Outcomes of Patients with Heart Failure and Kidney Disease Who Receive Intravenous Fluids for Sepsis

OAKLAND UNIVERSITY WILLIAM BEAUMONT

Melany Wiczorek[1], Ronny Otero M.D.[2], Stephen Knight M.D.[2], Kaitlin Ziadeh[4], James Blumline[1], Zachary Rollins[1], Hunter Littmann[7], Rebecca Hufstader[8]

[1] Class of 2022 M.D. Candidate, Oakland University William Beaumont School of Medicine

[2] Department of Emergency Medicine, Beaumont Health System

Introduction

Severe sepsis and septic shock are associated with high morbidity and high mortality. To combat this, early goal-directed therapy (EGDT) originally coined by Rivers et al has been used since 2001 with proven improved outcomes for septic patients[1]. EGDT calls for aggressive intravenous fluid (IVF) administration of >30cc/kg of crystalloid fluids in the first 6 hours of patient care. Because sepsis induces widespread systemic inflammation and an increased tendency for capillary leak, interventions including IVF and vasopressors are aimed at preventing hypotension which can lead to renal injury and multiorgan failure[2]. On the other hand, because septic patients have an increased tendency for capillary leak, IVF administration especially in large quantities can cause additional complications such as peripheral edema, pulmonary edema, respiratory failure, and increased cardiac load[10]. Since EGDT was made a standard practice, many publications including harmonized, multicenter trials ProCESS, ARISE, and ProMISe have concluded that EGDT was not more effective nor cost-effective when compared to usual care of sepsis[3-5]. While there are studies currently being done on liberal vs. restrictive fluids administration therapy, no studies have been published that specifically look at those patient populations most at risk for fluid overload and their outcomes with EGDT. Our primary goal was to evaluate outcomes such as length of stay, need for respiratory support, and mortality in patients at-risk for fluid overload and look for any association with whether or not they received the current fluid administration recommendation.

Aims and Objectives

- Define outcomes for control and at-risk patients in categories such as hospital length of stay, need for respiratory support, and mortality.
- Look for any association with these outcomes and amount of IVF received.

Methods

We performed an IRB-approved retrospective case-control study involving Beaumont Health System's three community hospitals. After chart review, we were able to select 745 patients with a history of CHF and/or CKD presenting with severe sepsis or septic shock to act as our at-risk (AR) group. An additional 570 patients were selected as a control group *without* a diagnosis of CHF and/or CKD with severe sepsis or septic shock.

Methods cont.

These patients' sepsis encounters occurred between April 2018 and May 2019. We decided to include a full year of data to eliminate any variation in infection prevalence during different seasons of the year. Data points were collected to determine the link between patient comorbidities, fluid administration, and outcomes of interest. These included but were not limited to fluids received within 3, 6, 12, and 24 hours from Emergency Department (ED) arrival, need for BiPAP, need for intubation, need for renal replacement therapy, ICU admission length of stay, total length of stay, as well as in-hospital mortality. Logistic regression analysis was used to compare the association between the amount of IVFs received and the outcomes of interest. Log-Rank test was used to adjust for multiple comparisons in survival analysis.

Results

Our cohort consisted of 745 patients with a history of CHF and/or CKD (AR group) and 570 patients without a history of CHF and/or CKD (control group). Beyond the history of CHF or CKD, there appeared to be a higher incidence of coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), and hypertension (HTN) in the control group (p-values of <0.001, <0.001, <0.001 respectively. The source of infection varied in a statistically significant way between the two groups (p-value <0.05).

Overall patients in the AR group received less IVFs than the control group at 24 hours (2530.6mL vs 3046.7mL, p-value <0.001). In the control group, 50 (9%) vs 126 (17%) in the AR group required BiPAP during their hospitalization. There was a significant association between receiving of >30mL/kg of IVFs in the AR group at three and six hours from ED arrival and the need for BiPAP (p-values of 0.006 and 0.02, respectively). However, there was no similar association between the receiving >30 mL/kg of IVFs at three and six hours in the at-risk group and the need for mechanical ventilation (p-values 0.1 and 0.02, respectively). Similarly, there was no association between the receiving >30mL/kg of IVF in the at-risk group at three hours and the need for renal replacement therapy (p-value 0.11). In-hospital mortality was found in 96 (13%) of the AR group vs 47 (8%) of the control group (p-value 0.007). There was no statistically significant association between receiving >30 mL/kg of IVF in the AR group compared to the control group at three or at six hours in terms of in-hospital mortality (p-values of 0.614 and 0.115, respectively). However, in-hospital mortality was higher for the at-risk group compared with the control group overall (12.9% vs 8.2% respectively with p-value 0.007).

Figures

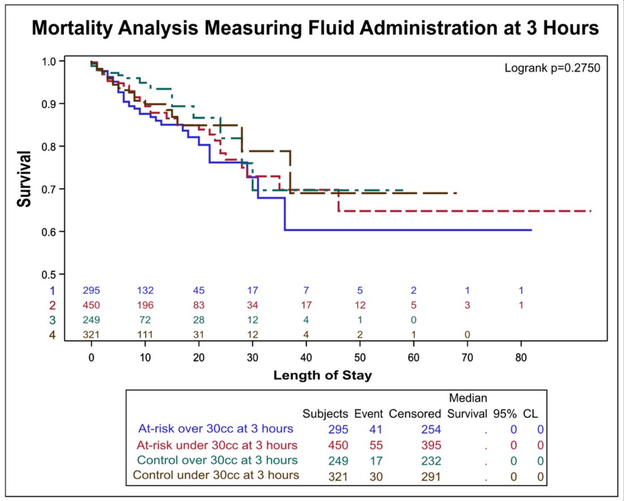

Figure 1: This is a Kaplan-Meier plot showing patient survival throughout their length of stay in the hospital. This shows a survival comparison between at-risk patients who received high or low fluid administration at 3 hours and control patients who received high or low fluid administration at 3 hours.

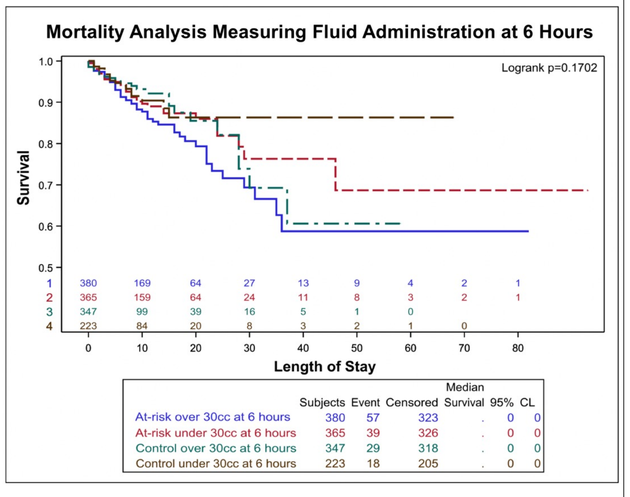

Figure 2: This is a Kaplan-Meier plot showing patient survival throughout their length of stay in the hospital. This shows a survival comparison between at-risk patients who received high or low fluid administration at 6 hours and control patients who received high or low fluid administration at 6 hours.

Conclusions

We identified a significant association of >30 mL/kg IVF administration and the need for BiPAP in AR patients. We did not find a similar association with the need for mechanical ventilation or renal replacement therapy. We identified higher in-hospital mortality in the AR group, but this was not associated with the amount of IVF resuscitation received. This finding may be due to increased comorbidities in the AR group. Overall our findings show that the current fluid administration guidelines of giving >30mL/kg of IVFs are not associated with increased mortality in patients with CHF and/or CKD.

Secondary analyses are currently being performed, including with collected ejection fraction data to further stratify type of CHF in AR patients and time to vasopressors in association with improved mortality. We are aware that there may be many confounding factors that may affect patient outcomes other than vasopressor use, fluid administration, and ejection fraction that limit this study. Given the retrospective nature of this study, data was absent in some patients. Despite these limitations, we hope that the results of this study help guide clinical decision making in the care of septic patients to further reduce mortality and enhance medical decision making and patient-centered care.

Acknowledgements

I would like to acknowledge Dr. Ronny Otero and Dr. Stephen Knight for their continued support in this project. I would also like to thank my data collectors for their hard, tedious work in collecting consistently accurate data. I have no conflicts of interest to disclose.

References

1. **Ford H, Systems H, Re- CW**. The New England Journal of Medicine EARLY GOAL DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK.2001;345(19):1368-1377.
2. **Kelm DJ, Perrin JT, Cartin-Ceba R, Gajic O, Schenck L et al.** Fluid overload in patients with severe sepsis and septic shock treated with early goal-directed therapy is associated with increased acute need for fluid-related medical interventions and hospital death. *Shock*. 2015;43(1):6873.doi:10.1097/SHK.0000000000000268
3. **Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G et al.** Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Critical Care Medicine. 2001; 29(7):1303–1310. [PubMed: 11445675]
4. **Bailey M, Bellomo R, Peter A, et al.** Goal-Directed Resuscitation for Patients with Early Septic Shock. *N Engl J Med*. 2014;371(16):1496-1506. doi:10.1056/NEJMoa1404380
5. **Mouncey PR, Osborn TM, Power GS, et al.** Trial of Early, Goal-Directed Resuscitation for Septic Shock. *N Engl J Med*. 2015;372(14):1301-1311. doi:10.1056/NEJMoa1500896