

# Association of Fluid Balance with All-Cause and Cause-Specific Mortality in Critically Ill Adult Patients Receiving Continuous Renal Replacement Therapy



Keisuke Okamoto MD and Blaithin A. McMahon MD, Ph.D.,  
Medical University of South Carolina, Division of Nephrology, Charleston, South Carolina.

## Background

Fluid overload is a frequent complication of critically ill patients with acute kidney injury (AKI) and is independently associated with mortality<sup>1</sup>. The use of ultrafiltration with continuous renal replacement therapy (CRRT) is commonly used for the management of fluid balance and/or electrolytes disturbances in the setting of AKI in critically ill patients in intensive care unit (ICU). The optimal rate of ultrafiltration in critically ill patients is unknown. A recent study<sup>2</sup> showed greater net ultrafiltration (NUF) rate is associated with lower survival among critically ill patients with acute kidney injury (AKI). A single-center observational study of critically ill patients receiving continuous venovenous hemodiafiltration (CVVHDF) showed that an NUF rate less than 20 mL/kg/d was associated with higher mortality compared with an NUF rate greater than 25 mL/kg/d<sup>3</sup>.

## Purpose of Study

The purpose of this study is to assess an association between daily fluid balance in critically ill patients with severe (AKI) receiving CRRT and mortality. More specifically, linking fluid balance, net ultrafiltration (UF), vasoactive medication requirement at the time of CRRT initiation and cause-specific mortality in patients with different grades of fluid balance.

## Methods

We consecutively evaluated 64 patients with severe AKI or ESRD requiring CRRT who were admitted to the medical ICU at Medical University of South Carolina (MUSC) between 1/1/2019 to 7/31/2019. We stratified patients into 3 categories according to the median daily net fluid balance while the patients were receiving CRRT (Group A : a net negative daily fluid balance group, Group B : a net even daily fluid balance group, and Group C : a net positive daily balance group), NUF and assessed 28-day all-cause and cause-specific mortality among these 3 groups. We defined Net UF as:

\* Net UF rate (mL/kg/hr) = Ultrafiltration rate – (Replacement fluid rate + Dialysate fluid rate)

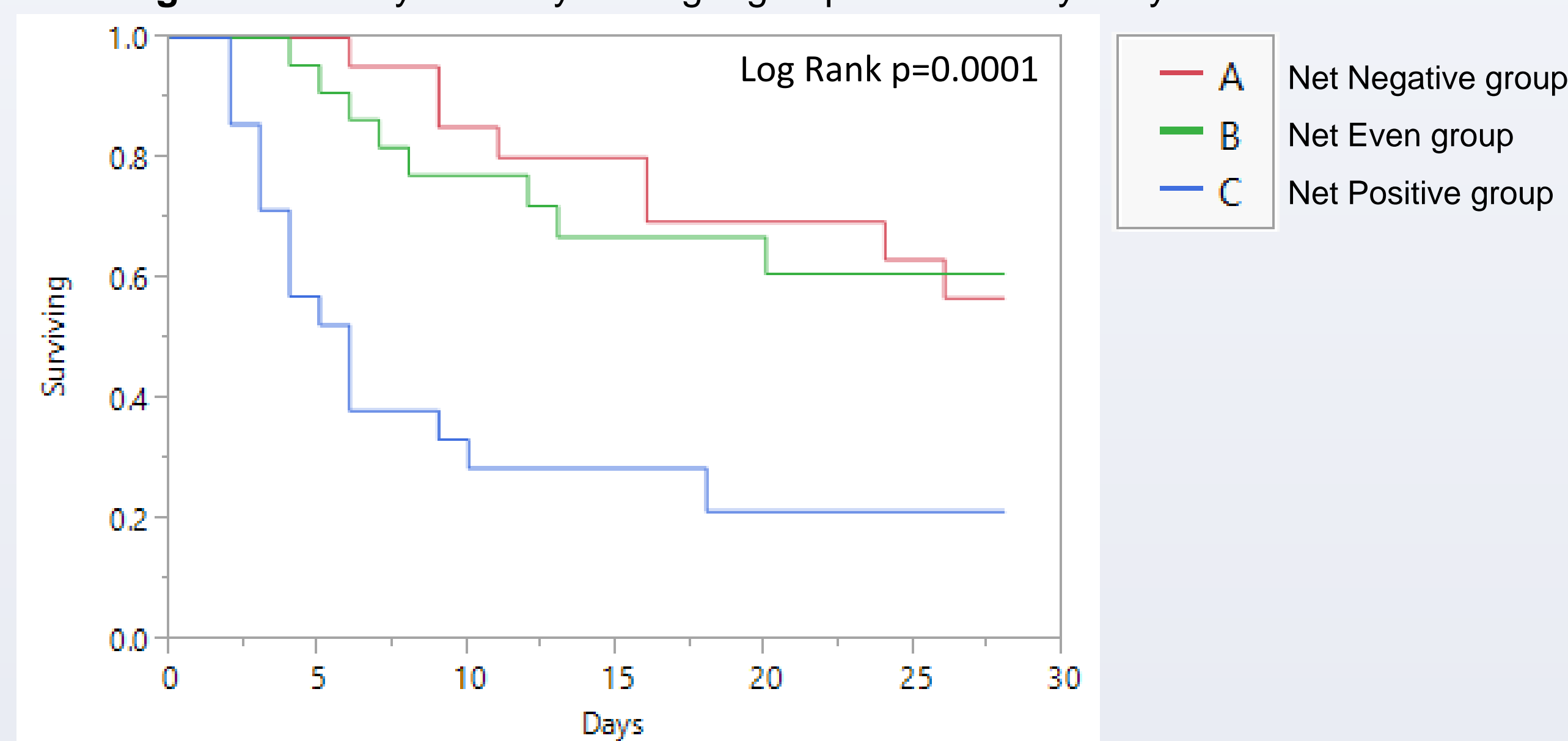
## Results

**Table 1.** Baseline characteristics of patients at medical ICU admission

	Group A (n=21) (Net Negative group) -1.2 L/day [-2.2, -0.9]	Group B (n=22) (Net Even Group) -0.2 L/day [-0.5, 0.1]	Group C (n=21) (Net Positive group) 1.6 L/day [0.6, 4.8]	P-value
<b>Demographics</b>				
Age (y/o)	62.1±7.5	58.4±7.3	53.6±7.5	0.28
Gender (male)	33.3 %	31.8 %	38.1 %	0.20
ICU admission BW (kg)	95.4±13.0	82.4±12.7	79.1±13.0	0.18
ICU admission BMI (%)	33.2±4.8	29.5±4.6	29.2±5.0	0.42
<b>Coexisting diseases</b>				
Hypertension	81.0 %	68.2 %	66.7 %	0.53
Diabetes	66.7 %	36.4 %	19.1 %	0.0063
ESRD	9.5 %	22.7 %	19.1 %	0.50
Transplant	19.1 %	9.1 %	9.5 %	0.54
<b>Findings at ICU admission</b>				
Mean arterial pressure (mmHg)	74.2±5.1	70.6±4.9	70.2±5.1	0.47
Pressor/inotrope requirement at time of CRRT initiation	47.6 %	77.3 %	90.5 %	0.0067
APACHE II	25.4±2.8	27.7±2.6	27.4±2.6	0.44
Serum creatinine at time of CRRT initiation (mg/dl)	4.9±1.2	5.1±1.2	4.7±1.2	0.91
<b>Sepsis</b>				
	14.3 %	36.4 %	38.1 %	0.17
*Net UF rate (mL/kg/hr)	2.20±0.56	1.49±0.55	1.32±0.56	0.07
Median daily net fluid balance [range] (mL/d)	-1188.3 [-2223.1, -890.1]	-206.8 [-453.7, 117.8]	1564.5 [605.1, 4787.5]	

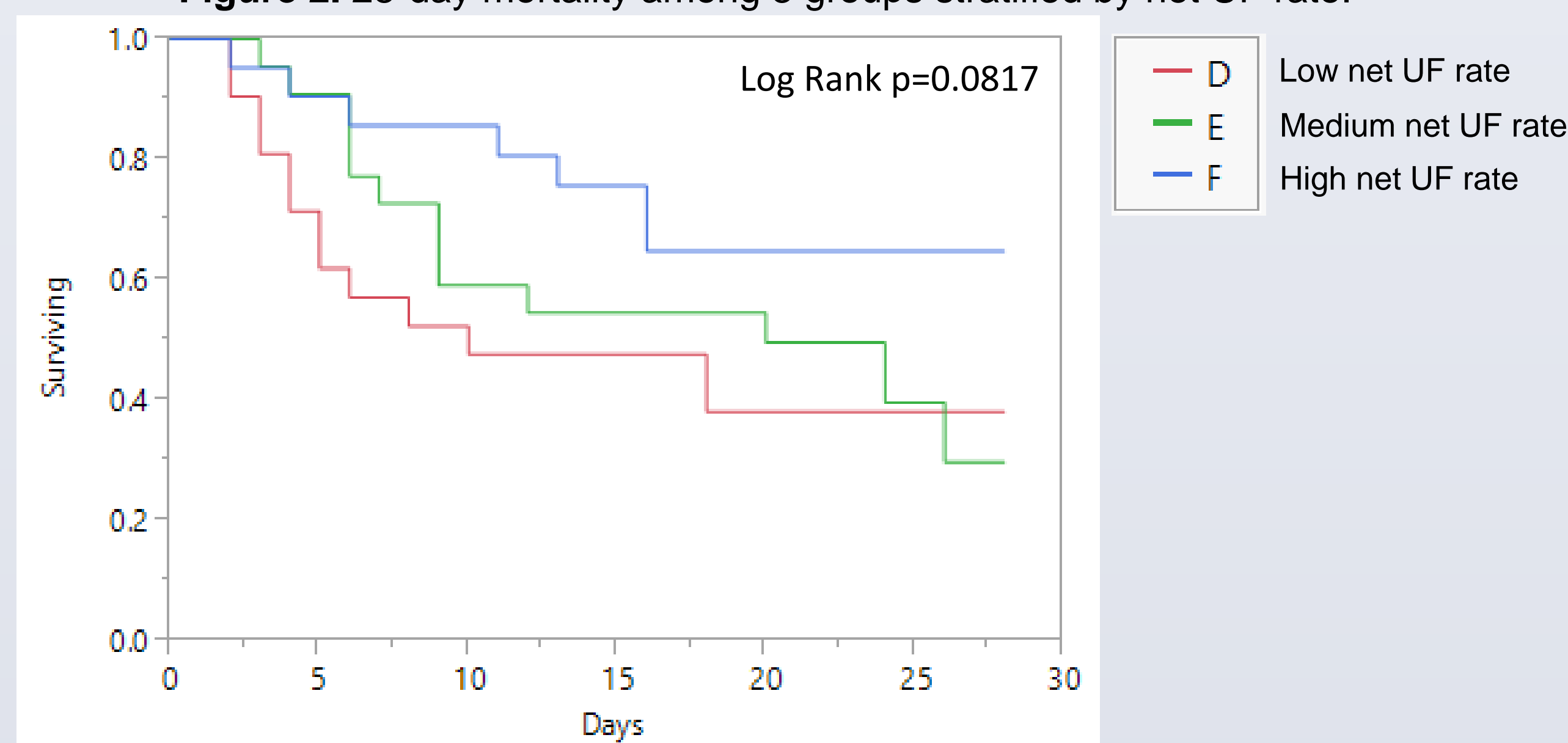
## Results (cont)

**Figure 1.** 28-day mortality among 3 groups stratified by daily fluid balance.



Among the 64 patients, 32 (50%) patients had a 28-day mortality. Group C, the net positive daily fluid balance group, was associated with the highest mortality rate of 76.2% (16 out of 21 patients died).

**Figure 2.** 28-day mortality among 3 groups stratified by net UF rate.



We, then, stratified patients into another 3 categories according to the median net UF rate (Group D : Low net UF rate (0.22184 [0.25489, 0.80982] mL/kg/hr), Group E : Medium net UF rate (1.40735 [1.20614, 1.53212] mL/kg/hr), and Group F : High net UF rate (2.40264 [2.20964, 3.7991] mL/kg/hr)), and assessed 28-day mortality. There was no statistical significance in mortality among these 3 groups.

**Table 2.** All-cause death and cause-specific death among three fluid balance tertile.

	Group A (n=21) (Net Negative group)	Group B (n=22) (Net Even Group)	Group C (n=21) (Net Positive group)	P-value
All-cause death No. (%)	9 (42.9%)	8 (36.4%)	12 (57.1%)	0.0136
<b>Cause-specific death</b>				
Infection	5 (55.6%)	5 (62.5%)	12 (70.6%)	0.9331
Cardiovascular	1 (11.1%)	1 (12.5%)	2 (11.8%)	1.00
Cancer	0 (0%)	1 (12.5%)	0 (0%)	0.2126
Other	3 (33.3%)	1 (12.5%)	3 (17.6%)	0.8145

Group C has the highest percentage of death, however there was no significant difference in the percentage of specific causes among these 3 groups.

## Conclusion

Positive daily net fluid balance on CRRT predicted worse 28-day survival rate compared with negative or intermediate daily net fluid balance ( $p < 0.001$ ). Although there was no significant difference between NET UF there was a signal toward lower UF. Further research into the cause-specific mortality of volume overloaded patients on CRRT is required.

## Limitations

- Small study population from a single institution
- Retrospective study and lack of prospective data
- Unadjusted analysis

## References

1. Morgan E. Grams et al., Fluid balance, diuretic use and mortality in acute kidney injury. CJASN May 2011, 6 (5) 966-9732.
2. Raghavan Murugan et al., Association of Net Ultrafiltration Rate With Mortality Among Critically Ill Adults With Acute Kidney Injury Receiving Continuous Venovenous Hemodiafiltration. JAMA Netw Open. 2019;2(6):e195418.
3. Raghavan Murugan et al., Net ultrafiltration intensity and mortality in critically ill patients with fluid overload. Crit Care. 2018 Sep 24;22(1):223.