standardized into equivalent units. For dichotomous variables such as mortality, rates in the experimental (SLEDD/EDD) and control (CRRT) groups were expressed as rate ratio and 95% CI. For continuous variables such as length of ICU stay, fluid removal, and biochemical parameters, mean difference, and 95% CI were calculated for each study. Heterogeneity in the studies was evaluated using the Cochrane Q test and I^2 statistic to assess the degree of inter study variation. I^2 values of 0% to 24.9%, 25% to 49.9%, 50% to 74.9%, and 75% to 100% were considered as having no, mild, moderate, and significant thresholds for statistical heterogeneity.

6. Results

6.1. Study selection

The combined literature search identified around 5497 studies which contained the MeSH terms either in the title or abstract. After reviewing the title, we included 98 studies for abstract review. Finally, only 11 studies matched the inclusion criteria. The excluded studies were on the basis of various reasons described in Fig. 1.

The eligible studies were conducted from year 2004 till 2017. Of the 11 eligible studies, 6 were RCTs[13,15,17,18,23,28] and 5 were prospective cohort studies[11,14,20,21] carried out among different parts of the world as depicted in Table 1. The total population covered was 1160. Of these, 530 (46%) individuals were allocated to SLED and rest were treated using the CRRT modality. The mean age of the study participants varied from 50 to 70 years. The proportion of men among the study population varied from 63% to 75%.

6.2. Assessment of methodological quality

The risk of bias among the RCTs included in the analysis are as summarized in Table 2. Of the 5 RCTs, 3 had low risk for random sequence generation[15,17,28]; while bias for allocation concealment was low in only one study.[28] There was high risk for blinding bias foe almost all the included studies except the study by Kielstein et al,[28] which had low risk of this bias. Incomplete outcome data bias was high in only one study.[23] Selective outcome reporting bias was also high in one study that was by Mishra et al.[23]

Similarly, Newcastle–Ottawa scale was used to assess bias among prospective cohort studies as presented in Table 3.

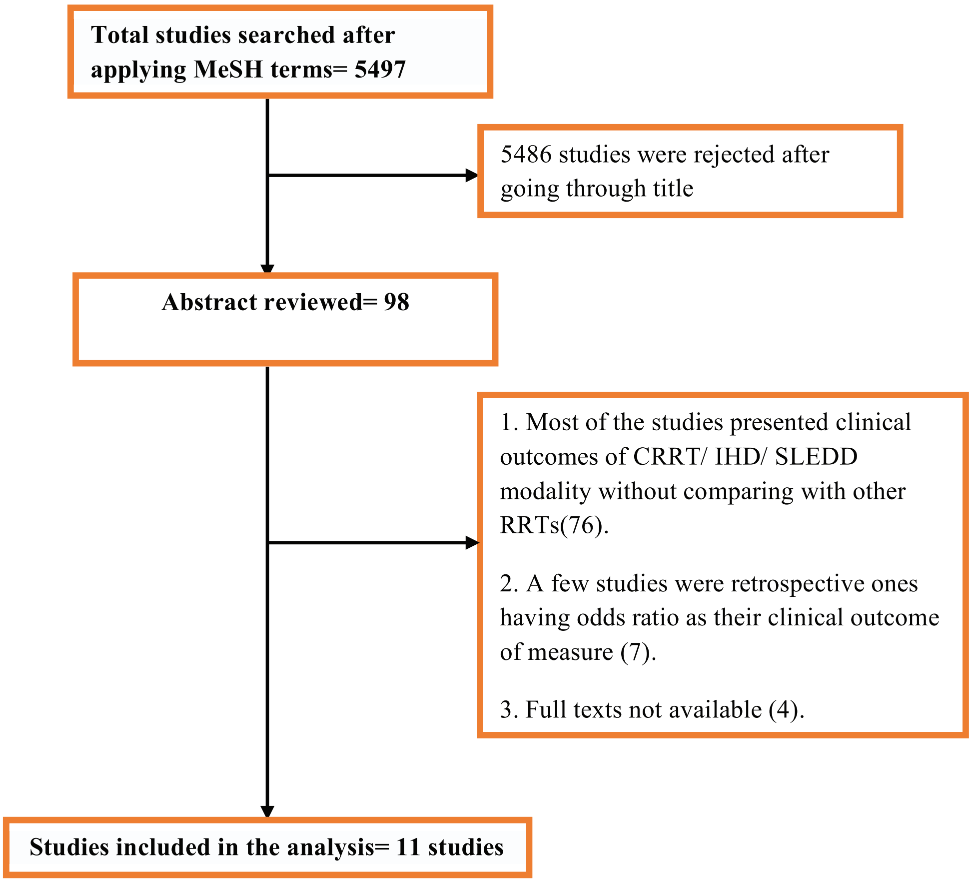

Figure 1. Flowchart showing selection of studies.

6.3. Outcome 1: mortality

Two types of mortality data were extracted from eligible studies; in-hospital and ICU mortality. In-hospital mortality was reported by 4 studies.[11,13,15,17] Their meta-analysis showed that there was no significant difference in the in-hospital mortality rates among patients treated with SLED compared with CRRT (RR = 0.67 [0.44–1.00], $P = .05$, $I^2 = 0\%$). This is shown in Fig. 2. There was no significant heterogeneity among the selected studies.

Similarly, the ICU mortality rate was reported by 9 studies.[13–15,17,18,20–22,28] The meta-analysis of these studies showed 0% heterogeneity and there was no significant difference in the ICU mortality rates among 2 treatment modalities as shown in Fig. 3 (RR = 0.88, 95% CI = 0.77–1.02, P value = .08, $I^2 = 0\%$).

6.4. Outcome 2: dialysis dependence

Figure 4 described the meta-analysis of 5 studies that assessed for dialysis dependence among the 2 treatment modalities.[11,13,15,18,22] The analysis revealed 0% heterogeneity and showed that there was no significant difference for rates of

Table 1

Matrix showing characteristics of selected studies.

First author, year	Design	Country	N	CRRT	SLED	Mean age	Sex (% males)	Main outcomes
Kielstein, 2004	RCT	Germany	39	19	20	50.5	62.9	Mortality, fluid removal, biochemical clearance
Kumar 2004	Prospective cohort	United States	54	28	26	52	63%	Mortality, kidney recovery, RRT dependence, ICU days.
Abe 2010	RCT	Japan	60	30	30	68.7	65	Mortality, kidney recovery, RRT dependence, ICU days
Wu 2010	Prospective cohort	Taiwan	101	63	38	67.3/67.5	66.6/63.1	Mortality
Abe 2011	RCT	Japan	50	25	25	65.9	66	Mortality, kidney recovery, RRT dependence, ICU days
Schwenger 2012	RCT	Germany	232	117	115	66.2	67.7	Mortality, fluid removal, ICU days, biochemical clearance
Badawy 2012	RCT	Egypt	80	40	40	47.5	65	Mortality, fluid removal, RRT dependence, ICU days, biochemical clearance
Chen 2014	Prospective cohort	China	107	55	52	59.27/59.83	NR	Mortality
Sun 2014	Prospective cohort	China	145	65	80	67.78/68.59	75.3/73.7	Mortality
Kitchlu 2015	Prospective cohort	Canada	232	158	74	62.1/60.6	59.5/67.6	Mortality, RRT dependence, clinical deterioration
Mishra 2017	RCT	India	60	30	30	47.8/49	70	Fluid removal

CRRT = continuous renal replacement therapy, ICU = intensive care unit, RCT = randomized controlled trials, RRT = renal replacement therapy, SLED = sustained low efficiency dialysis.

Table 2

Bias matrix among randomized controlled trial studies.

Parameters of bias in RCTs	Kielstein 2004	Abe 2010	Abe 2011	Schwenger 2012	Badawy 2012	Mishra 2017
Sequence generation	L	UC	L	L	UC	H
Allocation concealment	L	UC	UC	UC	UC	UC
Blinding of patients and personnel	L	H	H	H	H	H
Blinding of outcome assessors	L	UC	UC	H	H	H
Incomplete outcome data	L	L	L	L	L	H
Selective outcome reporting	UC	L	L	L	L	H
Other sources of bias	L	UC	UC	UC	UC	UC

L = low risk of bias, H = high risk of bias, RCT = randomized controlled trials, UC = unclear risk of bias.

Table 3

Bias matrix for prospective cohort studies.

Parameters of NOS scale	Kumar 2004	Wu 2010	Chen 2014	Sun 2014	Kitchlu 2015
Representatives of exposed cohort	L	L	L	L	L
Selection of non-exposed cohorts	L	L	L	L	L
Ascertainment of exposure	L	L	L	L	L
Outcome of interest not present	L	L	L	L	L
Comparability of cohort (age wise)	H	L	L	UC	L
Comparability of cohort (severity of illness wise)	H	L	L	UC	L
Assessment of outcome	L	L	L	L	L
Was follow-up long enough	L	L	L	L	L
Adequacy of follow up of cohorts	UC	L	L	L	L

L = low risk of bias, H = high risk of bias, UC = unclear risk of bias.

Study or Subgroup	SLED Events	SLED Total	CRRT Events	CRRT Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Abe 2010	5	30	11	30	16.3%	0.35 [0.10, 1.16]
Abe 2011	5	25	9	25	12.8%	0.44 [0.12, 1.59]
Kumar 2004	14	26	20	28	15.8%	0.47 [0.15, 1.44]
Schwenger 2012	57	115	62	117	55.1%	0.87 [0.52, 1.46]
Total (95% CI)		**196**		**200**	**100.0%**	**0.67 [0.44, 1.00]**
Total events	81		102			

Heterogeneity: Chi² = 2.94, df = 3 (P = 0.40); I² = 0%

Test for overall effect: Z = 1.94 (P = 0.05)

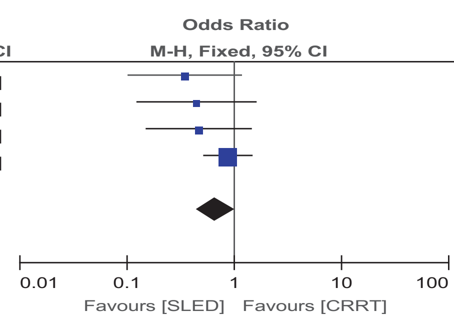

Figure 2. Forest plot comparing in-hospital mortality among patients of acute kidney injury treated by SLED versus CRRT. CRRT = continuous renal replacement therapy, SLED = sustained low efficiency dialysis.

Study or Subgroup	SLED Events	SLED Total	CRRT Events	CRRT Total	Weight	Risk Ratio M-H, Random, 95% CI
Abe 2010	5	30	10	30	2.2%	0.50 [0.19, 1.29]
Abe 2011	4	25	7	25	1.6%	0.57 [0.19, 1.71]
Badawy 2013	7	40	9	40	2.5%	0.78 [0.32, 1.88]
Chen 2014	4	52	6	55	1.4%	0.71 [0.21, 2.36]
Kielstein 2004	12	20	11	19	7.2%	1.04 [0.61, 1.75]
Kitchlu 2015	40	74	97	158	33.3%	0.88 [0.69, 1.12]
Schwenger 2012	49	115	49	117	21.9%	1.02 [0.75, 1.37]
Sun 2014	37	80	29	65	15.3%	1.04 [0.72, 1.48]
Wu 2010	18	38	45	63	14.5%	0.66 [0.46, 0.96]
Total (95% CI)		**474**		**572**	**100.0%**	**0.88 [0.77, 1.02]**
Total events	176		263			

Heterogeneity: Tau² = 0.00; Chi² = 6.51, df = 8 (P = 0.59); I² = 0%

Test for overall effect: Z = 1.75 (P = 0.08)

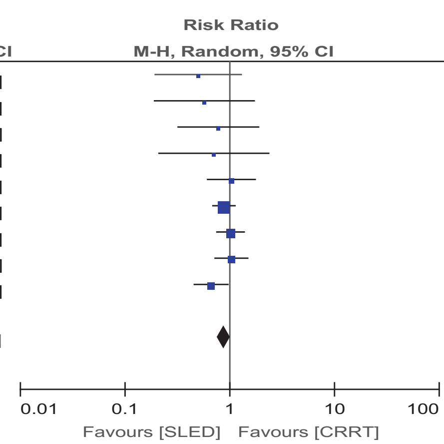

Figure 3. Forest plot comparing ICU mortality among critically ill-patients of acute kidney injury and hemodynamic instability. ICU = intensive care unit.

Study or Subgroup	SLED Events	SLED Total	CRRT Events	CRRT Total	Weight	Risk Ratio M-H, Random, 95% CI
Abe 2011	3	20	6	16	10.6%	0.40 [0.12, 1.35]
Abe 2010	2	25	3	19	5.5%	0.51 [0.09, 2.74]
Kumar 2004	2	10	2	8	5.3%	0.80 [0.14, 4.49]
Kitchlu 2015	13	34	20	61	50.5%	1.17 [0.67, 2.04]
Badawy 2013	12	33	8	31	28.1%	1.41 [0.67, 2.98]
Total (95% CI)		**122**		**135**	**100.0%**	**1.03 [0.69, 1.53]**
Total events	32		39			

Heterogeneity: Tau² = 0.00; Chi² = 3.97, df = 4 (P = 0.41); I² = 0%
Test for overall effect: Z = 0.14 (P = 0.89)

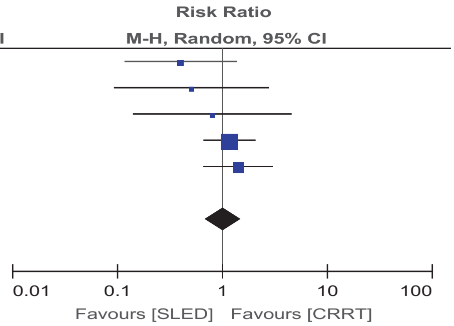

Figure 4. Forest plot of comparing dialysis dependence among patients of acute kidney injury and hemodynamic instability.

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Sun 2014	26	80	33	65	17.4%	0.64 [0.43, 0.95]
Badawy 2013	21	33	23	31	19.6%	0.86 [0.62, 1.19]
Chen 2014	32	52	30	55	19.8%	1.13 [0.82, 1.56]
Abe 2010	24	30	18	30	19.2%	1.33 [0.95, 1.88]
Wu 2010	13	38	15	63	11.2%	1.44 [0.77, 2.68]
Abe 2011	17	25	10	25	12.9%	1.70 [0.98, 2.95]
Total (95% CI)		**258**		**269**	**100.0%**	**1.08 [0.83, 1.42]**
Total events	133		129			

Heterogeneity: Tau² = 0.07; Chi² = 13.42, df = 5 (P = 0.02); I² = 63%
Test for overall effect: Z = 0.58 (P = 0.56)

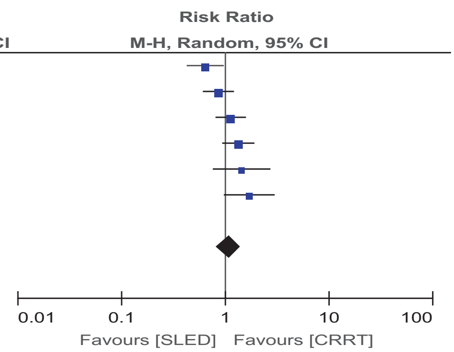

Figure 5. Forest plot of comparing renal recovery among critically ill-patients of acute kidney injury and hemodynamic instability.

dialysis dependence posttreatment among patients treated with SLED compared with CRRT (RR = 1.03, 95% CI = 0.69–1.53, P = .89, I^2 = 0%).

6.5. Outcome 3: renal recovery

The summary risk ratio of 6 studies[13–15,18,20,21] that assessed for renal recovery indicated that there was no significant difference in the renal recovery status among patients treated with SLED compared with CRRT (RR = 1.08, 95% CI = 0.83–1.42, P = .56). However, as shown in Fig. 5, there was significant heterogeneity among the selected studies for this outcome measure (τ^2 = 0.07, χ^2 = 13.42, df = 5, P = .02, I^2 = 63%).

6.6. Outcome 4: length of stay in ICU

The summary mean difference of 5 studies[11,13,15,17,18] that assessed length of stay in the ICU indicated that there was no significant difference in the ICU stay among patients treated with SLED versus CRRT (mean difference = –0.16, 95% CI = –0.56–0.22, P = .41). As shown in Fig. 6, there was significant heterogeneity among the selected studies for this outcome measure (τ^2 = 0.13, χ^2 = 13.96, df = 4, P = .007, I^2 = 71%).

6.7. Outcome 5: fluid removal

The summary mean differences in fluid removal among 4 selected studies[17,18,23,28] indicated that there was no significant differ-

Study or Subgroup	SLED Mean	SLED SD	SLED Total	CRRT Mean	CRRT SD	CRRT Total	Weight	Std. Mean Difference IV, Random, 95% CI
Abe 2011	14	7	25	19	11	25	18.1%	-0.53 [-1.10, 0.03]
Kumar 2004	16	8	14	24	20	20	15.2%	-0.48 [-1.17, 0.21]
Abe 2010	14	9	30	19	17	30	19.5%	-0.36 [-0.87, 0.15]
Schwenger 2012	20	20	115	24	22	117	26.0%	-0.19 [-0.45, 0.07]
Badawy 2013	23	5	40	19	8	40	21.1%	0.59 [0.15, 1.04]
Total (95% CI)			**224**			**232**	**100.0%**	**-0.16 [-0.55, 0.22]**

Heterogeneity: Tau² = 0.13; Chi² = 13.96, df = 4 (P = 0.007); I² = 71%
Test for overall effect: Z = 0.83 (P = 0.41)

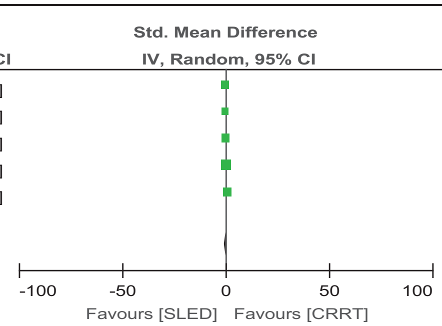

Figure 6. Forest plot of comparison in length of stay in ICU among Acute Kidney Injury patients treated by SLED vs CRRT. CRRT = continuous renal replacement therapy, ICU = intensive care unit, SLED = sustained low efficiency dialysis.

Study or Subgroup	SLED Mean	SLED SD	SLED Total	CRRT Mean	CRRT SD	CRRT Total	Weight	Std. Mean Difference IV, Random, 95% CI
Badawy 2013	1.9	0.25	40	2.1	0.29	40	25.4%	-0.73 [-1.19, -0.28]
Kielstein 2004	2.97	0.55	20	3.28	0.39	19	20.7%	-0.63 [-1.28, 0.01]
Schwenger 2012	0.533	1.36	115	0.736	1.44	117	30.0%	-0.14 [-0.40, 0.11]
Mishra 2017	0.79	0.24	30	0.68	0.2	30	23.9%	0.49 [-0.02, 1.01]
Total (95% CI)			**205**			**206**	**100.0%**	**-0.24 [-0.72, 0.24]**

Heterogeneity: Tau² = 0.18; Chi² = 14.14, df = 3 (P = 0.003); I² = 79%
Test for overall effect: Z = 0.99 (P = 0.32)

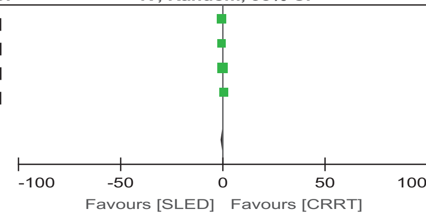

Figure 7. Forest plot of comparing fluid removal among patients of acute kidney injury treated with SLED versus CRRT. CRRT = continuous renal replacement therapy, SLED = sustained low efficiency dialysis.

ence in the fluid removal rates (L/24 h) among patients treated with SLED compared with CRRT (mean difference = –0.24, 95% CI = –0.72–0.24, $P = .32$). There was significant heterogeneity among the selected studies for this outcome measure ($\tau^2 = 0.18$, $\chi^2 = 14.14$, df = 3, $P = .003$, $I^2 = 79\%$) as shown in Fig. 7.

6.8. Outcome 6: biochemical clearance

The summary mean difference of 3 selected studies indicated that there was no significant difference in the clearance rates for serum creatinine, and serum uric acid among patients treated with SLED versus CRRT as shown in Figs. 8 and 9. However, there was significant heterogeneity among the selected studies for this outcome measure.

The summary mean difference of 2 selected studies indicated that there was a significant difference in the serum phosphate clearance among patients treated with SLED and CRRT (mean difference = –1.17, 95% CI = –1.90 to –0.44, $P = .002$).[17,28] There was significant heterogeneity among the selected studies for this outcome measure ($\tau^2 = 0.21$, $\chi^2 = 3.68$, df = 1, $P = .06$, $I^2 = 73\%$) as indicated in Fig. 10.

7. Discussion

This review identified 11 original studies that compared the performance of SLED versus CRRT among >1160 patients with AKI and hemodynamic instability.[11,13–15,17,18,20–23,28] When we analyzed data from RCTs and prospective cohort studies, we found that patients who received SLED as an initial RRT modality for AKI had a similar risk of death compared with those who initially received CRRT. Similarly, there were no significant differences in kidney recovery, dialysis dependence, ICU length of stay (in days), and fluid removal with SLED in comparison to CRRT. Also, SLED showed similar efficacy to CRRT in laboratory results for serum urea, and serum creatinine during RRT. However, the efficacy of SLED was statistically significant in clearing serum phosphates level as compared with CRRT.

Study or Subgroup	SLED Mean	SLED SD	SLED Total	CRRT Mean	CRRT SD	CRRT Total	Weight	Std. Mean Difference IV, Random, 95% CI
Schwenger 2012	1.26	0.8	115	1.66	0.65	117	34.5%	-0.55 [-0.81, -0.29]
Kielstein 2004	1.18	0.09	20	1.2	0.3	19	32.3%	-0.09 [-0.72, 0.54]
Badawy 2013	2.1	0.9	40	1.1	0.3	40	33.2%	1.48 [0.98, 1.97]
Total (95% CI)			**175**			**176**	**100.0%**	**0.27 [-1.02, 1.56]**

Heterogeneity: Tau² = 1.24; Chi² = 49.81, df = 2 (P < 0.00001); I² = 96%
Test for overall effect: Z = 0.41 (P = 0.68)

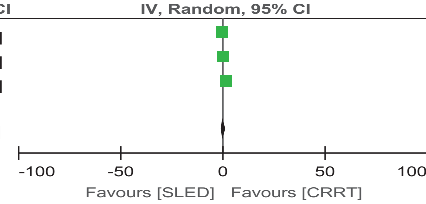

Figure 8. Forest plot of comparing serum creatinine among patients of acute kidney injury treated with SLED versus CRRT. CRRT = continuous renal replacement therapy, SLED = sustained low efficiency dialysis.

Study or Subgroup	SLED Mean	SLED SD	SLED Total	CRRT Mean	CRRT SD	CRRT Total	Weight	Std. Mean Difference IV, Random, 95% CI
Schwenger 2012	68.4	31.2	115	105.5	29.7	117	34.0%	-1.21 [-1.49, -0.93]
Kielstein 2004	71.8	7.2	20	73.1	7.7	19	32.7%	-0.17 [-0.80, 0.46]
Badawy 2013	38	1.4	40	26	12	40	33.3%	1.39 [0.90, 1.88]
Total (95% CI)			**175**			**176**	**100.0%**	**-0.00 [-1.68, 1.68]**

Heterogeneity: Tau² = 2.14; Chi² = 82.96, df = 2 (P < 0.00001); I² = 98%
Test for overall effect: Z = 0.01 (P = 1.00)

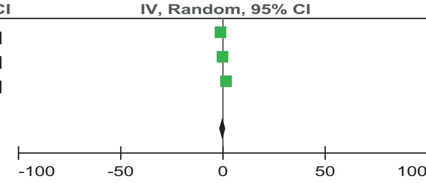

Figure 9. Forest plot of comparing serum urea among patients of acute kidney injury treated with SLED versus CRRT. CRRT = continuous renal replacement therapy, SLED = sustained low efficiency dialysis.

	SLED			CRRT				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Kielstein 2004	3.7	0.3	20	4.2	0.3	19	39.6%	-1.63 [-2.37, -0.90]
Schwenger 2012	0.88	0.34	115	1.18	0.35	117	60.4%	-0.87 [-1.14, -0.60]
Total (95% CI)			**135**			**136**	**100.0%**	**-1.17 [-1.90, -0.44]**

Heterogeneity: $Tau^2 = 0.21$; $Chi^2 = 3.68$, $df = 1$ ($P = 0.06$); $I^2 = 73\%$
Test for overall effect: $Z = 3.12$ ($P = 0.002$)

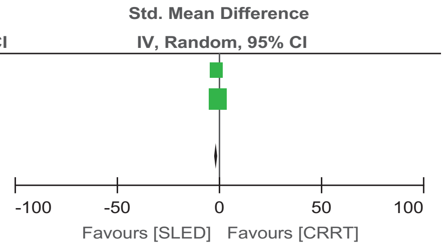

Figure 10. Forest plot of comparing serum phosphate among patients with acute kidney injury treated SLED versus CRRT. CRRT = continuous renal replacement therapy, SLED = sustained low efficiency dialysis.

In the past, many systematic reviews and meta-analysis have compared the performance of IHD with CRRT. They concluded that the mortality risk was similar for IHD and CRRT treated individuals. Both of these treatment modalities had their own advantages and disadvantages. These factors led to the development of hybrid technology of SLED. Researchers have tried to carry out independent studies to compare the performance of SLED and CRRT using varying methodologies of RCTs and cohort study designs. But due to limited 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. These limitations informed the need to conduct this systematic reviews and meta-analysis.

Our study builds on previous published meta-analyses by Zhang et al,[24] Nash et al,[25] and Tonelli et al.[30] We found 4 and 9 studies that reported on in-hospital mortality and ICU mortality rate, respectively. The analyses indicate that there were no statistically significant differences for the pooled results of in-hospital mortality and ICU mortality rates comparing patients who received CRRT compared with SLED. This suggests that in a setting where economic costs is a major consideration, the cost-effective RRT modality (SLED) should be the option of choice. Other advantages of performing SLED over CRRT includes: its ready availability and their need for less expertise compared with CRRT, its ability to achieve adequate renal replacement in hemodynamically unstable patients thereby gaining time for other procedures, lowered need for anticoagulation, and ability to provide slow solute and fluid removal ensuring hemodynamic stability.[31–33] Furthermore, this meta-analysis also found that there were no significant differences in the length of ICU stay, and rate of fluid removal among individuals who received SLED compared with CRRT. These findings are consistent with previous meta-analyses.[19,30,32,34,35]

In addition, another crucial outcome of RRT is dialysis dependence whether following hospital discharge or in the long-term and renal recovery. Previous cohort studies indicated that the type of RRT may affect the recovery of renal function among individuals having AKI. Thus, most of these studies reported that CRRT seem to decrease the need for dialysis compared with SLED.[32,36–38] In a recent study, individuals who received SLED had a higher rate of dialysis dependence following hospital discharge than those who were first given CRRT.[37] However, it was observed that the subjects in the SLED group had a lower baseline eGFR compared with those in the CRRT group.[34] In our meta-analysis, we found that there were no significant differences in the rates of dialysis dependence and renal recovery posttreatment among patients treated with SLED compared with CRRT. These findings are consistent with the results of previous analyses.[30,34,35] Theoretically, CRRT may be linked with the preservation of renal function, thereby maintaining the hemodynamic status and reducing hypotension episodes, especially during fluid withdrawal.[30,32,34–36] However, eGFR at hospital discharge may overestimate renal function of subjects undergoing RRT due to their accompanying loss of muscle mass that occurs during conditions of serious illness.[37,38]

Our analyses further revealed that there was no significant difference in the clearance rates of serum creatinine and serum uric acid among patients treated with SLED versus CRRT. However, the summary mean difference indicated that there was a significant difference in the serum phosphate clearance rates among patients treated with SLED compared with CRRT. Due to its prolonged nature, subjects who were given treatment with SLED usually require daily monitoring and often supplementation of potassium and phosphorus.[33,40,41] Our finding is consistent with the results of previous studies which reported that hypophosphatemia may occur in a significant proportion of subjects treated with SLED compared with those treated with CRRT.[33,40,41] Therefore, the dialysate phosphate concentration in individuals receiving SLED needs to be adjusted accordingly and the patients may require supplementation.[33,40,41]

Our study has some limitations. This is a purely statistical meta-analysis using published data of each study selected. This is per se may be a possible cause of bias. The number of studies and the number of patients included in the meta-analysis is not high. Therefore, study number, different study designs with small sample sizes can be considered limitations of our review. Third, one of the strongest limitations of this study is the fact that the studies included in the review were conducted in different periods of time, in different countries, with different methodologies and the only data in which we have access are the published reports from the various studies. An individual patient data meta-analysis may improve upon these limitations. Finally, one major limitation is the inclusion of all studies in the review despite some of the studies having low quality (as indicated by bias matrix for RCTs and prospective cohort studies) due to scarcity of existing literature.

However, based on the current meta-analysis and the reviews done in the past, we can draw some cautious conclusions. First, these 2 modalities of renal replacement do not produce different outcomes in adults with AKI and hemodynamic instability. Second, the overall risk of mortality was reduced in patients receiving SLED but this finding might have been diluted due to sample sizes of individual studies and variations in the design of the studies with shorter follow-up periods.

Hence, future research should focus on well-planned RCTs or cohort studies with longer duration of follow up along with addressal of key outcome measures like mortality, and renal outcomes along with biochemical profile. Hence, it can be concluded that there is no clear advantage for using continuous renal replacement in the hemodynamically unstable patient. Albeit, CRRT is more costly than SLED. Both the modalities are equally safe and effective in treating AKI among critically ill patients. Hence, SLED can be used in place of CRRT to cut costs as both have same efficacy.

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