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ORIGINAL ARTICLE

Net ultrafiltration rate and its impact on mortality in patients with acute kidney injury receiving continuous renal replacement therapy

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ABSTRACT

Background. Fluid overload, a critical consequence of acute kidney injury (AKI), is associated with worse outcomes. The optimal fluid removal rate per day during continuous renal replacement therapy (CRRT) is unknown. The purpose of this study is to evaluate the impact of the ultrafiltration rate on mortality in critically ill patients with AKI receiving CRRT.

Methods. This was a retrospective cohort study where we reviewed 1398 patients with AKI who received CRRT between December 2006 and November 2015 at the Mayo Clinic, Rochester, MN, USA. The net ultrafiltration rate (UF^{NET}) was categorized into low- and high-intensity groups (<35 and ≥ 35 mL/kg/day, respectively). The impact of different UF^{NET} intensities on 30-day mortality was assessed using logistic regression after adjusting for age, sex, body mass index, fluid balance from intensive care unit (ICU) admission to CRRT initiation, Acute Physiologic Assessment and Chronic Health Evaluation III and sequential organ failure assessment scores, baseline serum creatinine, ICU day at CRRT initiation, Charlson comorbidity index, CRRT duration and need of mechanical ventilation.

Results. The mean ± SD age was 62 ± 15 years, and 827 (59%) were male. There were 696 patients (49.7%) in the low- and 702 (50.2%) in the high-intensity group. Thirty-day mortality was 755 (54%). There were 420 (60%) deaths in the low-, and 335 (48%) in the high-intensity group ($P < 0.001$). $UF^{NET} \geq 35$ mL/kg/day remained independently associated with lower 30-day mortality (adjusted odds ratio = 0.47, 95% confidence interval 0.37–0.59; $P < 0.001$) compared with <35 mL/kg/day.

Conclusions. More intensive fluid removal, $UF^{NET} \geq 35$ mL/kg/day, among AKI patients receiving CRRT is associated with lower mortality. Future prospective studies are required to confirm this finding.

Keywords: acute kidney injury, dose–response relationship, fluid overload, mortality, net ultrafiltration, renal replacement therapy

INTRODUCTION

Acute kidney injury (AKI) represents a significant public health burden [1]. During the last decades, the incidence of AKI has increased in hospitalized patients and particularly in patients admitted to intensive care units (ICUs). This increase was mostly attributed to older age, higher incidence of comorbidities and higher severity of the acute illnesses [2].

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One of the most common complications of AKI is fluid overload. The management of fluid overload is crucial, given it is independently associated with a higher mortality rate in AKI. Based on the Kidney Disease: Improving Global Outcome (KDIGO) guidelines, continuous renal replacement therapy (CRRT) is the modality of choice among hemodynamically unstable patients with severe AKI requiring RRT [3–5]. CRRT allows overall more fluid removal over a more extended period of time. In the past two decades, in-hospital mortality in patients who develop AKI and require CRRT has remained high at around 50% [6].

In one study, fluid overload was significantly associated with a higher death rate at 90 days in patients who had AKI. It seemed that there was a dose–response relationship between fluid overload (as measured by percent of body weight) and mortality rate [7–10]. Multivariable logistic regression showed that fluid overload >10% was associated with a 58% increased odds of major adverse kidney events at 90 days (MAKE_{90}) [11]. The interplay between fluid overload and AKI is intriguing. In the Program to Improve Care in Acute Renal Disease, patients with fluid overload (defined as >10% body weight) when their serum creatinine reached its peak were significantly less likely to recover kidney function [12]. In a study by Dalfino *et al.* [13], intraabdominal hypertension (IAH) was an independent predictor of AKI. Cumulative fluid balance was among the independent predictors of IAH, suggesting the indirect role of fluid overload on the occurrence of AKI [13]. In a study utilizing data extracted from the Sepsis Occurrence in Acutely Ill Patients study, a multicenter observational cohort study, mean fluid balance was significantly more positive in patients with AKI [14]. These studies point to the relationship between venous congestion and the occurrence of AKI with or without IAH through interstitial edema and possibly decreased renal blood flow.

Among patients with end-stage renal disease (ESRD) receiving maintenance hemodialysis, a fluid removal rate of ≥10 mL/kg/h has been associated with coronary hypoperfusion, myocardial stunning and access-related adverse events [15–17]. In addition, a fluid removal rate of >13 mL/kg/h has been associated with increased mortality [15–17]. This is why The National Kidney Foundation-Kidney Disease Outcomes Quality Initiative has established that in patients with ESRD on maintenance dialysis for 240 min, ultrafiltration rate (UFR) should not exceed 13 mL/kg/h [18]. When it comes to patients with AKI who require CRRT, there is not much evidence to guide clinicians on the appropriate rate. While the situation differs with the burden of critical illness and fluid overload, investigating the efficacy and safety of different rates is essential.

The optimal net ultrafiltration rate (UF^{NET}) of delivery during CRRT still varies across institutions as the optimum UF^{NET} intensity in AKI is unknown. Our objective in this study was to investigate the impact of different ultrafiltration intensities on the outcomes of critically ill patients with AKI requiring CRRT. We hypothesized that higher UF^{NET} is associated with a lower risk of short-term mortality.

MATERIALS AND METHODS

Study population

This was a single-center retrospective cohort study between December 2006 and November 2015 at the Mayo Clinic, Rochester, MN, USA. We reviewed 1398 patients who were ≥18 years of age diagnosed with AKI and who received CRRT in the form of continuous veno–venous hemofiltration (CVVH). The exposure was CRRT. Patients had available data for follow-up for the outcome of interest. We utilized the data available in the electronic health records. AKI was defined according to the KDIGO criteria [5]. Exclusion criteria consisted of kidney transplantation, ESRD on maintenance hemodialysis or peritoneal dialysis, known pregnancy at admission, prisoners or those who did not provide research authorization (Figure 1). The institutional review board at the Mayo Clinic approved the study protocol and waived the requirement for obtaining informed consent for minimal risk clinical investigations.

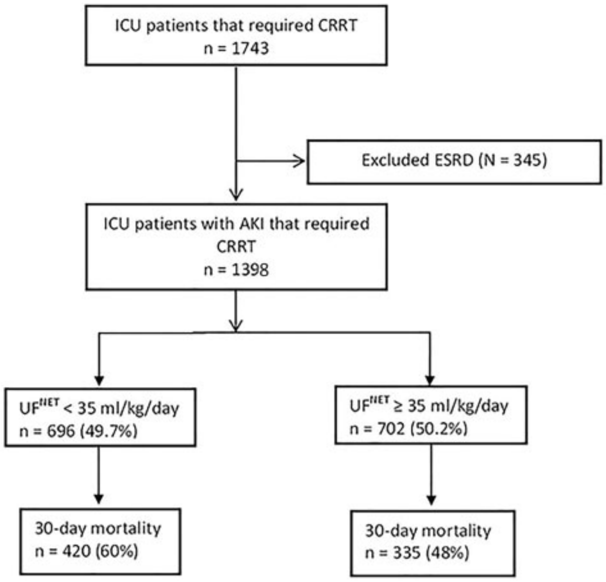

FIGURE 1: Patients flowchart.

Data collection and UF^{NET} intensity

Demographics, clinical characteristics and laboratory data were collected through electronic health records. Daily ultrafiltration volume was calculated from daily fluid balance. UF^{NET} intensity (mL/kg/day) was calculated by the following formula [19]:

$$\frac{\text{Total UF volume (mL)}}{\text{Hospital weight admission (kg)} \times \text{CRRT duration (days)}}$$

In the primary analysis, patients were divided into two groups based on their UF^{NET}, i.e. $\text{UF}^{\text{NET}} < 35$ and ≥35 mL/kg/day. This was based on the median UF^{NET} of the whole cohort. Also, the cutoff was chosen after exploring the relationship between the continuous value of UF^{NET} and 30-day mortality (Supplementary data, Figure S1).

Moreover, we performed sensitivity analyses using three different thresholds of UF^{NET} intensity: low (≤20 mL/kg/day), moderate (20–35 mL/kg/day) and high intensity (≥35 mL/kg/day).

Clinical outcome

The primary outcome was 30-day mortality. As secondary outcomes, we assessed in-hospital mortality, ICU and hospital length of stay (LOS) and MAKE_{90}, which is a composite endpoint of the need for RRT, persistent renal dysfunction (defined as a serum creatinine ≥200% of reference) or death at 90 days [20].

We determined early hypotension as any of the following criteria occurring during the first hour of CRRT initiation: mean arterial pressure <60 mmHg, systolic blood pressure (SBP) < 90 mmHg or a decline in SBP > 40 mmHg from baseline, a positive fluid balance >500 mL or increased vasopressor requirement [21].

Table 1. Baseline characteristics of patients

Characteristics	UF^{NET} <35 mL/kg/day (*n* = 696)	UF^{NET} ≥35 mL/kg/day (*n* = 702)	P-value
Age (mean ± SD), years	63 ± 15	60 ± 15	<0.001
Female, *n* (%)	251 (36)	320 (46)	0.002
BMI (mean ± SD), kg/cm^2	34.3 ± 19	29.4 ± 12.3	<0.001
UF (mean ± SD), mL	19 ± 11	59 ± 24	<0.001
UF [median (IQR)], mL	20.3 (9.6–28)	51.5 (42.2–67)	<0.001*
SOFA score on CRRT initiation (mean ± SD)	11.8 ± 3.8	12.2 ± 3.5	0.01
APACHE III score (mean ± SD)	103 ± 29	104 ± 30	0.3
Baseline serum creatinine, mg/dL	1.15 (0.6)	1.13 (0.6)	0.4
Time to CRRT [median (IQR)], days	1 (0–2)	1 (0–2)	0.02
Fluid balance before CRRT initiation (L), [median (IQR)]	4.2 (1–9.7)	5.8 (1.2–12.8)	0.003
CCI [median (IQR)]	5 (3–7)	5 (3–7)	0.17
Invasive mechanical ventilation at CRRT initiation, *n* (%)	586 (84)	648 (92)	<0.001
Early hypotension, *n* (%)	494 (71)	434 (62)	<0.001
ICU type, *n* (%)			0.001
Cardiac and coronary	65 (9.3)	34 (4.8)	
Cardiovascular surgery	164 (23.6)	166 (23.7)	
General surgery	102 (14.7)	143 (20.4)	
Medical	358 (51.4)	354 (50.4)	
Miscellaneous	7 (1)	5 (0.7)	
Early hypotension (%)	494 (71)	434 (62)	<0.001
30-day mortality, *n* (%)	420 (60)	335 (48)	<0.001
$MAKE_{90}$, *n* (%)	486 (70)	427 (61)	<0.001
Doubling of serum creatinine at 90 days	26	37	0.2
Need for RRT at 90 days	4	14	0.03**
Death at 90 days	456	378	<0.001

*Comparison was made using the Wilcoxon Rank-Sum test.

**Comparison was made using Fisher's exact test.

Statistical analysis

Depending on the normality of data distribution, we summarized continuous variables as mean and standard deviation (SD) or medians and interquartile range (IQR). Categorical variables were presented as counts and percentages. The two-way independent *t*-test was used for continuous variables, and the Chi-squared test and Fisher's exact test were utilized for categorical variables whenever deemed appropriate.

The impact of different UF^{NET} intensities on 30-day mortality rate was assessed using logistic regression after adjusting for age, sex, body mass index (BMI), fluid balance from ICU admission to CRRT initiation, Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) III score, sequential organ failure assessment (SOFA) score on the day of CRRT initiation, baseline serum creatinine, ICU day at CRRT initiation, Charlson comorbidity index (CCI), CRRT duration and need of mechanical ventilation. A $P < 0.05$ was considered significant. Hosmer–Lemeshow goodness of fit was performed using Stata (StataCorp 2017; Stata Statistical Software: Release 15; StataCorp LLC, College Station, TX, USA). All other analyses were performed using JMP statistical software version 14.0 (SAS Institute Inc., Cary, NC, USA).

RESULTS

We included 1398 AKI patients who underwent CRRT over the 8-year period of the study. Patients were categorized into two groups based on the median UF^{NET} of the whole cohort: 696 (49.7%) patients were in the low-intensity group (<35 mL/kg/day), and 702 patients (50.2%) patients were in the high-intensity group (≥35 mL/kg/day).

The majority of the patients (712, 51%) were admitted to the medical ICU, with a similar distribution in both the UF^{NET} groups.

The patients in the low-intensity group were older (63 versus 60 years; $P < 0.001$), had higher BMI (34.3 versus 29.4 kg/m^2; $P < 0.001$), lower SOFA score (11.8 versus 12.2; $P = 0.01$) and less fluid overload at the time of CRRT initiation (4.2 versus 5.8 L; $P = 0.003$) (Table 1).

In the entire cohort, 30-day mortality was 755 (54%). There were 420 (60%) deaths in the low-, and 335 (48%) deaths in the high-intensity group ($P < 0.001$). After adjustment for age, sex, BMI, fluid balance between ICU admission and CRRT initiation, APACHE III score, SOFA score on the day of CRRT initiation, baseline serum creatinine, ICU day at CRRT initiation, CCI, CRRT duration and need of mechanical ventilation, a UF^{NET} ≥35 mL/kg/day was independently associated with lower 30-day mortality [adjusted odds ratio (aOR) = 0.47, 95% confidence interval (CI) 0.37–0.59; $P < 0.001$) compared with <35 mL/kg/day (Table 2). We also performed Hosmer–Lemeshow goodness of fit for the model for 30-day mortality; it resulted in a P-value of 0.44, indicating appropriate calibration. The same finding was reached when 90-day mortality was considered as the outcome (Kaplan–Meier survival curve in Supplementary data, Figure S2). In the multivariate model, the OR for 90-day mortality for patients who had UF^{NET} <35 mL/kg/day was 1.79 (95% CI 1.41–2.27; $P < 0.001$) compared with patients who received UF^{NET} ≥35 mL/kg/day. Moreover, $MAKE_{90}$ occurred in 913 patients (65.3%), of whom 486 (70%) were in the low-, and 427 (61%) in the high-intensity group. UF^{NET} ≥35 mL/kg/day was associated with lower $MAKE_{90}$ (aOR = 0.58, 95% CI 0.45–0.74; $P < 0.001$) (Table 3). There were 334 patients who had serum creatinine measured at around 90 days (median: 90 days; IQR:

Table 2. aOR for 30-day mortality

Variables	aOR (95% CI)	P-value
Age	1.016 (1.01–1.02)	<0.001
≥35 mL/kg/day	0.49 (0.39–0.63)	<0.001
SOFA score	1.14 (1.1–1.2)	<0.001
APACHE III score (per 10 units increase)	1.05 (1.03–1.07)	0.02
ICU LOS at CRRT initiation	1.09 (1.05–1.14)	<0.001
Early hypotension	1.4 (1.11–1.82)	0.005

Model adjusted for age, sex, BMI, the fluid balance between ICU admission and CRRT initiation, APACHE III, SOFA score on the day of CRRT initiation, baseline serum creatinine, ICU day when CRRT was initiated, CCI, early hypotension and mechanical ventilation.

Table 3. aOR for $MAKE_{90}$

Variables	aOR (95% CI)	P-value
Age	1.02 (1.01–1.03)	<0.001
≥35 mL/kg/day	0.62 (0.48–0.78)	<0.001
SOFA score	1.13 (1.09–1.17)	<0.001
APACHE III score (per 10 U increase)	1.03 (0.98–1.08)	0.19
ICU LOS at CRRT initiation	1.08 (1.04–1.13)	<0.001
Early hypotension	1.32 (1.03–1.7)	0.03

Model adjusted for age, sex, BMI, the fluid balance between ICU admission and CRRT initiation, APACHE III, SOFA score on the day of CRRT initiation, baseline serum creatinine, ICU day when CRRT was initiated, CCI, early hypotension and mechanical ventilation.

80–94 days). There were 18 patients who required dialysis during the 90 days after CRRT initiation.

We then divided the cohort into three subcategories depending on their fluid overload status before CRRT initiation. There were 659 patients who had fluid overload <5%, 263 patients with fluid overload between 5% and 10% and 476 patients with fluid overload >10% of body weight. We then reanalyzed the data by stratifying by the fluid overload category. Patients with the highest fluid overload category had the greatest benefit from UF^{NET} ≥35 mL/kg/day (Table 4).

Early hypotension was more present in patients who received lower intensity UF^{NET} (71% versus 62%; $P < 0.001$).

Furthermore, we did four sensitivity analyses. In the first analysis, we excluded patients who had fluid overload <5% of body weight before CRRT initiation or patients who died within the first 24 h of CRRT initiation. The result showed a lower 30-day mortality rate in patients with UF^{NET} ≥35 mL/kg/day (aOR = 0.5, 95% CI 0.34–0.74; $P < 0.001$) (Table 5). In the second, we categorized patients into four quartiles based on the UF^{NET}: <20, 20–34, 35–50 and >50 mL/kg/day. As there was no difference between the third and fourth quartiles, they were combined into one group (UF^{NET} ≥35 mL/kg/day). In multivariate logistic regression, higher UF^{NET} was associated with lower odds of 30-day mortality (Table 6). Moreover, the Cochran Armitage test for trend was significant ($P < 0.001$), with a higher degree of UF^{NET} having lower mortality. We performed another sensitivity analysis to account for admission in different ICU types. We found that UF^{NET} ≥35 mL/kg/day was associated with lower 30-day mortality in the general surgical ICU (aOR = 0.25, 95% CI 0.13–0.5; $P < 0.001$) and the medical ICU (aOR = 0.4, 95% CI 0.28–0.58; $P < 0.001$) only. The effect of UF^{NET} was not statistically significant in multivariate model in the cardiovascular surgery ICU or in the cardiac/coronary ICU. The interaction term for ICU type and UF^{NET} was statistically significant, $P < 0.001$.

Since the proportional hazard assumption was violated in our cohort when assessed both visually and through the Schoenfeld residual test, we could not use the Cox proportional hazard model. Using Gray's survival analysis, we demonstrated that the higher UF^{NET} was only beneficial during the first 5 days of CRRT initiation (adjusted hazard ratio = 0.25, 95% CI 0.19–0.32) (Supplementary data, Table S1).

DISCUSSION

In this large cohort study, we evaluated the effect of different UF^{NET} on mortality in patients with AKI receiving CRRT. In critically ill patients, mechanical fluid removal requires consideration of the patients' clinical needs, hemodynamic status and concurrent morbidities. After adjusting for significant and clinically relevant factors, we found that UF^{NET} intensity ≥35 mL/kg/day was associated with a lower 30-day mortality rate. The results did not change after multiple sensitivity analyses.

There is a growing concern about the deleterious consequences of fluid overload in AKI patients. In the Randomized Evaluation of Normal versus Augmented Level (RENAL) replacement therapy study, an independent association was shown between positive fluid balance and higher 90-day mortality in critically ill AKI patients receiving CRRT [22]. These results were also replicated in other studies [11, 12, 23]. It is important to note that the longer the patients remained with fluid overload during the hospital stay, the higher its impact on mortality [12]. This can be overcome with CRRT; however, while the rate of fluid removal would depend on patients' characteristics (including their hemodynamic capacity to tolerate different rates), the optimal rate of fluid removal in this population remains unknown.

In the international Dialysis Outcomes and Practice Patterns Study, evaluating UFR in patients with ESRD on maintenance hemodialysis, UFR 10 mL/kg/h was associated with a higher risk of all-cause (Relative risk (RR) = 1.09; $P = 0.02$) and cardiopulmonary (Odds ratio (OR) = 1.04; $P = 0.03$) mortality rates [24]. Similar results have been reported in multiple observational studies that indicated a higher risk of death in UFR of 10 mL/kg/h or higher [25–27]. The 'dosing' of CRRT has been reported in several studies. Ronco *et al.* [28] observed an increased survival when the intensity of UFR was increased from 20 to 35 mL/kg/h in AKI patients receiving CRRT. This was also consistent with the 20% reduction in mortality at 90 days reported by Saudan *et al.* [29] following an increase in UFR. In a recent report of critically ill patients with AKI requiring dialysis (both intermittent and continuous modalities), among those with fluid overload >5% of admission weight, the UF^{NET} intensity of >25 mL/kg/day was associated with lower 1-year mortality compared with UF^{NET} <20 mL/kg/day [19]. The findings remained in favor of higher UF^{NET} in multiple sensitivity analyses, including propensity score matching. However, the effect seemed to be most pronounced during the first 39 days after RRT initiation. In a subgroup of 487 patients who only received CRRT, UF^{NET} intensity >1.0 mL/kg/h was associated with lower odds of death (aOR = 0.41, 95% CI 0.24–0.71) compared with intensity of <0.5 mL/kg/h [19]. Interestingly, a secondary analysis of the RENAL study in 2019 reported that UF^{NET} >1.75 mL/kg/h was associated with lower survival between Day 7 and 90. Moreover, it was shown that every 0.5 mL/kg/h increase was associated with a 7% increase in odds of death in critically ill patients with AKI required CVVH [30]. This interpretation was in contrast with both Murugan *et al.* [19], and our cohort, where it was shown that

Table 4. Adjusted or for 30-day mortality across different fluid overload categories

Variables	aOR for 30-day mortality for ≥35 mL/kg/day compared with <35 mL/kg/day	P-value
Fluid overload <5% ($n = 659$)	0.64 (95% CI 0.46–0.9)	0.01
Fluid overload 5–10% ($n = 263$)	0.38 (95% CI 0.21–0.7)	0.002
Fluid overload >10% ($n = 476$)	0.23 (95% CI 0.14–0.37)	<0.001

P-value for interaction was significant, P = 0.001 (between fluid overload category and UF^{NET}) when including the interaction term in the original full model (without stratification).

Table 5. aOR for 30-day mortality excluding moribund patients or with fluid overload <5%

Variables	aOR (95% CI)	P-value
Age	1.012 (1.001–1.024)	0.038
≥ 35 mL/kg/day	0.5 (0.34–0.74)	<0.001
SOFA score	1.13 (1.09–1.17)	<0.001
APACHE III score (per 10 units increase)	1.01 (0.99–1.01)	0.69
ICU LOS at CRRT initiation	1.16 (1.09–1.23)	<0.001

Model adjusted for age, sex, BMI, the fluid balance between ICU admission and CRRT initiation, APACHE III, SOFA score on the day of CRRT initiation, baseline serum creatinine, ICU day when CRRT was initiated, CCI, early hypotension and mechanical ventilation.

Table 6. aOR for 30-day mortality for different UF^{NET} cutoffs

Variables	aOR (95% Cl)	P-value
≥35 vs 20–34	0.59 (0.45–0.78)	<0.001
≥35 vs <20	0.41 (0.34–0.63)	<0.001
20–34 vs <20	0.68 (0.49–0.95)	0.023

Model adjusted for age, sex, BMI, the fluid balance between ICU admission and CRRT initiation, APACHE III, SOFA score on the day of CRRT initiation, baseline serum creatinine, ICU day when CRRT was initiated, CCI, early hypotension and mechanical ventilation.

higher UF^{NET} was associated with lower mortality. This rather contradictory result may be due to different population distributions among studies. In addition, in Murugan *et al.* [30], fluid balance prior to initiation of CRRT was unavailable, a limitation that the authors acknowledge. Also, in our cohort, the degree of fluid overload prior to CRRT initiation was higher compared with that of Murugan *et al.* [19]. The differences in the cohorts studied can explain the different findings reached in each study.

In a recent study of Woodward *et al.* [11], in multivariable analysis, fluid overload >10% was associated with a 58% increased odds of $MAKE_{90}$ (P = 0.046) and 82% increased odds of hospital mortality (P = 0.004). These results are similar to our findings regarding the mortality rate. They also reported a 2.7% increased odds of $MAKE_{90}$ for each 1-day increase in the time between ICU admission and CRRT initiation.

However, the previously mentioned studies looked at the dosing of solute removal; aside from Murugan *et al.*, there are no other studies evaluating the rate of fluid removal in patients with AKI on CRRT. Murugan *et al.* [19] found that mortality was higher in patients who underwent UF^{NET} <20 mL/kg/day. The results of this study are comparable to our cohort, as in their sensitivity analysis when including only patients on CRRT, higher intensity UF^{NET} was associated with lower 1-year mortality (OR = 0.41, 95% CI 0.24–0.71).

These results should be interpreted with caution as the UF^{NET} was the rate that patients received on average during CRRT. As stated by Murugan *et al.* [19], the day-to-day dosing will vary depending on the patients' needs, the severity of fluid overload and patient tolerability of the rate of fluid removal. Moreover, in our study, early hypotension was significantly higher in patients who received lower intensity UF^{NET}. This could indicate that the more severely ill patients with a higher risk of death might not have been able to tolerate a higher UF^{NET}. However, we accounted for such difference in both the multivariate logistic regression and the propensity score derived inverse probability weighting. Furthermore, the results were not different when we stratified our analysis based on the presence or absence of early hypotension (data not shown).

Our study has several strengths. It includes one of the largest cohorts of patients who required CRRT for AKI. Our findings are consistent with other reported studies, and therefore confirm such associations.

We do note some limitations to our study as well. Due to the inherent nature of the retrospective observational studies, it is not possible to ascertain the causal relationship between higher UF^{NET} and improved outcomes. We have tried to overcome that by conducting several sensitivity analyses that did not change our findings. Second, the study remains the experience of one center. However, we think that our results would contribute to the literature given the sparsity of data in this domain. By including patients from different ICUs, we tried to add to the diversity in our cohort and hence the generalizability of our results. Another limitation is the cutoff chosen to dichotomize patients as low or high based on 35 mL/kg/day. Aside from it being the median UF^{NET}, we did explore the relationship between the values of UF^{NET} and mortality through Locally Weighted Scatterplot Smoothing (LOWESS) plot. It did suggest that there is monotonicity, and that supported our decision by choosing this cutoff. The study could also have an unmeasured bias, although both sampling and measurement biases are less likely to occur as we included all patients who met our criteria. Also, measurement bias was reduced as most patients had complete follow-up (for the primary outcome).

CONCLUSIONS

Several methods have been attempted to mitigate the risks incurred by fluid overload in patients with AKI, among them ultrafiltration. We showed that higher UFR was associated with improved outcomes. It remains unknown whether there is a causal relationship between the higher fluid removal rate and lower mortality. This can only be definitively answered in prospective interventional clinical trials.

SUPPLEMENTARY DATA

Supplementary data are available at ckj online.

CONFLICT OF INTEREST STATEMENT

None declared.

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