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 (UFNET) was categorized into low- and high-intensity groups (<35 and ≥35 mL/kg/day, respectively). The impact of different UFNET 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). UFNET ≥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, UFNET ≥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].
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 (MAKE90) [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 registry, 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 hyperperfusion, 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 (UFNET) of delivery during CRRT still varies across institutions as the optimum UFNET 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 UFNET 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.

**Data collection and UFNET intensity**

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

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

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

Moreover, we performed sensitivity analyses using three different thresholds of UFNET 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 MAKE90, 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].
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 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.

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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 UFNET >35 mL/kg/day (Table 4).

Early hypotension was more present in patients who received lower intensity UFNET (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 UFNET >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 UFNET: <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 (UFNET >35 mL/kg/day). In multivariate logistic regression, higher UFNET was associated with lower odds of 30-day mortality (Table 6).

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 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 (1.03–1.17) | 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  |

### Table 3. aOR for MAKE<sub>90</sub>

| 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.

DISCUSSION

In this large cohort study, we evaluated the effect of different UFNET 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 UFNET 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, 29]. 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 UFNET intensity of ≥25 mL/kg/day was associated with lower 1-year mortality compared with UFNET <20 mL/kg/day [19]. The findings remained in favor of higher UFNET 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, UFNET 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 UFNET >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
higher UFNET was associated with lower mortality. This rather contradictory result may be due to different population distributions among studies. In addition, in Murugan et al., 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 MAKE90 (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 MAKE90 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 UFNET <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 UFNET 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 UFNET 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 UFNET. This could indicate that the more severely ill patients with a higher risk of death might not have been able to tolerate a higher UFNET. 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 UFNET 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 UFNET, we did explore the relationship between the values of UFNET 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 cjonline.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Lewington AJ, Cerda J, Mehta RL. Raising awareness of acute kidney injury: a global perspective of a silent killer. Kidney Int 2013; 84: 457–467
2. Ostermann ME, Taube D, Morgan CJ et al. Acute renal failure following cardiopulmonary bypass: a changing picture. Intensive Care Med 2000; 26: 565–571
3. Mc Causland FR, Brunelli SM, Waikar SS. Dialysate sodium, serum sodium and mortality in maintenance hemodialysis. Nephrol Dial Transplant 2012; 27: 1613–1618
4. Schoenfelder T, Chen X, Bless HH. Effects of continuous and intermittent renal replacement therapies among adult patients with acute kidney injury. GMS Health Technol Assess 2017; 13: doi: 10.3205/hta000127
5. Kellum JA, Lameire N, Group K. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care 2013; 17: 204
6. Iwagami M, Yasunaga H, Noiri E et al. Current state of continuous renal replacement therapy for acute kidney injury in Japanese intensive care units in 2011: analysis of a national administrative database. Nephrol Dial Transplant 2015; 30: 988–995
7. Choi SJ, Ha EJ, Jhang WK et al. Factors associated with mortality in continuous renal replacement therapy for pediatric patients with acute kidney injury. Pediatr Crit Care Med 2017; 18: e56–e61
8. Dos Santos TOC, Oliveira MAS, Monte JCM et al. Outcomes from a cohort of patients with acute kidney injury subjected to continuous venous hemodiafiltration: the role of negative fluid balance. PLoS One 2017; 12: e0175897
9. Kim IY, Kim JH, Lee DW et al. Fluid overload and survival in critically ill patients with acute kidney injury receiving continuous renal replacement therapy. PLoS One 2017; 12: e0172137
10. Sharma S, Waikar SS. Intradialytic hypotension in acute kidney injury requiring renal replacement therapy. Semin Dial 2017; 30: 553–558
11. Woodward CW, Lambert J, Ortiz-Soriano V et al. Fluid overload associates with major adverse kidney events in critically ill patients with acute kidney injury requiring continuous renal replacement therapy. Crit Care Med 2019; 47: e753–e760
12. Bouchard J, Soroko SB, Chertow GM et al. Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. Kidney Int 2009; 76: 422–427
13. Dalfino L, Tullo L, Donadio I et al. Intra-abdominal hypertension and acute renal failure in critically ill patients. Intensive Care Med 2008; 34: 707–713
14. Payen D, de Pont AC, Sakr Y et al. A positive fluid balance is associated with a worse outcome in patients with acute renal failure. Crit Care 2008; 12: R74
15. Jaeger JQ, Mehta RL. Assessment of dry weight in hemodialysis: an overview. J Am Soc Nephrol 1999; 10: 392–403
16. Kashani K, Mehta RL. We restrict CRRT to only the most hemodynamically unstable patients. Semin Dial 2016; 29: 268–271
17. Selby NM, Burton JO, Chesterton LJ et al. Dialysis-induced regional left ventricular dysfunction is ameliorated by cooling the dialysate. Clin J Am Soc Nephrol 2006; 1: 1216–1225
18. Kramer H, Yee J, Weiner DE et al. Ultrafiltration rate thresholds in maintenance hemodialysis: an NKF-KDOQI controversies report. Am J Kidney Dis 2016; 68: 522–532
19. Murugan R, Balakumar V, Kerti SJ et al. Net ultrafiltration intensity and mortality in critically ill patients with fluid overload. Crit Care 2018; 22: 223
20. Palevsky PM, Molitoris BA, Okusa MD et al. Design of clinical trials in acute kidney injury: report from an NIDDK workshop on trial methodology. Clin J Am Soc Nephrol 2012; 7: 844–850
21. Akhoudi A, Singh B, Vela M et al. Incidence of adverse events during continuous renal replacement therapy. Blood Purif 2015; 39: 333–339
22. RENAL Replacement Therapy Study Investigators; Bellomo R, Cass A, Cole L et al. An observational study fluid balance and patient outcomes in the randomized evaluation of normal vs. augmented level of replacement therapy trial. Crit Care Med 2012; 40: 1753–1760
23. Vaara ST, Korhonen AM, Kaukonen KM et al. Fluid overload is associated with an increased risk for 90-day mortality in critically ill patients with renal replacement therapy: data from the prospective FINNAKI study. Crit Care 2012; 16: R197
24. Saran R, Bragg-Gresham JL, Levin NW et al. Longer treatment time and slower ultrafiltration in hemodialysis: associations with reduced mortality in the DOPPS. Kidney Int 2006; 69: 1222–1228
25. Assimon MM, Wenger JB, Wang L et al. Ultrafiltration rate and mortality in maintenance hemodialysis patients. Am J Kidney Dis 2016; 68: 911–922
26. Flythe JE, Kimmel SE, Brunelli SM. Rapid fluid removal during dialysis is associated with cardiovascular morbidity and mortality. Kidney Int 2011; 79: 250–257
27. Kim JK, Song YR, Park G et al. Impact of rapid ultrafiltration rate on changes in the echocardiographic left atrial volume index in patients undergoing haemodialysis: a longitudinal observational study. BMJ Open 2017; 7: e013990
28. Ronco C, Bellomo R, Homel P et al. Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomised trial. Lancet 2000; 356: 26–30
29. Saudan P, Niederberger M, De Seigneur S et al. Adding a dialysis dose to continuous haemofiltration increases survival in patients with acute renal failure. Kidney Int 2006; 70: 1312–1317
30. Murugan R, Kerti SJ, Chang CH et al. Association of net ultrafiltration rate with mortality among critically ill adults with acute kidney injury receiving continuous venous veno hemodiafiltration: a secondary analysis of the randomized evaluation of normal vs. augmented level (RENAL) of renal replacement therapy trial. JAMA Netw Open 2019; 2: e195418