Renal Replacement Therapy for Burn Patients: A Systematic Review and Meta-Analysis

ZhiYu Duan

Chinese PLA General Hospital <https://orcid.org/0000-0002-5761-0964>

FengKun Chen

PLA 304 Hospital: Chinese PLA General Hospital

GuangYan Cai (✉ caiguangyan@sina.com)

Chinese PLA General Hospital <https://orcid.org/0000-0001-8586-6353>

JiJun Li

PLA 304 Hospital: Chinese PLA General Hospital

XiangMei Chen

Chinese PLA General Hospital

Research

Keywords: Renal replacement therapy, burn patients, acute kidney injury, meta-analysis, regional citrate anticoagulation

Posted Date: September 15th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-72357/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Background: To improve the prognosis of burn patients with renal replacement therapy (RRT), we performed this systematic review and meta-analysis.

Methods: We searched multiple databases for studies published before February 2020. Studies about adult populations with burn injury, providing epidemiologic data on prevalence or mortality of RRT, were included.

Results: A total of selected 58 studies, including 38,787 patients were enrolled in our analysis. The prevalence rates of RRT were 5.14% (95%CI 4.54%-5.74%) in all burn patients and 35.8% (95%CI 29.54%-42.07%) in acute kidney injury (AKI) patients. The prevalence of RRT among burn patients in the intensive care unit (ICU) was 10.92% (95%CI 8.71%-13.14%). The mortality of all burn patients with RRT was 65.52% (95%CI 58.41%-72.64%). The mortality of patients with RRT in ICU was 62.7% (95%CI 53.7%-71.7%). The mortality rate of RRT patients was 30.33% (95%CI 22.06%-38.59%) of the total. There was no significant correlation ($r=-0.224$, $P=0.159$) between the year of publication and the mortality of burn patients with RRT. Neither cohort studies nor RCT studies of subgroup analyses show that RRT could reduce the risk of death in burn patients with AKI. Bleeding (10.92%) and secondary infection (9.61%) were the most common RRT-related adverse reactions. Compared with heparin, regional citrate anticoagulation has advantages in superior filter life spans and fewer bleeding episodes. Dialysis-requiring AKI in burn patients could increase the risk of chronic kidney disease progression and end-stage renal disease. About 35% of RRT patients need to maintain hemodialysis temporarily, even if they survive and leave hospital.

Conclusions: The prevalence of RRT is not low; approximately, one-third of burn patients with AKI need RRT. The mortality of burn patients with RRT is very high and accounts for 1/3 of the total deaths. There is no evidence that RRT can improve the prognosis of burn patients with AKI. Regional citrate anticoagulation has some advantages in reducing bleeding and extending filter life spans, which may be more suitable for severe burn patients with CRRT.

Introduction:

Acute kidney injury (AKI) is one of the common complications of burn patients that seriously threatens the life of patients and increases the length of stay, intensive care unit (ICU) length of stay and treatment costs (1, 2). In 2010, meta-analysis reported that the prevalence of AKI in burn patients ranged from 16–26.6% (3), depending on the severity of the burns and on the definition of AKI. The prevalence of AKI in burn patients ranged from 18.4–47.4% with the RIFLE standard (2). Burn patients with AKI had a significantly increased risk of death. The mortality of burn patients with AKI was 16.95–100%, significantly higher than that of their control group (7%-29.41%) (4–7).

However, the prevalence and mortality of renal replacement therapy (RRT) for burn patients are still unclear. A meta-analysis in 2010 conducted a subgroup analysis of the prevalence and mortality of RRT in burn AKI patients. The results showed that the prevalence of RRT was 3.2% in all burn patients and 27.1% in burn patients with AKI. The mortality of burn patients with RRT was as high as 80% (95%CI 72-88.6%) (3). However, the updated meta-analysis of burn patients admitted to the ICU showed that the prevalence of RRT in all burn patients was 12%, and the mortality was 74% (95%CI 58–87%) (8). The mortality of burn patients with RRT was very high. However, due to the different directions of attention, the literature of RRT for burn patients included in these studies is incomplete. At present, there is a lack of meta-analysis of RRT for burn patients. Moreover, to reduce the mortality of severe burn patients with AKI after 2010, many researchers have made many attempts for different dialysis modalities (continuous or intermittent), different treatment doses (high-volume or standard) and different anticoagulant methods (regional citrate anticoagulation vs heparin). Chung 2017 conducted a multicentre, prospective, randomized, controlled clinical trial to evaluate the impact of high-volume haemofiltration (HVHF) on the haemodynamic profile of burn patients with septic shock and AKI. They concluded that HVHF was effective in reversing shock and improving organ function in burn patients with septic shock and AKI, but the data were insufficient to comment on improving survival (9). Another random prospective study concluded that HVHF conducted in the early stage (within 3 days) could reduce the incidence of sepsis and the mortality of patients with severe burns (10). Yoon 2017-burns found that early or late continuous renal replacement therapy (CRRT) did not change the prognosis of burn patients with AKI. In their multivariate logistic regression analysis, only sepsis had an independent association with mortality (11). Most of the existing studies are single-centre, small-sample, retrospective or involved the examination of a single or a few variables. Moreover, the findings on RRT for burn patients were varied or contradictory. To improve the prognosis of burn patients with RRT, we selected eligible studies related to RRT in burn

patients with or without AKI and then performed this systematic review and meta-analysis of its prevalence, dialysis modality, therapeutic dose, anticoagulation, and prognosis.

Methods:

This systematic review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines (12, 13).

Eligibility criteria

Studies on adult populations with burn injury, providing epidemiologic data on prevalence and mortality of RRT, were included. Randomized controlled trials (RCTs) comparing the clinical efficacy of intermittent haemodialysis (IHD), peritoneal dialysis (PD) or CRRT for adult patients with burn injury receiving treatment for AKI were also included. We did not limit the total body surface area (TBSA) of burns. Studies conducted only in patients with chemical or electrical burns were not included because of the different pathophysiologies. We excluded studies with a sample size of less than 10. Other blood purification techniques, such as plasma exchange (non-RRT), are not included in this study.

Search strategy

We used the following terms for standard medical subject headings and free-text words: burn, burns, renal, kidney, kidney injury, kidney diseases, renal insufficiency, renal failure, and kidney failure. We also reviewed the references cited in all of the studies selected for review. An extensive search of literature published until January 2020 was conducted using the databases PubMed/MEDLINE, Embase, Science Citation Index (Web of Science), and the Cochrane Central Register of Controlled Trials (CENTRAL) database. Two searchers (D.ZY. and C.FK.) conducted the search independently. If one of the searchers thought that the article was appropriate, the study was selected.

Study selection

Two reviews (D.ZY. and C.FK.) independently screened studies for eligibility according to study selection criteria. The inclusion criteria were RCT, case-control and cohort studies. Cross-sectional studies were excluded because they cannot clearly identify the causal relationship between observed indicators and diseases. Only articles in English, Japanese or Chinese were included. Populations with paediatric patients, animal studies, case reports and reviews were excluded. Any disagreement between reviewers were resolved by consensus. RRTs included slow low-efficiency dialysis (SLED), IHD, PD and CRRT. If the patients used CRRT during hospitalization, we still classified them into the CRRT group even if other dialysis methods were also used. If the patient used peritoneal dialysis during hospitalization, even if other dialysis methods were used, we still classified them into the peritoneal dialysis group. We excluded the study of plasma exchange in burn patients because the mechanism and mode of treatment of plasma exchange are different from those of dialysis. We excluded the lack of mortality studies aimed at studying antibiotic pharmacokinetics in burn patients with RRT. For studies that gave multiple mortalities, we took the longest mortality, such as 28, 60, 90, or in-hospital mortality.

Study quality

We assessed risk of bias for RCTs using the Cochrane Collaboration's tool for assessing bias(14). We assessed risk of bias for case-control and cohort studies using the Newcastle-Ottawa Scale (NOS) (15). The NOS allocates nine points for quality of the selection (four items, four points), comparability (one item, two points), and outcome or exposure (three items, three points). Publication bias was assessed by creating and examining funnel plots. The robustness of the results was evaluated using sensitivity analyses. Each study included in this review was assessed for quality as good (7–9), moderate (4–6), or poor (≤ 3) based on scores.

Data extraction and statistical analysis

Two independent reviewers (D.ZY. and C.FK.) extracted the following information from the included studies: title, author, year, journal, study design, nationality, sample size, definition of AKI, number of patients with or without AKI, number of patients with or without RRT, RRT details (modalities, device and manufacturer, dose, anticoagulants), and results (mortality of AKI patients, mortality of RRT patients). We also reported other outcomes (RRT complications, renal outcome-long-term dialysis, temporarily required dialysis, CKD progress).

All ambiguities in data extraction were double-checked and resolved. Relative risks (RRs) and 95% confidence intervals were obtained using a random effects model. I^2 derived from the chi-squared test was used to evaluate the heterogeneity across the included studies. An I^2 less than 50% indicated that there was no significant heterogeneity(16). Sensitivity analysis was performed by sequentially removing each individual study. We assessed publication bias by constructing a funnel plot. Pearson or Spearman's correlation was used to analyse correlations. A two-tailed P value of < 0.05 was considered statistically significant. All statistical analyses were performed using Review Manager version 5.3, R 3.5.1, SPSS 24.0 and R 3.5.1 software were used for meta-analyses of prevalence and mortality.

Results:

Quality assessment and study characteristics

We screened and evaluated 4720 studies, assessing 194 for eligibility. The selected 58 studies, including 38,787 patients, were enrolled in our analysis (Fig. 1) (1, 4–7, 9–11, 17–65). There were 4718 burn patients with AKI and 1764 burn patients with RRT. A total of 93.53% of the burn patients with RRT were AKI patients. Figure 1 shows a flow chart of the identification and selection of the studies.

The main features of these studies are shown in Table 1. Risk of bias is summarized in Additional file 1: Table S1 (cohort or case-control studies) and Fig. S1 (RCT studies). Among the 58 included studies, 23 were from North America (1, 4, 9, 17–19, 27, 29, 31, 33, 34, 36, 37, 42–44, 48–50, 54, 59, 61, 62), 18 were from Asia (5, 7, 10, 11, 22, 24–26, 28, 39, 40, 46, 47, 51, 52, 58, 64, 66), 15 were from European countries (6, 20, 21, 23, 30, 35, 38, 45, 53, 55–57, 60, 65, 67), one was from South America (32), one was Africa (41). A total of 12 studies could not be used for analysis of the prevalence of RRT, seven of which only reported on RRT patients (11, 18, 21, 37, 40, 43, 45), four of which were RCT studies (9, 10, 51, 52), and the remaining one of which were historical controls (44). Most of the 58 studies (41/60) were retrospective cohort studies, but 12 were prospective cohort studies (7, 35, 39, 41, 43, 46, 47, 50, 57, 58, 64, 65), and 5 RCT studies (9, 10, 51, 52, 56).

Table 1
Summary of the baseline characteristics of the studies included in the meta-analysis.

Study	Nationality	Study type	Sample size	AKI definition	Admitted time	AKI numbers	RRT numbers	RRT mortality (%)
Akers 2012	America	Retrospective cohort	171	≥ 0.5 mg/dL SCr increase, any time during therapy	2006–2009	38	33	19(57.58)
Béchir 2010	Switzerland	Prospective cohort	30	Dialysis	1997.8-1999.7	5	5	NA
Béchir 2013	Switzerland	Randomized controlled trial	45	Dialysis	2009.11-2013.1	12	12	NA
Boucher 2016	America	Prospective cohort	10	AKIN criteria	NA	9	10	3(30)
Chrysopoulo 1999	America	Retrospective cohort	1404	Oliguria for at least 36 hours (urine output < 350 mL/d), a blood urea nitrogen-creatinine ratio of less than 20, Scr > 2 mg/dL, and the requirement for dialysis after injury	1981–1998	76	67	61(91.04)
Chun 2018	Korea	Prospective cohort	76	AKIN criteria	2014.2-2015.9	32	20	19(95)
Chung 2008	America	Retrospective cohort	102	RIFLE classification	2003–2007	34	18	10(55.56)
Chung 2017	America	Randomized controlled trial	37	Oliguria (< 20 ml/hour) for > 24 hours or an increase Scr > 2 mg/dl in males or > 1.5 mg/dl in females over a period of < 4days	2012–2016	37	37	23(62.16)
Chung 2018	America	Retrospective cohort	4086	KDIGO criteria	2012–2016	160	170	85(50)
Clark 2019	America	Retrospective cohort	1040	KDIGO criteria	2008–2015	601	58	36(62.07)
Coca 2007	America	Retrospective cohort	304	RIFLE classification	1998–2003	81	11	8(72.73)
Damkat-Thomas 2011	America	Retrospective cohort	41	RIFLE classification	2006–2010	17	5	2(40)
Davies 1979	England	Retrospective cohort	1064	NA	1958–1979	28	25	22(88)

NA, not available; Scr, serum creatine.

Study	Nationality	Study type	Sample size	AKI definition	Admitted time	AKI numbers	RRT numbers	RRT mortality (%)
Demsey 2019	Canada	Retrospective cohort	151	AKIN criteria	2010–2016	64	18	7(38.89)
Dépret 2018	France	Retrospective cohort	87	KDIGO criteria	2012.1-2015.1	55	21	NA
Gille 2014	Germany	Retrospective cohort	18	NA	2004–2009	18	18	2(11.11)
Haberal 1993	Turkey	Retrospective cohort	915	NA	1979–1989	19	19	15(78.95)
Hladik 2001	Czech	Retrospective cohort	40	NA	1996–2000	10	40	28(70)
Holm 1999	Germany	Retrospective cohort	328	Scr > 2.0 mg/dl (with rising tendency) combined with a blood urea nitrogen level > 200 mg/dl or in patients with anuria or oliguria (urine volume < 400 ml/24 h) with anasarca and/or hyperkalemia	1994–1998	48	48	41(85.42)
Hong 2013	Korea	Prospective cohort	45	RIFLE classification	2011–2012	11	5	4(80)
Hu 2012	China	Retrospective cohort	396	RIFLE classification	2006–2010	151	25	NA
Hundeshagen 2017	America	Retrospective cohort	246(adults)	KDIGO criteria	2004–2016	26	3	NA
Kim 2003	Korea	Retrospective cohort	147	Scr ≥ 2 mg/dL	2000.1-2000.12	28	3	3(100)
Knowlin 2018	America	Retrospective cohort	7539	Using ICD-9 codes	2002–2012	194	1	NA
Kumar 2016	America	Retrospective cohort	254	AKIN criteria	2011–2013	190	10	NA
Kuo 2016	China	Retrospective cohort	145	KDIGO criteria	2004–2006	59	9	7(77.78)
Kuo 2018	China	Retrospective cohort	301	AKIN criteria	2006–2011	34	28	NA
Kym 2015	Korea	Prospective cohort	85	RIFLE classification	2012–2013	48	22	NA
Leblanc 1997	Canada	Retrospective cohort	970	NA	1987–1994	16	16	13(81.25)
Liu 2016	China	Randomized controlled trial	41	NA	2013.1-2015.7	NA	20	7(35)
NA, not available; Scr, serum creatine.								

Study	Nationality	Study type	Sample size	AKI definition	Admitted time	AKI numbers	RRT numbers	RRT mortality (%)
Liu 1986	China	Retrospective cohort	6050	NA	1958–1983	53	15	8(53.33)
Lopes 2007	Portugal	Retrospective cohort	126	Doubling of baseline Scr	2004–2006	32	11	NA
Mariano 2010	Italy	Retrospective cohort	548	NA	2000–2007	98	70	50(71.43)
Mason 2016	Canada	Retrospective cohort	330	Scr > 1.5 mg/dL	2004–2011	48	37	NA
Muñoz 2017	Spain	Retrospective cohort	840	KDIGO criteria	1992–2012	466	34	NA
Mustonen 2008	Finland	Retrospective cohort	1380	Scr > 120μmol/L (1.4 mg/dL); for chronic renal insufficiency patients, 2-fold rise in Scr or Scr rose > 100 μmol/l during 1 day	1988–2001	93	32	20(62.5)
Peng 2005	China	Randomized controlled trial	20	NA	2001.6–2001.10	NA	10	1(10)
Planas 1982	America	Retrospective cohort	29	Scr level above initial values to a level equal to or greater than 1.5 mg/dL	1980–1982	11	3	2(66.67)
Pronina 2015	Canada	Retrospective cohort	1405	AKIN or RIFLE criteria	2006–2014	53	21	7(33.33)
Queiroz 2016	Brazil	Retrospective cohort	293	An elevation in baseline serum creatinine greater than or equal to 50% from baseline	2010–2012	77	52	NA
Rakkolainen 2018	Finland	Retrospective cohort	187	Scr ≥ 120μmol/L (1.4 mg/dl)	2006–2015	51	21	9(42.86)
Ren 2015	China	Prospective cohort	95	KDIGO criteria	2013.4–2013.9	11	5	4(80)
Sabry 2009	Egypt	Prospective cohort	40	Scr > 2 mg/dL and blood urea nitrogen > 25 mg/dL	2007.5–2007.12	9	4	2(50)

NA, not available; Scr, serum creatine.

Study	Nationality	Study type	Sample size	AKI definition	Admitted time	AKI numbers	RRT numbers	RRT mortality (%)
Saffle 1993	America	Retrospective cohort	529	Scr > 132.6umol/L (1.5 mg/dL)	1987–1991	143	5	5(100)
Sánchez-Sánchez 2016	Spain	Prospective cohort	165	RIFLE classification	2008.10-2011.12	32	15	14(93.33)
Schneider 2012	America	Retrospective cohort	220	RIFLE classification	2006–2008	103	25	NA
Sen 2015	America	Prospective cohort	30	RIFLE classification	NA	14	3	NA
Soltani 2009	America	Retrospective cohort	3356	NA	1994–2004	38	33	23(69.7)
Steinvall 2008	Sweden	Prospective cohort	127	RIFLE classification	1997–2005	31	4	3(75)
Stewart 2013	America	Retrospective cohort	1967	AKIN criteria	2003–2008	640	70	49(70)
Tang 2018	China	Retrospective cohort	157	AKIN criteria	2014.8	89	82	NA
Tremblay 2000	Canada	Retrospective cohort	12	NA	1995–1998	12	12	6(50)
Witkowski 2016	Poland	Retrospective cohort	225	Decrease in GFR of less than 60 ml/min at admission, decrease in GFR of more than 75% compared to baseline or decrease in the daily diuresis of less than 500 ml for at least 24 h	2012–2013	135	9	9(100)
Yang 2014	Korea	Prospective cohort	90	RIFLE classification	2011–2012	55	22	17(77.27)
Yim 2015	Korea	Prospective cohort	97	AKIN criteria	2012–2013	40	23	NA
Yoon 2017-Burns	Korea	Retrospective cohort	84	RIFLE classification	2007–2010	84	84	71(84.5)
Yoon 2017-PLOS ONE	Korea	Retrospective cohort	216	AKIN criteria	2009–2015	190	216	176(81.48)
You 2018	China	Randomized controlled trial	82	KDIGO stage 3	2014–2017	9	41	11(26.83)
NA, not available; Scr, serum creatine.								

Prevalence and mortality of RRT under different AKI diagnostic criteria

We analysed 46 literatures that reported the prevalence of RRT in burn patients (Table 2) (1, 4–7, 17, 19, 22–36, 38, 39, 41, 42, 46–50, 53–62, 64–68). The prevalence rates of RRT were 5.14% (95%CI 4.54%-5.74%) in all burn patients and 35.8% (95%CI 29.54%-42.07%) in AKI patients. The prevalence of RRT among burn patients in the ICU was 10.92% (95%CI 8.71%-13.14%)(4–7, 19, 25, 30, 32, 34, 39, 42, 46, 47, 50, 54, 56, 57, 59, 60, 62, 65, 67). A total of 25 studies with RIFLE, AKIN and KDIGO as AKI diagnostic criteria were analysed (4, 6, 7, 19, 24–26, 31, 35, 36, 38, 39, 46, 47, 49, 50, 54, 58–62, 64–66). The prevalence of RRT in these burn patients was 29.58% (95%CI 23.65%-35.52%).

Moreover, we analysed the results of 41 studies that reported RRT mortality in burn patients (Table 3). The mortality of all burn patients with RRT was 65.52% (95%CI 58.41%-72.64%) (4, 5, 9–11, 17–23, 25, 27, 28, 30, 31, 33–46, 48, 51, 52, 54, 55, 58, 59, 64, 65, 67). The mortality of patients with RRT in ICU was 62.7% (95%CI 53.7%-71.7%) (4, 5, 9, 10, 18, 19, 25, 30, 34, 39, 40, 42–46, 54, 59, 65, 67). Of the 41 studies, excluding those only conducted in RRT patients, 20 gave not only the mortality rate of all burn patients but also the mortality rate of burn patients with RRT (4, 5, 19, 23, 25, 30, 33–36, 38, 39, 42, 46, 48, 54, 58, 59, 65, 67). Based on the results of the above 20 articles, it was found that the mortality rate of RRT patients was 30.33% (95%CI 22.06%-38.59%) of the total. The results of 20 studies with RIFLE, AKIN, and KDIGO as AKI diagnostic criteria showed that the mortality of RRT in burn patients was 67.16% (95%CI 57.40%-76.93%) (4, 10, 11, 18, 19, 25, 31, 35, 36, 38–40, 43, 44, 46, 54, 58, 59, 64, 65). Three studies reported deaths in all burn patients undergoing RRT (5, 33, 38, 42). According to different mortality categories, the mortalities of 14 days, 28 days and 60 days ranged from 30–50%, while those of ICU and hospital were 56.98% and 68.89%, and overall mortality further increased to 75.24% (Additional file 1: Table S2).

According to the three diagnostic criteria of RIFLE, AKIN, and KDIGO, the prevalence of RRT was KDIGO<RIFLE<AKIN, and that of mortality was KDIGO<AKIN<RIFLE. The prevalence of RRT was 14.79% (95%CI 9.02%-20.56%) and that of mortality was 55.29% (95%CI 39.46%-71.12%) in the six literatures with KDIGO classification as the diagnostic standard, which was lower than other AKI diagnostic standards.

There was no significant correlation ($r=-0.224$, $P = 0.159$) between the year of publication and the mortality of burn patients with RRT (Additional file 1: Fig. S2). According to the year of publication, the patients were divided into four subgroups (Additional file 1: Fig. S3) from 2010–2020, 2000–2009, 1990–1999, 1989 and before. The mortality of the 2010–2020 group was $60.42\pm25.35\%$, that of the 2000–2009 group was $61.55\pm23.29\%$, that of the 1990–1999 group was $87.33\pm8.44\%$, and that of the 1989 and before group was $63.52\pm25.05\%$. There was no significant difference between groups ($P = 0.139$). After 2010, three studies still reported that the mortality of RRT patients was more than 90% (38, 58, 65).

Table 2
The prevalence of RRT in burn patients with different diagnostic criteria.

Diagnosis	N. of Trials	Patients	I^2 (%)	P	Prevalence (%)	95%CI
All burn patients	46	34076	97	<0.01	5.14	4.54–5.74
RRT of AKI patients	39	3929	98	<0.01	35.8	29.54–42.07
ICU	22	5628	90%	<0.01	10.92	8.71–13.14
RIFLE classification	11	596	78	<0.01	28.85	21-36.69
AKIN classification	9	1180	98	<0.01	43.96	28-59.91
KDIGO classification	6	1218	83	<0.01	14.79	9.02–20.56
Summary of RIFLE, AKIN, KDIGO	25	3044	96	<0.01	29.58	23.65–35.52

Table 3
The mortality of RRT in burn patients with different diagnostic criteria.

Diagnosis	N. of Trials	Patients	I^2 (%)	P	RRT mortality (%)	95%CI
Summary of all literatures	41	1342	90	<0.01	65.52	58.41–72.64
ICU	20	797	85%	<0.01	62.7%	53.7–71.7
RIFLE classification	9	185	77	<0.01	70.08	56.4–83.75
AKIN classification	7	370	90	<0.01	66.73	52.01–81.45
KDIGO classification	5	283	81	<0.01	55.29	39.46–71.12
Summary of RIFLE, AKIN, KDIGO	20	811	90	<0.01	67.16	57.40–76.93

The effect of RRT on the mortality of burn patients

Compared with the absolute values of serum creatinine or urine volume as the grading standard defined by AKI (such as SOFA or other definition), RIFLE, AKIN, and KDIGO grading can more accurately reflect the actual incidence of AKI. Therefore, we used cohort studies with RIFLE, AKIN, and KDIGO as diagnostic criteria for subgroup analysis. The standard of ARF was defined as RIFLE-Failure level and above, AKIN-3 or KDIGO Level 3. The results showed that the risks of death in burn patients with AKI and ARF were 5.19 times (95%CI 3.87–6.97) and 4.77 times (95%CI 3.01–7.57) higher than those in non-AKI patients, while the risk of death in RRT patients was increased to 5.78 (95%CI 3.43–9.75), but there was no significant difference between groups ($P = 0.87$, Fig. 2). A meta-analysis of the cohort study did not show that RRT could reduce the risk of death in burn patients with AKI.

Three RCT studies compared the effects of standard care (non-RRT) and CRRT on patients' prognosis (10, 51, 52). Two RCT studies did not find that CRRT had a positive effect on the mortality of burn patients (51, 52). You 2018 (10) found that early HVHF treatment may reduce 90-day mortality of patients with severe burns ($\geq 80\%$ TBSA) ($P = 0.049$). A meta-analysis of these three RCT studies also did not show that CRRT could reduce the risk of death in burn patients with AKI compared with the standard care (non-RRT) ($RR = 0.64$, 95%CI 0.40–1.03, $P = 0.06$; Fig. 3).

Regional Citrate Anticoagulation

Four articles reported the studies of regional citrate anticoagulation (RCA) for CRRT in burn patients, including 3 retrospective cohort studies (21, 55, 69) and 1 RCT study (70). The cohort studies found that the filter survival time (CRRT) of the citrate group was significantly longer than that of the heparin group (average 28.5–28.7 h vs 19–19.4 h) (55, 69). When the dialysis mode was SLED, the filter survival time of the citrate group was still better than that of the heparin group (average 8–13 h vs 6.5–7 h) (55, 70). Moreover, the citric acid group also had some advantages in the recovery time of urine volume and the length of stay in ICU (69). After 24 h of treatment, the coagulation index (PT and APTT) and the inflammation index (PCT and CRP) of the citric acid group were significantly lower than those of the heparin group (69). However, there was no significant difference in the risk of death between the two groups ($P = 0.51$, Additional file 1: Fig. S4). Only a small-sample RCT study was conducted to compare the effects of local heparin anticoagulation and local citrate anticoagulation for SLED-HF in severe burn patients (TBSA greater than 50%) with sepsis (70). The results also showed that the citric acid group had significant advantages in single treatment time, treatment time reaching rate (12 h), coagulation index (PT and APTT), and inflammation index (PCT and CRP) (70). All these literatures suggest that the incidence of bleeding events in the heparin group was significantly higher than that in the citric acid group (55, 69, 70). The incidence of hypocalcaemia in the citric acid group was 7.27% (4/55). The incidence rates of metabolic acidosis and metabolic alkalosis in the citric acid group were slightly higher than those in the heparin group, but the differences were not statistically significant (69).

RRT-related adverse reactions

Nine articles reported the incidence of RRT-related adverse reactions. The total incidence was 28.77% (63/229) (9, 10, 21, 23, 27, 28, 30, 37, 51), including thrombocytopenia 0.44% (1/229), bleeding 10.92% (25/229), thromboembolism 1.75% (4/229), secondary infection 9.61% (22/229), electrolyte disorder 2.62% (6/229), and imbalance syndrome 0.44% (1/229). Among them, only Chung 2017 reported 6 patients with electrolyte disorder. Other literatures may not mention the occurrence of electrolyte disorder due to certain concerns, which may underestimate the prevalence of electrolyte disorder. A total of 16 patients with peritoneal dialysis were

reported in 9 articles; most of these patients were from Liu 1986 (28). Among the 16 patients, 1 had "unbalanced syndrome" and improved after stopping dialysis; 4 had abdominal infection, 3 survived, and 1 changed to haemodialysis and ultimately died. Considering the immature technology at that time, the incidence of PD adverse reactions may be overestimated.

Renal outcome

A recent study found an odds of dialysis of 2.40 in burn patients who developed AKI compared with the general Finnish population (71). Eleven studies followed up the long-term renal outcomes of burn patients who survived RRT (9, 18, 19, 21, 27, 30, 34, 36, 37, 50, 54). A total of 184 patients survived after renal replacement therapy; 64.13% of them (118/184) were dialysis-independent after discharge, 25% (46/184) needed temporary required dialysis, and 10.87% (20/184) needed long-term dialysis (more than 6 months after discharge). Thalji 2017 found that one year after burn, the proportion of chronic dialysis in non-AKI patients was 0.33% (56/16985), significantly lower than that in patients with AKI, which was 4.58% (26/568) (72). The proportion of severe CKD (defined as stage 3–5 CKD) in non-AKI patients (0.71%) was also lower than those in AKI patients (5.81%) (72). Gille reported that 3 of the 16 surviving burn patients undergoing CRRT had CKD progression ($\text{GFR} < 45 \text{ ml/min.1.73 m}^2$, CKD 3b) (18.75%) (21). Two patients had slightly impaired GFR ($< 90 \text{ ml/min.1.73 m}^2$, CKD 2) before the burn trauma. One patient had normal GFR (21).

Discussion:

Acute renal injury is one of the common complications in burn patients. The incidence of AKI varied from 16–26.6% according to the definition of AKI in different populations (3). The incidence of AKI in burn ICUs was 38% (30–46%) (8). Renal replacement therapy was often needed by some severe burn patients with AKI. According to the subgroup analysis in the previous meta-analysis of burn patients with AKI, the proportion of all burn patients requiring RRT was approximately 3% (3). The proportion of burn patients admitted to the ICU was 12% (8–16%) (8), and the proportion of burn patients with AKI who needed RRT was as high as 30% (3). Moreover, the mortality of RRT in burn patients was as high as 80% (3). Such high mortality rates were the reasons we wanted to conduct a meta-analysis of RRT in burn patients. A total of 38,787 burn patients were enrolled in this study from 58 literatures from 1979 to 2019. The results showed that the prevalence rates of RRT were 5.14% (95%CI 4.54%-5.74%) in all burn patients and 35.8% (95%CI 29.54%-42.07%) in AKI patients. The mortality of all burn patients with RRT was 65.52% (95%CI 58.41%-72.64%). Although burn patients with RRT only accounted for approximately 5% of all burn patients, patients treated with RRT accounted for 1/3 of the total dead patients (95%CI 22.06%-38.59%).

RIFLE (73), AKIN (74) and KDIGO (75) are three commonly used AKI grading standards. The KDIGO diagnostic standard proposed in 2012 had been reported to improve the early diagnosis of kidney injury (59, 76) and to reduce the missed diagnosis rate (77), which was conducive to the early diagnosis and treatment of AKI. Our results showed that, compared with RIFLE and AKIN, the prevalence and mortality of RRT in KDIGO were relatively low. We speculate that early diagnosis and early treatment may help some burn patients with AKI avoid further deterioration of renal function, reduce the need for dialysis, and improve the prognosis of patients. Ren et al defined AKI according to KDIGO guidelines by 48 h after admission. That prospective study reported 11.2% (11/95) AKI and only 35.4% mortality in the AKI group (64).

For burn patients with AKI, especially those with continuous deterioration of renal function, renal replacement therapy was one of the standard treatment methods. In the principle of treatment, RRT can maintain the stability of the internal environment by controlling capacity overload, reducing organ damage, clearing inflammatory mediators, and correcting electrolyte and acid-base balance disorders to benefit AKI patients. At present, only a few retrospective match historical cohort studies had found that CRRT had better prognosis than conventional non-RRT therapy (44, 78). However, in a meta-analysis of the cohort studies included, we did not find that RRT could reduce mortality. Compared with AKI or ARF, the risk of death in RRT patients was not significantly reduced. A meta-analysis of three RCT studies also did not show that CRRT could reduce the risk of death in burn patients with AKI compared with the standard care. You 2018 found that administration of HVHF within 3 days after admission may reduce the 90-day mortality of patients with large-area severe burns ($\geq 80\%$ TBSA) ($P = 0.049$). This RCT study excluded burn patients with sepsis or multiple organ failure on admission (10). Early (0–3 days after injury) burn AKI is typically due to hypovolemia, poor renal perfusion, direct cardiac suppression from TNF- α , and precipitation of denatured proteins (79). The therapeutic effect of renal replacement therapy in the above aetiology is better. However, late AKI is often due to sepsis, multi-organ failure, and nephrotoxic drugs (79). Thus far, it is often believed that AKI related to these aetiologies cannot reduce mortality and improve the prognosis of patients. The beginning time of CRRT was different in Liu 2016 and only lasted until 72 hours after the injury. The results showed that CRRT could not improve the

prognosis of burn patients (52). Peng et al. performed an RCT study in patients with TBSA greater than 50% having sepsis. The treatment time of CRRT varied from 3 days to 8 days after burn, and the time of treatment was relatively late. There were only 10 patients each in the CRRT and control groups. The mortality rates were 10% in the CRRT group and 20% in control group, but no statistical significance was found (51). We speculate that early CRRT (within 3 days) may improve the prognosis of severely burned patients with early AKI. In the future, RCT studies should consider grouping burn patients with AKI according to the aetiology or time and then evaluate the therapeutic effect of RRT and its impact on the prognosis of patients. All the above three studies were from the same hospital, and the results may be biased.

Although CRRT has the advantages of stable haemodynamics and efficient clearance of inflammatory factors and metabolites, its shortcomings are that it needs systemic or regional anticoagulation. Compared with systematic anticoagulation, the risk of bleeding of regional citrate anticoagulation is smaller. The KDIGO guidelines (75) suggest the use of RCA in patients without contraindications rather than systemic heparin anticoagulation (SHA). The results of three recent RCT studies in critically ill patients showed that the RCA group had superior filter life spans and fewer adverse events than those of the SHA group (80–82). However, there was no difference in survival rate between the two groups (80, 81). Cohort studies in burn patients also found that RCA had some advantages over SHA in terms of filter survival time and coagulation index. Compared with local heparin anticoagulation, RCA also has advantages in single treatment time, target rate of treatment time, coagulation index and inflammation index (70). However, anticoagulation with citric acid also has the risk of hypocalcaemia, accumulation of citric acid and aggravation of metabolic acidosis (83). Our results showed that the incidence of hypocalcaemia in the citrate group was 7.27%. Compared with the heparin group, the incidence of metabolic acidosis in the citric acid group was slightly higher, but the difference was not statistically significant. Regarding the side effects of RRT, the results of this study suggest that bleeding is the most common incidence of RRT in burn patients, with an incidence of approximately 11%. The advantage of citric acid in reducing bleeding may be more suitable for burn patients with AKI. Moreover, there is new evidence that RCA can safely be used in patients with liver failure (84, 85) and after liver transplant (86), suggesting that local citrate anticoagulation may also be used in severe burn patients with MOF combined with renal and liver failure. Other common adverse effects of RRT include secondary infection, electrolyte disorder, thromboembolism, disequilibrium syndrome and thrombocytopenia. Compared with haemodialysis, peritoneal dialysis has some advantages in bleeding, but its risk of secondary infection is also higher. Moreover, the peritoneal dialysis catheter placement area is a common donor site or burned area (79). This limits the use of peritoneal dialysis in burn patients.

AKI in burn patients not only increases mortality (87), but also increases the risk of CKD progression and ESRD (71, 72). When severe burn patients have dialysis-requiring AKI, approximately 35% of the patients need to maintain haemodialysis temporarily, even if they survive and leave the hospital. Among them, 10% of the surviving patients need haemodialysis for more than half a year. Therefore, for burn AKI or dialysis-requiring AKI survivors, it is recommended to monitor the renal function regularly within one year after discharge and to avoid the use of nephrotoxic drugs, excessive diuresis, and diarrhoea (79), to reduce the progress of CKD and to avoid the recurrence of AKI.

This systematic review has several limitations. First, there was significant heterogeneity in most results of RRT prevalence and mortality in this study. The clinical heterogeneity of this study may be due to the differences in the study population, RRT modalities and the end-point indicators observed in the study. The inclusion and exclusion criteria were different among different studies. There were controversies on modalities, timing, and dosage of RRT, and the standards reported in different literatures are not the same. Outcome variables, such as mortality, also varied from study to study. Although we conducted a series of subgroup analyses on AKI diagnostic criteria, the intensive care unit and different mortality criteria, the results still showed heterogeneity. Because we were unable to obtain the original data for each patient, we cannot completely control the above confounding factors. Therefore, we used the random effect model to analyse the results. Second, we only included documents in English, Japanese and Chinese, and there may be omissions in documents reported in other languages, such as Russian. There was no literature from Russia in the studies we included. However, 58 articles and nearly 40,000 burn patients from five continents were included in this meta-analysis, most of which were in North America, Asia, and Europe. The inclusion of a large number of literatures and patients can ensure that the results of this study were well representative, especially in North America, Asia, and Europe. Finally, this study did not analyse the starting time of RRT for burn patients with AKI. At present, the timing of RRT for critically ill patients is still controversial. At the beginning of this study, we plan to analyse the timing of RRT in burn patients. However, even if 58 articles were included, there is still a lack of head-to-head study on the starting time of RRT for burn patients with AKI. There was only one cohort study that was divided into groups according to the AKI level of patients at the beginning of CRRT. The early CRRT group was defined according to the patients who started CRRT at the risk stage of the RIFLE criteria. The results showed there were no significant differences in mortality by the

severity of AKI at the time of CRRT initiation (11). We suggest that more head-to-head cohort studies or RCT studies can be designed in the future regarding the timing of RRT in burn patients.

Our meta-analysis had a number of strengths. In this study, 58 articles from 1979 to 2019 were included, involving nearly 40,000 burn patients. It has obvious representative advantages for the prevalence and mortality of RRT for burn patients with high statistical variability. Second, we analysed comprehensively and systematically whether RRT can improve the prognosis (mainly mortality) of burn patients and performed a subgroup analysis from different anticoagulation methods, RRT-related adverse reactions and renal outcome. There is certain value in designing RRT schemes for severe burn patients with AKI in the future.

Conclusions:

The prevalence of RRT is not low; approximately, one-third of burn patients with AKI need RRT. The mortality of burn patients with RRT is very high and accounts for 1/3 of the total deaths. There is no evidence that RRT can improve the prognosis of burn patients with AKI. Regional citrate anticoagulation has some advantages in reducing bleeding and extending filter life spans, which may be more suitable for severe burn patients with CRRT.

Declarations:

Authors' contributions

C.GY and L.JJ contributed to the conception and design of the study. D.ZY and C.FK selected the studies and extracted the data. D.ZY evaluated the study quality. D.ZY and C.FK performed the statistical analyses and data presentation. The manuscript was drafted by D.ZY, with assistance by C.FK and L.JJ, and the manuscript was critically revised by C.XM and C.GY. All authors have read and approved the final manuscript.

Funding

This study was supported by National Key R&D Program of China (2018YFA0108803), Logistics research project (BLB19J009), Science and Technology Project of Beijing, China (D181100000118004, Z161100000516225, D1771100002817002), Natural Science Foundation of China (NSFC) (81600548, 81670694). They have no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Acknowledgements

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article

Ethics approval and consent to participate

Not applicable

Conflict of interest

All authors have no conflict of interest of any type.

Consent for publication

Not applicable.

References:

1. Knowlin LT, Purcell L, Cairns BA, Charles AG. Burn injury mortality in patients with preexisting and new onset renal disease. *Am J Surg*. 2018;215(6):1011-5.

2. Wu G, Xiao Y, Wang C, Hong X, Sun Y, Ma B, et al. Risk Factors for Acute Kidney Injury in Patients With Burn Injury: A Meta-Analysis and Systematic Review. *J Burn Care Res.* 2017;38(5):271-82.
3. Brusselaers N, Monstrey S, Colpaert K, Decruyenaere J, Blot SI, Hoste EA. Outcome of acute kidney injury in severe burns: a systematic review and meta-analysis. *Intensive Care Med.* 2010;36(6):915-25.
4. Coca SG, Bauling P, Schiffner T, Howard CS, Teitelbaum I, Parikh CR. Contribution of acute kidney injury toward morbidity and mortality in burns: a contemporary analysis. *Am J Kidney Dis.* 2007;49(4):517-23.
5. Kim GH, Oh KH, Yoon JW, Koo JW, Kim HJ, Chae DW, et al. Impact of burn size and initial serum albumin level on acute renal failure occurring in major burn. *Am J Nephrol.* 2003;23(1):55-60.
6. Martins Munoz J, Nin N, Penuelas O, Muriel A, Abril J, Lorente Balanza JA. Acute Kidney Injury in Critically Ill Burned Patients Is Independently Associated with Increased Mortality. *Nephrology Dialysis Transplantation.* 2017;32:528-.
7. Yim H, Kym D, Seo DK, Yoon J, Yang HT, Lee J, et al. Serum cystatin C and microalbuminuria in burn patients with acute kidney injury. *Eur J Clin Invest.* 2015;45(6):594-600.
8. Folkestad T, Brurberg KG, Nordhuus KM, Tveiten CK, Guttormsen AB, Os I, et al. Acute kidney injury in burn patients admitted to the intensive care unit: a systematic review and meta-analysis. *Crit Care.* 2020;24(1):2.
9. Chung KK, Coates EC, Smith DJ, Jr., Karlinski RA, Hickerson WL, Arnold-Ross AL, et al. High-volume hemofiltration in adult burn patients with septic shock and acute kidney injury: a multicenter randomized controlled trial. *Crit Care.* 2017;21(1):289.
10. You B, Zhang YL, Luo GX, Dang YM, Jiang B, Huang GT, et al. Early application of continuous high-volume haemofiltration can reduce sepsis and improve the prognosis of patients with severe burns. *Crit Care.* 2018;22(1):173.
11. Yoon J, Kim Y, Yim H, Cho YS, Kym D, Hur J, et al. Analysis of prognostic factors for acute kidney injury with continuous renal replacement therapy in severely burned patients. *Burns.* 2017;43(7):1418-26.
12. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ.* 2009;339:b2535.
13. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA.* 2000;283(15):2008-12.
14. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ.* 2011;343:d5928.
15. Wells GS, B.; O'Connell, D.; Peterson, P.; Welch, V.; Losos, M.; Tugwell, P. Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses 2014 [Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
16. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ.* 2003;327(7414):557-60.
17. Chrysopoulou MT, Jeschke MG, Dziewulski P, Barrow RE, Herndon DN. Acute renal dysfunction in severely burned adults. *J Trauma.* 1999;46(1):141-4.
18. Chung KK, Coates EC, Hickerson WL, Arnold-Ross AL, Caruso DM, Albrecht M, et al. Renal Replacement Therapy in Severe Burns: A Multicenter Observational Study. *J Burn Care Res.* 2018;39(6):1017-21.
19. Damkat-Thomas L, Black CE, Bedi A. Acute kidney injury and the burned patient: Progression and outcomes. *Burns.* 2011;37(1):175-6; author reply 6-7.
20. Davies DM, Pusey CD, Rainford DJ, Brown JM, Bennett JP. Acute renal failure in burns. *Scand J Plast Reconstr Surg.* 1979;13(1):189-92.
21. Gille J, Sablotzki A, Malcharek M, Raff T, Mogk M, Parentin T. Regional citrate anticoagulation for continuous renal replacement therapy in severe burns-a retrospective analysis of a protocol-guided approach. *Burns.* 2014;40(8):1593-601.
22. Haberal M, Ozdemir A, Bayraktar U, Oner Z, Bilgin N, Collini FJ. Gastrointestinal and renal complications in burned patients. *European Journal of Plastic Surgery.* 1993;16(1):17-21.
23. Holm C, Horbrand F, von Donnersmarck GH, Muhlbauer W. Acute renal failure in severely burned patients. *Burns.* 1999;25(2):171-8.
24. Hu JY, Meng XC, Han J, Xiang F, Fang YD, Wu J, et al. Relation between proteinuria and acute kidney injury in patients with severe burns. *Crit Care.* 2012;16(5):R172.

25. Kuo G, Yang SY, Chuang SS, Fan PC, Chang CH, Hsiao YC, et al. Using acute kidney injury severity and scoring systems to predict outcome in patients with burn injury. *J Formos Med Assoc.* 2016;115(12):1046-52.
26. Kuo G, Lee CC, Yang SY, Hsiao YC, Chuang SS, Chang SW, et al. Hyperphosphatemia is associated with high mortality in severe burns. *PLoS One.* 2018;13(1):e0190978.
27. Leblanc M, Thibeault Y, Querin S. Continuous haemofiltration and haemodiafiltration for acute renal failure in severely burned patients. *Burns.* 1997;23(2):160-5.
28. Liu YL. [Experiences in the treatment of 53 cases of major burns with acute renal failure]. *Zhonghua Zheng Xing Shao Shang Wai Ke Za Zhi.* 1986;2(2):103-5, 8.
29. Mason SA, Nathens AB, Finnerty CC, Gamelli RL, Gibran NS, Arnoldo BD, et al. Hold the Pendulum: Rates of Acute Kidney Injury are Increased in Patients Who Receive Resuscitation Volumes Less than Predicted by the Parkland Equation. *Ann Surg.* 2016;264(6):1142-7.
30. Mustonen KM, Vuola J. Acute renal failure in intensive care burn patients (ARF in burn patients). *J Burn Care Res.* 2008;29(1):227-37.
31. Pronina I, Malic C, Radulovic N, Bian J, Burnett MA, Jeschke MG. Acute kidney injury in burn victims: Progression to dialysis. *Journal of Burn Care and Research.* 2015;36:S66.
32. Queiroz LF, Anami EH, Zampar EF, Tanita MT, Cardoso LT, Grion CM. Epidemiology and outcome analysis of burn patients admitted to an Intensive Care Unit in a University Hospital. *Burns.* 2016;42(3):655-62.
33. Saffle JR, Sullivan JJ, Tuohig GM, Larson CM. Multiple organ failure in patients with thermal injury. *Crit Care Med.* 1993;21(11):1673-83.
34. Soltani A, Karsidag S, Garner W. A ten-year experience with hemodialysis in burn patients at Los Angeles County + USC Medical Center. *J Burn Care Res.* 2009;30(5):832-5.
35. Steinvall I, Bak Z, Sjoberg F. Acute kidney injury is common, parallels organ dysfunction or failure, and carries appreciable mortality in patients with major burns: a prospective exploratory cohort study. *Crit Care.* 2008;12(5):R124.
36. Stewart IJ, Cotant CL, Tilley MA, Huzar TF, Aden JK, Snow BD, et al. Association of rhabdomyolysis with renal outcomes and mortality in burn patients. *J Burn Care Res.* 2013;34(3):318-25.
37. Tremblay R, Ethier J, Querin S, Beroniade V, Falardeau P, Leblanc M. Veno-venous continuous renal replacement therapy for burned patients with acute renal failure. *Burns.* 2000;26(7):638-43.
38. Witkowski W, Kawecki M, Surowiecka-Pastewka A, Klimm W, Szamotulska K, Niemczyk S. Early and Late Acute Kidney Injury in Severely Burned Patients. *Med Sci Monit.* 2016;22:3755-63.
39. Yang HT, Yim H, Cho YS, Kym D, Hur J, Kim JH, et al. Assessment of biochemical markers in the early post-burn period for predicting acute kidney injury and mortality in patients with major burn injury: comparison of serum creatinine, serum cystatin-C, plasma and urine neutrophil gelatinase-associated lipocalin. *Crit Care.* 2014;18(4):R151.
40. Yoon J, Kim Y, Kym D, Hur J, Yim H, Cho YS, et al. Subgroup analysis of continuous renal replacement therapy in severely burned patients. *PLoS One.* 2017;12(11):e0189057.
41. Sabry A, Wafa I, El-Din AB, El-Hadidy AM, Hassan M. Early markers of renal injury in predicting outcome in thermal burn patients. *Saudi J Kidney Dis Transpl.* 2009;20(4):632-8.
42. Akers KS, Cota JM, Chung KK, Renz EM, Mende K, Murray CK. Serum vancomycin levels resulting from continuous or intermittent infusion in critically ill burn patients with or without continuous renal replacement therapy. *J Burn Care Res.* 2012;33(6):e254-62.
43. Boucher BA, Hudson JQ, Hill DM, Swanson JM, Wood GC, Laizure SC, et al. Pharmacokinetics of Imipenem/Cilastatin Burn Intensive Care Unit Patients Undergoing High-Dose Continuous Venovenous Hemofiltration. *Pharmacotherapy.* 2016;36(12):1229-37.
44. Chung KK, Juncos LA, Wolf SE, Mann EE, Renz EM, White CE, et al. Continuous renal replacement therapy improves survival in severely burned military casualties with acute kidney injury. *J Trauma.* 2008;64(2 Suppl):S179-85; discussion S85-7.
45. Hladik M, Tymonova J, Zaoral T, Kadlcik M, Adamkova M. Treatment by continuous renal replacement therapy in patients with burn injuries. *Acta Chir Plast.* 2001;43(1):21-5.
46. Hong DY, Lee JH, Park SO, Baek KJ, Lee KR. Plasma neutrophil gelatinase-associated lipocalin as early biomarker for acute kidney injury in burn patients. *J Burn Care Res.* 2013;34(6):e326-32.

47. Kym D, Cho YS, Yoon J, Yim H, Yang HT. Evaluation of diagnostic biomarkers for acute kidney injury in major burn patients. *Ann Surg Treat Res.* 2015;88(5):281-8.
48. Planas M, Wachtel T, Frank H, Henderson LW. Characterization of acute renal failure in the burned patient. *Arch Intern Med.* 1982;142(12):2087-91.
49. Schneider DF, Dobrowolsky A, Shakir IA, Sinacore JM, Mosier MJ, Gamelli RL. Predicting acute kidney injury among burn patients in the 21st century: a classification and regression tree analysis. *J Burn Care Res.* 2012;33(2):242-51.
50. Sen S, Godwin ZR, Palmieri T, Greenhalgh D, Steele AN, Tran NK. Whole blood neutrophil gelatinase-associated lipocalin predicts acute kidney injury in burn patients. *J Surg Res.* 2015;196(2):382-7.
51. Peng Y, Yuan Z, Li H. Removal of inflammatory cytokines and endotoxin by veno-venous continuous renal replacement therapy for burned patients with sepsis. *Burns.* 2005;31(5):623-8.
52. Liu F, Huang ZG, Peng YZ, Wu J, He WF, Yuan ZQ, et al. [Clinical randomized controlled trial on the feasibility and validity of continuous blood purification during the early stage of severe burn]. *Zhonghua Shao Shang Za Zhi.* 2016;32(3):133-9.
53. Lopes JA, Jorge S, Neves FC, Costa AG, Prata MM, Caneira M, et al. Acute renal failure in severely burned patients. *Resuscitation.* 2007;73(2):318.
54. Demsey D, Mordhorst A, Griesdale DEG, Papp A. Improved outcomes of renal injury following burn trauma. *Burns.* 2019;45(5):1024-30.
55. Mariano F, Tedeschi L, Morselli M, Stella M, Triolo G. Normal citratemia and metabolic tolerance of citrate anticoagulation for hemodiafiltration in severe septic shock burn patients. *Intensive Care Med.* 2010;36(10):1735-43.
56. Bechir M, Puhan MA, Fasshauer M, Schuepbach RA, Stocker R, Neff TA. Early fluid resuscitation with hydroxyethyl starch 130/0.4 (6%) in severe burn injury: a randomized, controlled, double-blind clinical trial. *Crit Care.* 2013;17(6):R299.
57. Bechir M, Puhan MA, Neff SB, Guggenheim M, Wedler V, Stover JF, et al. Early fluid resuscitation with hyperoncotic hydroxyethyl starch 200/0.5 (10%) in severe burn injury. *Crit Care.* 2010;14(3):R123.
58. Chun W, Kim Y, Yoon J, Lee S, Yim H, Cho YS, et al. Assessment of Plasma Neutrophil Gelatinase-Associated Lipocalin for Early Detection of Acute Kidney Injury and Prediction of Mortality in Severely Burned Patients. *J Burn Care Res.* 2018;39(3):387-93.
59. Clark AT, Li X, Kulangara R, Adams-Huet B, Huen SC, Madni TD, et al. Acute Kidney Injury After Burn: A Cohort Study From the Parkland Burn Intensive Care Unit. *J Burn Care Res.* 2019;40(1):72-8.
60. Depret F, Boutin L, Jarkovsky J, Chaussard M, Soussi S, Bataille A, et al. Prediction of major adverse kidney events in critically ill burn patients. *Burns.* 2018;44(8):1887-94.
61. Hundeshagen G, Herndon DN, Capek KD, Branski LK, Voigt CD, Killion EA, et al. Co-administration of vancomycin and piperacillin-tazobactam is associated with increased renal dysfunction in adult and pediatric burn patients. *Crit Care.* 2017;21(1):318.
62. Kumar AB, Andrews W, Shi Y, Shotwell MS, Dennis S, Wanderer J, et al. Fluid resuscitation mediates the association between inhalational burn injury and acute kidney injury in the major burn population. *J Crit Care.* 2017;38:62-7.
63. Rakkolainen I, Vuola J. Plasma NGAL predicts early acute kidney injury no earlier than s-creatinine or cystatin C in severely burned patients. *Burns.* 2016;42(2):322-8.
64. Ren H, Zhou X, Dai D, Liu X, Wang L, Zhou Y, et al. Assessment of urinary kidney injury molecule-1 and interleukin-18 in the early post-burn period to predict acute kidney injury for various degrees of burn injury. *BMC Nephrol.* 2015;16:142.
65. Sanchez-Sanchez M, Garcia-de-Lorenzo A, Cachafeiro L, Herrero E, Asensio MJ, Agrifoglio A, et al. Acute kidney injury in critically burned patients resuscitated with a protocol that includes low doses of Hydroxyethyl Starch. *Ann Burns Fire Disasters.* 2016;29(3):183-8.
66. Tang CQ, Li JQ, Xu DY, Liu XB, Hou WJ, Lyu KY, et al. [Comparison of machine learning method and logistic regression model in prediction of acute kidney injury in severely burned patients]. *Zhonghua Shao Shang Za Zhi.* 2018;34(6):343-8.
67. Rakkolainen I, Lindbohm JV, Vuola J. Factors associated with acute kidney injury in the Helsinki Burn Centre in 2006-2015. *Scand J Trauma Resusc Emerg Med.* 2018;26(1):105.
68. Davies MP, Evans J, McGonigle RJ. The dialysis debate: acute renal failure in burns patients. *Burns.* 1994;20(1):71-3.
69. Li XL, Xiao HT, Li YC, Li YG, Zhang J, Feng K, et al. [Effects of citric acid on patients with severe burn complicated with acute renal injury treated by continuous renal replacement therapy]. *Zhonghua Shao Shang Za Zhi.* 2019;35(8):568-73.

70. Ding LT, Yang ML, Zhu YG, Yan J, Xie LW, Lyu GZ. [Effects of application of citrate anticoagulation in bedside continuous blood purification of severe burn patients with sepsis]. *Zhonghua Shao Shang Za Zhi*. 2018;34(2):73-7.
71. Helanterä I, Koljonen V, Finne P, Tukiainen E, Gissler M. The risk for end-stage renal disease is increased after burn. *Burns*. 2016;42(2):316-21.
72. Thalji SZ, Kothari AN, Kuo PC, Mosier MJ. Acute Kidney Injury in Burn Patients: Clinically Significant Over the Initial Hospitalization and 1 Year After Injury: An Original Retrospective Cohort Study. *Ann Surg*. 2017;266(2):376-82.
73. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P, Acute Dialysis Quality Initiative w. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care*. 2004;8(4):R204-12.
74. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care*. 2007;11(2):R31.
75. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract*. 2012;120(4):c179-84.
76. Rodrigues FB, Bruetto RG, Torres US, Otaviano AP, Zanetta DM, Burdmann EA. Incidence and mortality of acute kidney injury after myocardial infarction: a comparison between KDIGO and RIFLE criteria. *PLoS One*. 2013;8(7):e69998.
77. Ulger F, Pehlivanlar Kucuk M, Kucuk AO, Ilkaya NK, Murat N, Bilgic B, et al. Evaluation of acute kidney injury (AKI) with RIFLE, AKIN, CK, and KDIGO in critically ill trauma patients. *Eur J Trauma Emerg Surg*. 2018;44(4):597-605.
78. Chung KK, Lundy JB, Matson JR, Renz EM, White CE, King BT, et al. Continuous venovenous hemofiltration in severely burned patients with acute kidney injury: a cohort study. *Crit Care*. 2009;13(3):R62.
79. Clark A, Neyra JA, Madni T, Imran J, Phelan H, Arnoldo B, et al. Acute kidney injury after burn. *Burns*. 2017;43(5):898-908.
80. Hetzel GR, Schmitz M, Wissing H, Ries W, Schott G, Heering PJ, et al. Regional citrate versus systemic heparin for anticoagulation in critically ill patients on continuous venovenous haemofiltration: a prospective randomized multicentre trial. *Nephrol Dial Transplant*. 2011;26(1):232-9.
81. Schilder L, Nurmohamed SA, Bosch FH, Purmer IM, den Boer SS, Kleppe CG, et al. Citrate anticoagulation versus systemic heparinisation in continuous venovenous hemofiltration in critically ill patients with acute kidney injury: a multi-center randomized clinical trial. *Crit Care*. 2014;18(4):472.
82. Gattas DJ, Rajbhandari D, Bradford C, Buhr H, Lo S, Bellomo R. A Randomized Controlled Trial of Regional Citrate Versus Regional Heparin Anticoagulation for Continuous Renal Replacement Therapy in Critically Ill Adults. *Crit Care Med*. 2015;43(8):1622-9.
83. Khadzhyrov D, Dahlinger A, Schelter C, Peters H, Kindgen-Milles D, Budde K, et al. Hyperlactatemia, Lactate Kinetics and Prediction of Citrate Accumulation in Critically Ill Patients Undergoing Continuous Renal Replacement Therapy With Regional Citrate Anticoagulation. *Crit Care Med*. 2017;45(9):e941-e6.
84. Slowinski T, Morgera S, Joannidis M, Henneberg T, Stocker R, Helset E, et al. Safety and efficacy of regional citrate anticoagulation in continuous venovenous hemodialysis in the presence of liver failure: the Liver Citrate Anticoagulation Threshold (L-CAT) observational study. *Crit Care*. 2015;19:349.
85. Zhang W, Bai M, Yu Y, Li L, Zhao L, Sun S, et al. Safety and efficacy of regional citrate anticoagulation for continuous renal replacement therapy in liver failure patients: a systematic review and meta-analysis. *Crit Care*. 2019;23(1):22.
86. Sponholz C, Settmacher U, Bauer M, Kortgen A. Regional citrate anticoagulation for continuous renal replacement therapy in the perioperative care of liver transplant recipients: a single center experience. *Ther Apher Dial*. 2015;19(1):8-15.
87. Mosier MJ, Pham TN, Klein MB, Gibran NS, Arnoldo BD, Gamelli RL, et al. Early acute kidney injury predicts progressive renal dysfunction and higher mortality in severely burned adults. *J Burn Care Res*. 2010;31(1):83-92.

Figures

Figure 1

Flow diagram of the study selection process.

Figure 2

Risk ratios for mortality of burn patients with AKI, ARF, and RRT in cohort studies.

Figure 3

Risk ratio for mortality of burned patients with CRRT in RCT studies.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Additionalfile12020.8.24.docx](#)