# Even Modest Fluid Overload is Associated with Mortality in Critically Ill Patients with Acute Kidney Injury

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## Background

- Positive fluid balance (FB) is associated with short-term morbidity and mortality in the critically ill patients with Acute Kidney Injury (AKI).
- Magnitude of the association between FB and short-term mortality is unknown.

## Objective

- To examine the association between fluid balance and risk-adjusted hospital mortality among critically ill patients with AKI.

## Methods

- We analyzed a large intensive care unit (ICU) dataset involving adults admitted to a tertiary care academic medical center over an 8-year period.
- Cumulative FB is described here:

$$\%FB = \frac{\text{Sum of daily (fluid in – fluid out) until RRT or end of ICU stay}}{\text{Hospital admission weight}} \times 100$$

- AKI was defined & classified using the KDIGO guidelines
- In the overall population, a propensity score was developed to account for indication bias for fluid administration using:
  - Baseline characteristics: age, sex, race, BMI, comorbidity, malignancy, surgery, reference creatinine
  - Risk factors in the 24hrs of ICU admission: vasopressors, mechanical ventilation, suspected sepsis, APS-III score, severity of hypotension, KDIGO Stage and oliguria
- Patients with ≥ 5% FB were matched with 3 controls (<5% FB) using PS matching without replacement with a caliper distance of 0.001
- Baseline characteristics of patients were compared between the 3 categories of FB (<0%; 0% to <5% and ≥ 5%). (Table 1)
- Association between FB and mortality was studied in the AKI cohort using logistic regression adjusted for several risk factors and the propensity for ≥ 5% FB.

## Results

- In the 13,358 patients the distribution of cumulative FB for <0%, 0% to <5% and ≥ 5% was 81.8%, 13.3%, and 4.9%, respectively.
- After matching, 441 patients with ≥ 5% FB were compared to 1231 patients with < 5% FB in the AKI population. (Table 3)

## Results

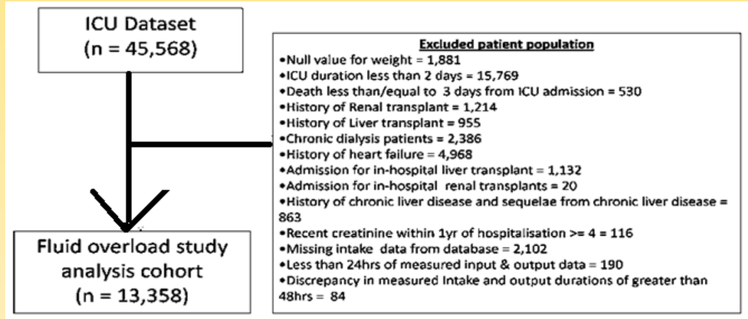


**TABLE 1: CHARACTERISTICS OF PATIENTS BY CATEGORIES OF FLUID BALANCE IN OVERALL POPULATION**

| Variable | N 13,358 | <0% 10,925 | 0% to <5% 1780 | ≥5% 653 | P value |
|---|---|---|---|---|---|
| Age | 13332 | 60 (47-73) | 65 (51-77) | 65 (51-78) | <0.001 |
| BMI | 10,788 | 26.8 (23.4 - 31.2) | 27.1 (23.6 - 31.6) | 24.6 (21.3 - 28.7) | <0.001 |
| H/o malignancy | 487 | 361(3.3%) | 84(4.7%) | 42(6.4%) | <0.001 |
| Multiple comorbidities | 3772 | 2951(27%) | 553(31%) | 268(41%) | <0.001 |
| Surgical admission* | 8584 | 7127(65.2%) | 1047(58.8%) | 410 (62.8%) | <0.001 |
| Vasopressors | 3211 | 2622(24%) | 396(22.3%) | 193(29.6%) | <0.001 |
| Mechanical ventilation | 8524 | 7136(65.3%) | 995(55.9%) | 393(60.2%) | <0.001 |
| Suspected sepsis* | 1871 | 1508(13.8%) | 246(13.8%) | 117(17.9%) | 0.01 |
| APS-III score* | 13,338 | 62.8 (26.2) | 65.6 (29.2) | 72.3 (29.9) | <0.001 |
| Average daily FB | | -0.9 (-1.4 -0.5) | 0.3 (0.1 - 0.6) | 1 (0.5 - 1.7) | <0.001 |
| Reference creatinine* | 13,357 | 0.81 (0.7 - 1.01) | 0.84 (0.7 - 1.02) | 0.82 (0.7 - 1.03) | 0.003 |
| AKI | 4056 | 3110 | 686 | 260 | |
| Stage 1 | 1049 | 891(8.2%) | 118 (6.6%) | 40 (6.1%) | |
| Stage 2 | 2326 | 1821 (16.7%) | 379 (21.3%) | 126 (19.3%) | <0.001 |
| Stage 3 | 681 | 398 (3.6%) | 189 (10.6%) | 94 (14.4%) | |

* see references for previous definitions of the variables used

**TABLE 2: DISTRIBUTION OF OUTCOMES IN AKI POPULATION BEFORE MATCHING**

| Variable | N | <0% | 0% to <5% | ≥5% | P value |
|---|---|---|---|---|---|
| Hospital mortality | 1591 | 1095 (12.5%) | 304 (19.9%) | 192 (32.2%) | <0.001 |
| ICU LOS* | 10,865 | 7 (5-14) | 5 (4-8) | 6 (4-14) | <0.001 |
| Hospital LOS* | 10,865 | 17 (10-28) | 12 (8-21) | 17 (10-29) | <0.001 |
| RRT | 719 | 362 (4.1%) | 229 (15%) | 128 (21.4%) | <0.001 |
| Initial RRT | | | | | |
| Hemodialysis | 268 | 131 (36.2%) | 90 (39.3%) | 47 (36.7%) | 0.74 |
| CRRT | 451 | 231 (63.8%) | 139 (60.7%) | 81 (63.3%) | |
| Days from ICU to RRT | 716 | 12 (6-20) | 3 (2-6) | 4 (3-9) | <0.001 |
| AKI | 10,865 | 8741 | 1527 | 597 | |
| Stage 1 | 2582 | 2255 (25.8%) | 252 (16.5%) | 75 (12.6%) | <0.001 |
| Stage 2 | 5684 | 4707 (53.9%) | 748 (50%) | 229 (38.4%) | |
| Stage 3 | 2599 | 1779 (20.4%) | 527 (34.5%) | 293 (49.1%) | |

*LOS length of stay

## Results

**TABLE 3: DISTRIBUTION OF OUTCOMES IN AKI POPULATION AFTER MATCHING**

| Outcomes | N | Controls <5% | Cases ≥5% | P value |
|---|---|---|---|---|
| Hospital mortality | 406 | 262 (21%) | 144 (33%) | <0.001 |
| ICU LOS* | 1672 | 8 (5-16) | 6 (4-14) | 0.004 |
| Hospital LOS* | 1672 | 18 (11-31) | 17 (10-29) | 0.19 |
| RRT | 275 | 171 (13.9%) | 104 (23.6%) | <0.001 |
| Initial RRT | 275 | | | |
| Hemodialysis | 91 | 57 (33.3%) | 34 (32.7%) | 0.91 |
| CRRT | 184 | 114 (66.7%) | 70 (67.3%) | |
| Days from ICU to RRT | 275 | 6 (3-14) | 4 (3-8..5) | 0.03 |
| AKI | 1672 | | | |
| Stage 1 | 237 | 179 (14.5%) | 58 (13.2%) | 0.08 |
| Stage 2 | 669 | 508 (41.3%) | 161 (36.5%) | |
| Stage 3 | 766 | 544 (44.2%) | 222 (50.3%) | |

*LOS length of stay

- After the propensity score matching patients with ≥ 5% FB had higher mortality compared with controls (33% vs. 21%, P<0.001). (Table 3)
- After accounting for baseline differences ≥ 5% FB compared with 0% to 5% FB was associated with increased odds of mortality (adjusted OR, 1.62; 95% CI, 1.24 - 2.13; P<0.001). Whereas <0% FB compared with 0% to 5% FB was associated with lower odds of mortality (adjusted OR, 0.75; 95%CI, 0.63-0.90; P=0.002).

## Conclusion

- While modest fluid overload is associated with increased mortality, negative balance is associated with lower mortality; thus association of fluid balance with mortality is variable.

## Limitations

- It is not possible to estimate if the fluid overload was the cause or the result of the severity of the underlying illnesses in the population.
- There is no acceptable definition of fluid overload and the model that we are using has not been validated.

## References

- Teixeira et al., Fluid balance and urine volume are independent predictors of mortality in acute kidney injury. Critical Care 2013 17(1), R14
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- Sileanu FE et al., AKI in Low-Risk versus High-Risk Patients in Intensive Care. *Clin J Am Soc Nephrol*. 2014:1–10. doi:10.2215/CJN.03200314.