



# Fluid Administration in Community Acquired Sepsis: Examination of a Large Administrative Database

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Fluid therapy is a cornerstone in the management of sepsis. Early titrated fluid administration impacts organ function and outcome. Guidelines from the Surviving Sepsis campaign recommend a minimum initial fluid administration of 30cc/kg in patients with sepsis-induced tissue hypoperfusion. This study used the Premier administrative database containing 17% of US hospital discharges to examine variation in fluid administration practices and compliance with recommended fluid guidelines in community acquired sepsis.

The study population consisted of patients aged 18 or older who were admitted to the ICU with a diagnosis of community acquired sepsis in septic shock who were medically managed during the year 2013. Fluid administration patterns were analyzed by hospital characteristics (size, teaching vs. nonteaching, urban vs. rural) and extent of organ dysfunction and support.

30,663 patients were analyzed. 49.9 % were female and mean age was  $67.8 \pm 15.1$  years. Patients were grouped into quartiles based on fluid administration. The quartile boundaries were 1110 ml, 3000 ml and 5276 ml respectively during the first 24 hours. Assuming an average body weight of 86.1kg for males and 74kg for females in the US, 47.4 % of patients received less than 30cc/kg within the first 24 hours. Using a more conservative average adult weight of 60kg (1800 cc fluid bolus @ 30cc/kg), 39% did not meet the sepsis guidelines in the first 24 hours. There were no significant differences in fluid administration across hospital types or by the extent of organ dysfunction and support.

Results provide new insight into the fluid administration practice for management of community acquired sepsis presenting in septic shock across US hospitals. While there is considerable homogeneity in fluid administration by hospital type, a substantial proportion of patients receive less initial fluid administration than recommended by consensus guidelines. Further studies are needed to determine the reasons for this discrepancy and to examine the impact and implications of current fluid management in septic patients.

# Fluid Prescription in Hospitalised Patients with Renal Failure : Evidence for a Therapeutic Index for Volume Therapy:

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**Introduction:** AKI complicating acute illness has significant implications with volume resuscitation seen as integral to the management of AKI <sup>1,2</sup>. There has been much recent debate regarding the overall volume balance achieved, with important treatment implications.<sup>3</sup>

**Objectives:** We decided to examine the relationship between fluid prescription and patient outcomes in patients with AKI.

**Method:** From the Premier database we identified a study population consisting of 62,695 from 493 hospitals. Patients were admitted to the ICU with AKI on the first day of the hospitalization, received at least 1L of Day 1 fluids and survived to Day 2. A multivariate model was built to predict mortality with a case-mix adjustment model applied to the data set in order to adjust for severity of illness together with premorbid assessment.

**Results:** Mean patient age was 65 years, 55% male, 75% emergencies, 43% diabetic and 36% had CKD. Mean LOS: 8.7 days with 4.6 days in the ICU. Average Day 1 fluids were 3.7L (median 3.1L), lowest in those without pressors (3.2L) and highest in those with MV and septic shock (5.4L). Hospital mortality was 16.5% for Day 1 survivors, varying from 7.8% in those with no mechanical ventilation (MV) and no pressors (NMNP), to 53% among those with MV and pressors (MVAP). Significant associations between volume of Day 1 fluids and hospital survival were seen. Overall mortality was ca. 15%, 19.4% and 29.3% for those receiving 1-5L of fluid, 6L fluid and (9+L) respectively. For NMNP cases (57%) both actual and expected mortality rates with increased fluid volume (8.3% at 1L to 6.6% at 9+L). Patients receiving pressors and MV (17% of cases) exhibited minimal variation in expected mortality but presented both a decrease in mortality from low to middle ranges (23.2% at 1L to 15.7% at 5L) and an increase in mortality from middle to high ranges (15.7% at 5L to 25.4% at 8L). The highest severity group exhibited no change in actual or expected mortality with fluid administration. Septic shock requiring MV (13% of cases) had no variation in actual mortality across the lower groups of day 1 fluid use (1L to 5L). However, higher ranges of 6+L (38% of the group) presented increased actual mortality rates (40% at 6L to 45% at 9+L), which was higher than predicted.

**Conclusions:** A potential for both under resuscitation and over resuscitation is observed in patients with AKI who received treatment with vasopressors. In those requiring pressor and MV support a clear association existed between volume excess and outcomes, emphasizing a better understanding of individual fluid needs in this important population.

# Effects of fluids administration in patients with septic shock with or without heart failure.

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**Rationale:** Fluid resuscitation has been a primary component of early goal-directed therapy of septic shock (SS) since the seminal study of Rivers et al, but recent data question the reproducibility of those original findings. [ProCESS 2014 ProMISE 2015 & ARISE 2014] Also, aggressive fluid administration has been associated with signs of volume overload and increased morbidity. [Kelm et al, 2015] The present study investigated the relationship between indications of fluid overload in septic patients with and without a history of diastolic heart failure (HF) and patient outcome.

**Methods:** From the Premier database we extracted a study population of 29,098 adult patients who were admitted through the ER and admitted to the ICU on day 1 with the ICD-9 code of septic shock POA, and receiving parental antibiotics. Indications of fluid overload were defined as the presence of 2 or more new variables, first occurring Days 2-4 after admission: diuretics, renal replacement therapy, mechanical ventilation, echocardiogram, pulmonary artery catheter, pleural effusion, and pulmonary vascular congestion. Fluid intake propensity and admission severity models were developed based on characteristics present on admission.

**Results:** The population had a mean age  $67 \pm 15$  years, and was 50% female, with (8,926) and without (20,172) a history of heart failure (HF), including 3,075 with diastolic heart failure. Across all patients, mortality was highest in the highest quantiles of fluid propensity and fluids received (31 – 36%). On Day 1, patients without HF received more fluids than those with HF. While those without HF exhibited no difference between actual and expected mortality rates, patients with HF had significantly lower mortality rates than expected ( $P < 0.001$ ). Table 1 compares outcomes of patients with and without indications of fluid overload, in patients with and without diastolic HF. Results indicate that 1 in 3 patients with diastolic HF received an intervention associated with fluid overload, such as diuretics, compared to 1 in 4 for those without diastolic HF.

**Conclusions:** Adult ICU patients with SS that received the highest volume of fluids on day 1 also had the highest mortality. Patients with diastolic HF received less fluids and exhibited a significantly lower mortality than predicted. The lowest mortality was found in patients with diastolic HF who exhibited evidence of fluid overload. Providers may recognize that patients with diastolic heart failure are susceptible to fluid overload, and subsequently prescribing less fluid and a more aggressive treatment in response to signs of fluid overload.

# Potential Harm Associated with Severity-Adjusted Treatment Variability in Fluid Resuscitation of Critically Ill Septic Patients

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**Rationale:** In the management of patients with severe sepsis and septic shock, recent high-profile studies demonstrated that protocolized early-goal directed resuscitation provided no additional benefit compared to a narrow spectrum of non-protocolized usual care resuscitation (Angus et. al. Intensive Care Med. 2015). However, the translation of clinical evidence to usual care practice in critically ill patients with sepsis is highly variable and the etiology of this variability is poorly understood. Clinical decisions based on usual care and outside of strict protocols raise the potential for harmful practice.

**Objective:** To determine the effect on hospital mortality of severity-adjusted treatment variability in fluid resuscitation of critically ill patients with severe sepsis.

**Methods:** We conducted a retrospective analysis using a large administrative database (Premier Inc, representing ~40% of patients discharged nationally in the USA) of day-one fluid resuscitation practices in critically ill adult patients discharged with ICD-9-CM codes compatible with severe sepsis. A model for propensity to receive five or more liters of fluid on day one was developed and applied, assessing for severity-adjusted treatment variability and comparing predicted to actual hospital mortality.

**Results:** 77,032 patients met the discharge diagnosis criteria. The propensity model identified seventeen statistically significant admission diagnoses for receiving five or more liters of fluid on day one. The model accounted for 22.6% of variation and demonstrated good calibration for the very large sample size (HL-statistic 46.53, p=0.000) and fair discrimination (AUROC 0.62). Overall, there was a wide range of prescribed fluid resuscitation volumes (median volume 2000mL, IQR 500-4000mL). Within propensity quintiles, there was also a wide range of fluid resuscitation but without a statistically significant difference in predicted or actual hospital mortality in quintiles 1-4. In propensity quintile 5, median day-one fluid resuscitation ranged from 250mL to 7000mL between the 1st and 4th quartile of actual prescribed fluid volume. Notably, patients in this highest fluid volume quartile experienced significantly higher actual hospital mortality than predicted (absolute difference of 7.4%, p<0.0001).

**Conclusion:** These data demonstrate a high degree of severity-adjusted treatment variability for fluid resuscitation amongst patients discharged with a diagnosis of severe sepsis present-on-admission. For those patients who receive less fluid and have a lower propensity for receiving fluids, there was no apparent mortality harm or benefit. However, in patients who receive the most fluid and have the highest propensity for receiving fluids, there was a strong association with worse hospital mortality.

## Disclosure

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# Association of fluids and outcomes in emergency department patients hospitalized with community-acquired pneumonia.

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**Introduction:** Emergency department (ED) patients admitted to the hospital with community-acquired pneumonia (CAP) may be at particular risk for volume overload related complications due to their infected lungs. This study used the Premier administrative database containing 17% of US hospital discharges in 2013 to examine the association between a higher amount of fluids administered on day 1, hospital mortality and ventilator free days (VFD)

**Methods:** CAP was defined as a bacterial pneumonia diagnosis present on admission in ED patients receiving chest x-ray and parenteral antibiotics on Day 1. Day 1 total fluid volume was stratified into quartiles. The primary outcome was hospital mortality, and secondary outcome was VFDs over a 30 day period. To adjust for potential confounds, patients were stratified into 5 severity groups based on their modeled predicted mortality, and a propensity model for giving fluids was built using clinical characteristics, severity of illness scores, and ICD-9-CM codes present on admission for important acute and chronic conditions. Patients were then grouped by severity of illness quintiles of predicted risk of death for the CAP population. The association of fluid administration with outcome was assessed within each quintile of mortality risk using chi-square analysis

**Results:** 192,806 adult ED patients with CAP were analyzed. Patients were 51.3% female with a mean age of 69. Overall mortality rate was 7.4% with an average of 24.6 VFDs. After propensity adjustment by severity of illness, mean amount of fluid administered on day 1 ranged from 842 ml to 2,189 ml. Within the fifth severity quintile we found a significant difference in the hospital (22.5%) vs. predicted (18.3%) mortality rate in the highest fluid quartile. Similarly, within the fifth severity quintile, we found a significant difference in the number of VFDs in the highest fluid quartile (16.1) compared to the rest of the quartiles (19.3-20.3)

**Conclusions:** For adult ED patients with CAP, we found significant associations between day 1 fluids and increased mortality and decreased VFDs in the highest fluid quartile and severity group, after adjusting for severity of illness and acuity level. This study may have identified the subset of ED patients who may benefit from a more restrictive fluid strategy when presenting to the hospital with CAP.

# Wide Practice Variability in Fluid Resuscitation of Critically Ill Patients with ARDS

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**Background:** Practice variability, including in the intensive care unit, is pervasive in the way tests are ordered and medical or surgical treatments are prescribed.<sup>1</sup> However, there is little systematic quantitation of the variability in usual care of critically ill patients with ARDS. In critically ill patients where the value proposition is high, unwarranted variability in clinical decision-making is a considerable threat to high-value care.

**Objective:** To determine the magnitude and scope of variable fluid resuscitation and associated outcomes in patients with ARDS.

**Methods:** A retrospective outcomes analysis of day-one fluid resuscitation practices in adult patients admitted to the ICU with ICD-9-CM codes compatible with ARDS was performed using the Premier Inc administrative database, representing ~40% of patients discharged nationally. We excluded those less than 18 years of age who were not admitted via the emergency department, were not mechanically ventilated during the admission, and had surgery during the admission. A propensity for day one fluid resuscitation model was applied to assess for severity-adjusted treatment variability.

**Results:** After exclusion, 1,052 patients with an overall hospital mortality of 32.8% were analyzed for day-one fluid resuscitation. There was a wide range of interquartile fluid resuscitation (42-3000mL). There was no significant difference in hospital mortality between the first quartile (27.8%, SD 2.8%) compared with the fourth quartile (33.7%, SD 2.9%). The propensity model demonstrated satisfactory performance with an area under the receiver operator curve of 0.70. Within the highest severity-adjusted treatment quartile, the interquartile fluid resuscitation range remained wide (1,015-5000mL) without a significant difference in hospital mortality between the first and fourth quartile (Figure 4, 53.6% vs 51.5%, SD 6%).

**Conclusion:** Despite highly variable day-one fluid resuscitation demonstrated in this study, there was no difference in hospital mortality for patients with ARDS even after disease severity adjustment. These findings suggest a widespread variability in provider decision-making, illustrated by clinical decisions regarding fluid resuscitation. While the causes are unclear, variable decision-making may be detrimental to both quality and cost, thereby lowering the value of care.

## Disclosure

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# Fluid Administration in Open and Laparoscopic Abdominal Surgery: Results from Examination of a Large Administrative Database

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**Introduction:** Intraoperative fluid therapy may impact perioperative patient outcome. Unstructured intraoperative fluid administration remains current practice at some hospitals, while other institutions have adopted a fluid restrictive or a goal directed approach. The aim of this study was to use a large administrative database to examine the effect of fluid use and any other relevant factors on postoperative complications following abdominal surgery.

**Methods:** We examined fluid use on day of surgery (DOS) within the 2013 Premier database. The study population consisted of patients 18 years or older who underwent major abdominal surgery during the index hospital admission. Only hospitals that recorded fluid use of at least 1,000 ml on DOS in at least 90% of patients were included in the analysis. DOS fluid use was segmented into eight quantiles by 1L increments with the final category for 8+ L. Patient outcome variables were analyzed by fluid quantile and surgery type (open or laparoscopic), including postoperative pulmonary and cardiac complications, postoperative ileus, length of stay (LOS) of more than 10 days, and discharge to a healthcare facility. To avoid potential confounders, the models were constructed for the incidence of each outcome and adjusted for contributing factors such as age, time in OR, health status, diagnosis, and surgery type.

**Results:** The analysis set consisted of 18,633 discharges from 344 hospitals. The mean patient age was 61.9 and 45.9% were male. Just over half of patients (50.7%) had cancer and nearly two-thirds (66.2%) underwent large bowel surgeries. An open surgical approach was used in 61.2% of cases. The mean DOS fluid use was 4.2 L, with 25<sup>th</sup>ile, median and 75<sup>th</sup>iles of 3.0, 4.0 and 5.2 L respectively. Only 7.8% of patients received less than 2 L of fluid and 9.7% received more than 7.0 L of fluid on DOS. The overall mean LOS was 6.1 days which increased from 5.9 days in the Median Fluid Quantile (MFQ) (4-4.99 L) to 7.7 days in the Highest Fluid Quantile (HFQ) (8+ L). Similarly, cost increased from \$15.7K at MFQ to \$24.0K at HFQ. Post-operative pulmonary complications increased from 4.5% at MFQ to 10.6% at HFQ, with similar results for other complications observed: postoperative cardiac complications (increase from 1.0% to 2.7%); ileus (increase of 14.4% to 18.8%); any postop complication (increase of 22.4% to 33.3%); LOS>10 day (increase of 8.4% to 17.0%); and discharge to a healthcare facility (increase of 7.4% to 12.9%). All comparisons were statistically significant with a p<0.05. After controlling for patient and surgical factors, rates of complications were generally higher in the open versus laparoscopic surgical groups. Overall there was a trend for increasing incidence of complications with DOS fluid use above 5 L in open procedures but not in laparoscopic (Figure 1).

**Conclusions:** Results suggest intraoperative fluid administration impacts observed surgical outcomes. This relationship was maintained when all other confounds were adjusted. Targeted, individualized fluid therapy on the DOS could reduce the potentially negative downstream effects arising from under or over resuscitation with intravenous fluids.