**SUPPLEMENTAL DIGITAL CONTENT**

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**Operational ESRD definition:** end-stage renal disease (ESRD), defined as having an International Classification of Diseases, Ninth Revision (ICD-9) diagnosis code for ESRD (585.6) or having an ICD-9 code for a dialysis procedure (39.95 for hemodialysis or 54.98 for peritoneal dialysis) without an ICD-9 code for acute kidney injury (AKI; 584.5, 584.6, 584.7, 584.8, 584.9)

**Ascertainment period:** Apart from in-hospital mortality and length of stay which were ascertained for the entire hospitalization, our follow-up period for ascertaining outcomes began after the first 24 hours in the ICU (i.e., the exposure period) and continued through the seventh day after ICU admission. We chose this time period because the direct effects of diuretics last a matter of hours, and we felt that a longer follow-up period would introduce random error and potential bias in our analyses. Information on net fluid balance was only available for the ICU portion of the hospitalization. We examined AKI and electrolyte abnormalities based on laboratory data available during both the ICU and non-ICU portions of the hospitalization, within the 7-day follow-up period discussed above.

**Table S1. SOFA scores by component in the unmatched and propensity-score matched cohorts.**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Unmatched Cohort** | | |  | | **Propensity-Score-Matched Cohort** | | | |
| **Score Components** | **Diuretics**  **(N=2606)** | **No Diuretics**  **(N=10983)** | **Std diff** | |  | | **Diuretics**  **(N=2523)** | **No Diuretics**  **(N=2523)** | **Std diff** | |
| **ICU admission SOFA** |  |  |  | |  | |  |  |  | |
| Cardiovascular | 1.3 +/- 1.0  1 [1-1] | 1.3 +/- 1.1  1 [1-1] | 0.01 | |  | | 1.3 +/- 1.0  1 [1-1] | 1.3 +/- 1.1  1 [1-1] | 0.00 | |
| Respiration | 0.9 +/- 1.3  0 [0-2] | 0.6 +/- 1.2  0 [0-0] | 0.24 | |  | | 0.9 +/- 1.3  0 [0-2] | 0.8 +/- 1.3  0 [0-2] | 0.01 | |
| Renal | 0.9 +/- 1.0  1 [0-1] | 0.8 +/- 1.1  0 [0-1] | 0.13 | |  | | 0.9 +/- 1.0  1 [0-1] | 0.9 +/- 1.1  1 [0-1] | 0.00 | |
| Coagulation | 0.4 +/- 0.8  0 [0-1] | 0.5 +/- 0.9  0 [0-1] | 0.05 | |  | | 0.4 +/- 0.8  0 [0-1] | 0.4 +/- 0.8  0 [0-1] | 0.02 | |
| Liver | 0.3 +/- 0.7  0 [0-0] | 0.4 +/- 0.9  0 [0-0] | 0.08 | |  | | 0.3 +/- 0.8  0 [0-0] | 0.3 +/- 0.8  0 [0-0] | 0.00 | |
| CNS | 1.3 +/- 1.4  1 [0-3] | 1.4 +/- 1.5  1 [0-3] | 0.03 | |  | | 1.4 +/- 1.5  1 [0-3] | 1.4 +/- 1.5  1 [0-3] | 0.01 | |

Mean +/- standard deviation and median [25th-75th percentiles].

**Table S2. Baseline characteristics of persons with diuretic use as compared with persons without diuretic use on the first day of ICU admission in the subset with heart failure**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Unmatched Cohort** | | |  | **Propensity-Score-Matched Cohort** | | |
| **Characteristics** | **Diuretics**  **(N=1787)** | **No Diuretics**  **(N=2643)** | **Std diff** |  | **Diuretics**  **(N=1692)** | **No Diuretics**  **(N=1692)** | **Std diff** |
| **Age (yrs)** | 74 +/- 13  76 [66-84] | 73 +/- 14 76 [64-84] | 0.05 |  | 74 +/- 13  76 [66-84] | 73 +/- 13 76 [64-84] | 0.01 |
| **Female sex** | 48% | 48% | 0.01 |  | 48% | 47% | 0.02 |
| **White race** | 73% | 75% | 0.04 |  | 73% | 75% | 0.03 |
| **Comorbidities** |  |  |  |  |  |  |  |
| Diabetes mellitus | 38% | 33% | 0.10 |  | 36% | 36% | 0.01 |
| Heart failure | 100% | 100% | 0.00 |  | 100% | 100% | 0.00 |
| Hypertension | 64% | 58% | 0.12 |  | 63% | 62% | 0.02 |
| Chronic kidney disease | 26% | 23% | 0.07 |  | 25% | 24% | 0.02 |
| Liver disease | 4% | 6% | 0.08 |  | 4% | 5% | 0.04 |
| **Admit type** |  |  |  |  |  |  |  |
| Cardiovascular | 57% | 38% | 0.38 |  | 55% | 53% | 0.03 |
| Gastrointestinal | 7% | 10% | 0.10 |  | 7% | 8% | 0.01 |
| Infectious | 7% | 16% | 0.26 |  | 8% | 7% | 0.02 |
| Respiratory | 15% | 15% | 0.00 |  | 15% | 16% | 0.02 |
| Neoplasm | 3% | 4% | 0.04 |  | 4% | 4% | 0.01 |
| Injuries/Poisonings | 4% | 7% | 0.12 |  | 5% | 5% | 0.03 |
| Other | 6% | 10% | 0.14 |  | 6% | 6% | 0.00 |
| **ICU Type** |  |  |  |  |  |  |  |
| Cardiac unit | 51% | 38% | 0.26 |  | 50% | 49% | 0.02 |
| Medical unit | 49% | 62% | 0.26 |  | 50% | 51% | 0.02 |
| **Vasopressor use** | 19% | 28% | 0.21 |  | 20% | 20% | 0.00 |
| **Admission serum**  **creatinine (mg/dL)** | 1.5 +/- 0.9 1.3 [ 0.9-1.7] | 1.6 +/- 1.3 1.2 [0.9-1.9] | 0.14 |  | 1.5 +/- 0.9 1.2 [0.9-1.7] | 1.5 +/- 0.9 1.2 [0.9-1.7] | 0.02 |
| **ICU admission SOFA**  **score** | 5.0 +/- 3.4 4 [2-7] | 5.7 +/- 3.9 5 [3-8] | 0.21 |  | 5.0 +/- 3.5 4 [2-7] | 5.0 +/- 3.6 4 [2-7] | 0.01 |
| **Mechanically ventilated**  **on first ICU day** | 37% | 39% | 0.03 |  | 36% | 37% | 0.01 |

Categorical variables are given as percentages. Continuous variables are given as both mean +/- standard deviation and median [25th-75th percentiles].

**Table S3. Baseline characteristics of persons with diuretic use as compared with persons without diuretic use on the first day of ICU admission in the subset with chronic kidney disease**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Unmatched Cohort** | | |  | **Propensity-Score-Matched Cohort** | | |
| **Characteristics** | **Diuretics**  **(N=554)** | **No Diuretics**  **(N=1327)** | **Std diff** |  | **Diuretics**  **(N=474)** | **No Diuretics**  **(N=474)** | **Std diff** |
| **Age (yrs)** | 76 +/- 11 78 [70-85] | 74 +/- 14 77 [65-85] | 0.20 |  | 76 +/- 12 78 [70 - 85] | 76 +/- 13 79 [69-86] | 0.01 |
| **Female sex** | 43% | 38% | 0.10 |  | 43% | 43% | 0.01 |
| **White race** | 77% | 72% | 0.13 |  | 75% | 77% | 0.03 |
| **Comorbidities** |  |  |  |  |  |  |  |
| Diabetes mellitus | 50% | 45% | 0.11 |  | 49% | 52% | 0.06 |
| Heart failure | 84% | 46% | 0.88 |  | 81% | 81% | 0.01 |
| Hypertension | 81% | 82% | 0.02 |  | 81% | 82% | 0.03 |
| Chronic kidney disease | 100% | 100% | 0.00 |  | 100% | 100% | 0.00 |
| Liver disease | 6% | 9% | 0.10 |  | 6% | 7% | 0.04 |
| **Admit type** |  |  |  |  |  |  |  |
| Cardiovascular | 53% | 27% | 0.55 |  | 47% | 46% | 0.04 |
| Gastrointestinal | 9% | 14% | 0.15 |  | 11% | 12% | 0.05 |
| Infectious | 6% | 17% | 0.36 |  | 7% | 7% | 0.02 |
| Respiratory | 13% | 12% | 0.02 |  | 14% | 14% | 0.01 |
| Neoplasm | 4% | 5% | 0.05 |  | 5% | 5% | 0.02 |
| Injuries/Poisonings | 6% | 8% | 0.10 |  | 7% | 7% | 0.01 |
| Other | 8% | 15% | 0.22 |  | 9% | 9% | 0.01 |
| **ICU Type** |  |  |  |  |  |  |  |
| Cardiac unit | 50% | 27% | 0.49 |  | 44% | 44% | 0.00 |
| Medical unit | 50% | 73% | 0.49 |  | 56% | 56% | 0.00 |
| **Vasopressor use** | 18% | 21% | 0.10 |  | 19% | 17% | 0.04 |
| **Admission serum**  **creatinine (mg/dL)** | 2.2 +/- 1.1 1.8 [1.4-2.5] | 2.5 +/- 1.7 2.0 [1.5-3.0] | 0.26 |  | 2.2 +/- 1.2 1.9 [1.5-2.6] | 2.1 +/- 1.1 1.8 [1.4-2.6] | 0.05 |
| **ICU admission SOFA**  **score** | 5.4 +/- 3.2 5 [3-7] | 6.0 +/- 3.6 5 [3-8] | 0.18 |  | 5.6 +/- 3.3 5 [3-7] | 5.6 +/- 3.3 5 [3-7] | 0.00 |
| **Mechanically ventilated**  **on first ICU day** | 33% | 30% | 0.06 |  | 33% | 32% | 0.02 |

Categorical variables are given as percentages. Continuous variables are given as both mean +/- standard deviation and median [25th-75th percentiles].

**Table S4. Baseline characteristics of persons with diuretic use as compared with persons without diuretic use on the first day of ICU admission in the subset with acute lung injury**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Unmatched Cohort** | | |  | **Propensity-Score-Matched Cohort** | | |
| **Characteristics** | **Diuretics**  **(N=828)** | **No Diuretics**  **(N=2234)** | **Std diff** |  | **Diuretics**  **(N=761)** | **No Diuretics**  **(N=761)** | **Std diff** |
| **Age (yrs)** | 69 +/- 15 71 [60-81] | 64 +/- 17 65 [52-77] | 0.37 |  | 69 +/- 15 70 [59-81] | 69 +/- 15 71 [59-80] | 0.01 |
| **Female sex** | 49% | 44% | 0.11 |  | 48% | 50% | 0.05 |
| **White race** | 72% | 70% | 0.04 |  | 72% | 74% | 0.04 |
| **Comorbidities** |  |  |  |  |  |  |  |
| Diabetes mellitus | 33% | 27% | 0.14 |  | 32% | 32% | 0.00 |
| Heart failure | 68% | 33% | 0.76 |  | 65% | 63% | 0.04 |
| Hypertension | 57% | 47% | 0.22 |  | 56% | 56% | 0.02 |
| Chronic kidney disease | 18% | 12% | 0.16 |  | 16% | 15% | 0.02 |
| Liver disease | 6% | 10% | 0.17 |  | 6% | 5% | 0.02 |
| **Admit type** |  |  |  |  |  |  |  |
| Cardiovascular | 41% | 19% | 0.49 |  | 37% | 36% | 0.02 |
| Gastrointestinal | 7% | 8% | 0.04 |  | 7% | 7% | 0.01 |
| Infectious | 11% | 22% | 0.31 |  | 11% | 11% | 0.00 |
| Respiratory | 25% | 25% | 0.01 |  | 27% | 29% | 0.04 |
| Neoplasm | 6% | 8% | 0.06 |  | 6% | 6% | 0.01 |
| Injuries/Poisonings | 4% | 10% | 0.21 |  | 5% | 4% | 0.03 |
| Other | 6% | 9% | 0.11 |  | 6% | 6% | 0.01 |
| **ICU Type** |  |  |  |  |  |  |  |
| Cardiac unit | 38% | 20% | 0.40 |  | 35% | 35% | 0.01 |
| Medical unit | 62% | 80% | 0.40 |  | 65% | 65% | 0.01 |
| **Vasopressor use** | 31% | 40% | 0.18 |  | 33% | 33% | 0.01 |
| **Admission serum**  **creatinine (mg/dL)** | 1.4 +/- 1.0 1.1 [0.9-1.6] | 1.5 +/- 1.3 1.1 [0.8-1.7] | 0.05 |  | 1.4 +/- 1.0 1.1 [0.9-1.6] | 1.4 +/- 1.2 1.1 [0.8-1.5] | 0.03 |
| **ICU admission SOFA**  **score** | 8.4 +/- 3.4 8 [6-10] | 9.5 +/- 3.9 9 [7-12] | 0.31 |  | 8.6 +/- 3.4 8 [6-11] | 8.7 +/- 3.5 8 [6-11] | 0.01 |
| **Mechanically ventilated**  **on first ICU day** | 78% | 85% | 0.18 |  | 81% | 81% | 0.01 |

Categorical variables are given as percentages. Continuous variables are given as both mean +/- standard deviation and median [25th-75th percentiles].

**Table S5. Outcomes from propensity-matched cohort with heart failure**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcomes** | **Diuretics**  **(N=1692)** | | **No Diuretics**  **(N=1692)** | | **Risk ratio or difference in mean** | | **99.5% CI** | | **P-value** | |
| **In-hospital mortality** | | 14% | | 14% | | 0.97 | | [0.76, 1.24] | | 0.73 | |
| **Any mechanical ventilation** | | 31% | | 34% | | 0.91 | | [0.80, 1.05] | | 0.07 | |
| **Acute kidney injury** | | 38% | | 29% | | 1.30 | | [1.13, 1.49] | | <0.001 | |
| **Renal replacement therapy** | | 2% | | 2% | | 1.03 | | [0.50, 2.15] | | 0.90 | |
| **Hyponatremia** | | 30% | | 29% | | 1.03 | | [0.88, 1.20] | | 0.61 | |
| **Severe hyponatremia** | | 9% | | 9% | | 0.91 | | [0.67, 1.24] | | 0.40 | |
| **Hypokalemia** | | 40% | | 34% | | 1.19 | | [1.04, 1.35] | | <0.001 | |
| **Severe hypokalemia** | | 6% | | 7% | | 0.92 | | [0.64, 1.33] | | 0.54 | |
| **Metabolic alkalosis** | | 42% | | 28% | | 1.51 | | [1.32, 1.74] | | <0.001 | |
| **Severe metabolic alkalosis** | | 4% | | 2% | | 2.19 | | [1.20, 3.98] | | <0.001 | |
|  | |  | |  | |  | |  | |  | |
| **Duration of mechanical ventilation, hours** | | 18.9 +/- 38.9 0 [0-12.3] | | 22.2 +/- 41.9 0 [0-20.0] | | -3.38 | | [-7.31, 0.55] | | 0.02 | |
| **ICU length of stay, days** | | 5.1 +/- 5.9 3.2 [2.0-5.9] | | 5.1 +/- 6.3 3.0 [1.9-5.7] | | -0.02 | | [-0.62, 0.58] | | 0.91 | |
| **Total length of stay, days** | | 10.8 +/- 9.2 8.1 [5.3-13.0] | | 10.8 +/- 9.3 8.0 [5.0-13.8] | | -0.03 | | [-0.94, 0.87] | | 0.92 | |
| **Fluid balance, liters** | | 0.0 +/- 5.1 -0.4 [-1.9-0.5] | | 1.4 +/- 5.2 0.1 [-0.7-1.9] | | -1.41 | | [-1.77, -1.05] | | <0.001 | |

Binary outcomes are given as percentages and risk ratios. Continuous variables are expressed as mean +/- standard deviation, median [25th-75th percentiles], and differences in mean.

**Table S6. Outcomes from propensity-matched cohort with chronic kidney disease**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Outcomes** | **Diuretics**  **(N=474)** | **No Diuretics**  **(N=474)** | **Risk ratio or difference in mean** | **99.5% CI** | **P-value** |
| **In-hospital mortality** | 17% | 13% | 1.30 | [0.83, 2.01] | 0.10 |
| **Any mechanical ventilation** | 26% | 24% | 1.06 | [0.77, 1.46] | 0.60 |
| **Acute kidney injury** | 52% | 38% | 1.39 | [1.14, 1.67] | <0.001 |
| **Renal replacement therapy** | 4% | 3% | 1.29 | [0.47, 3.50] | 0.48 |
| **Hyponatremia** | 34% | 31% | 1.10 | [0.84, 1.42] | 0.33 |
| **Severe hyponatremia** | 11% | 12% | 0.93 | [0.57, 1.52] | 0.67 |
| **Hypokalemia** | 36% | 32% | 1.12 | [0.88, 1.44] | 0.18 |
| **Severe hypokalemia** | 6% | 8% | 0.73 | [0.37, 1.45] | 0.20 |
| **Metabolic alkalosis** | 29% | 18% | 1.62 | [1.16, 2.26] | <0.001 |
| **Severe metabolic alkalosis** | 3% | 1% | 3.25 | [0.65, 16.21] | 0.04 |
|  |  |  |  |  |  |
| **Duration of mechanical**  **ventilation, hours** | 14.4 +/- 34.1 0.0 [0.0-1.7] | 13.7 +/- 34.5 0.0 [0.0-0.0] | 0.67 | [-5.50, 6.85] | 0.76 |
| **ICU length of stay, days** | 4.8 +/- 6.0 3.0 [1.9-5.2] | 4.3 +/- 5.6 2.6 [1.7-4.4] | 0.51 | [-0.56, 1.58] | 0.18 |
| **Total length of stay, days** | 11.2 +/- 10.8 8.2 [5.6-13.2] | 10.1 +/- 8.6 8.6 [4.9-12.9] | 1.10 | [-0.55, 2.76] | 0.06 |
| **Fluid balance, liters** | 0.2 +/-5.8 -0.2 [-1.7-0.7] | 0.9 +/- 4.3 0.0 [-0.7-1.3] | -0.62 | [-1.55, 0.30] | 0.06 |

Binary outcomes are given as percentages and risk ratios. Continuous variables are expressed as mean +/- standard deviation, median [25th-75th percentiles], and differences in mean.

**Table S7. Outcomes from propensity-matched cohort with acute lung injury**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Outcomes** | **Diuretics**  **(N=761)** | **No Diuretics**  **(N=761)** | **Risk ratio or difference in mean** | **99.5% CI** | **P-value** |
| **In-hospital mortality** | 22% | 25% | 0.89 | [0.69, 1.16] | 0.22 |
| **Any mechanical ventilation** | 63% | 68% | 0.92 | [0.83, 1.03] | 0.03 |
| **Acute kidney injury** | 40% | 33% | 1.23 | [1.02, 1.49] | 0.002 |
| **Renal replacement therapy** | 3% | 3% | 1.09 | [0.48, 2.50] | 0.77 |
| **Hyponatremia** | 27% | 30% | 0.91 | [0.73, 1.14] | 0.25 |
| **Severe hyponatremia** | 8% | 9% | 0.85 | [0.53, 1.35] | 0.31 |
| **Hypokalemia** | 53% | 45% | 1.19 | [1.03, 1.38] | 0.001 |
| **Severe hypokalemia** | 10% | 10% | 1.00 | [0.65, 1.54] | 1.00 |
| **Metabolic alkalosis** | 43% | 36% | 1.20 | [1.00, 1.43] | 0.004 |
| **Severe metabolic alkalosis** | 5% | 3% | 1.50 | [0.75, 2.99] | 0.10 |
|  |  |  |  |  |  |
| **Duration of mechanical ventilation, hours** | 43.5 +/- 51.2 17.8 [0-88.9] | 47.3 +/- 51.4 22.6 [0-97.9] | -3.81 | [-11.09, 3.47] | 0.14 |
| **ICU length of stay, days** | 7.5 +/- 8.0 4.9 [2.7-8.8] | 7.6 +/- 8.2 4.9 [2.7-9.6] | -0.15 | [-1.28, 0.98] | 0.71 |
| **Total length of stay, days** | 13.0 +/- 12.4 9.5 [6.1-15.2] | 12.8 +/- 11.0 9.7 [6.0-16.7] | 0.24 | [-1.45, 1.92] | 0.69 |
| **Fluid balance, liters** | 1.2 +/- 6.8 -0.2 [-2.1-2.6] | 2.7 +/- 6.6 0.8 [-0.7-4.5] | -1.51 | [-2.46, -0.55] | <0.001 |

Binary outcomes are given as percentages and risk ratios. Continuous variables are expressed as mean +/- standard deviation, median [25th-75th percentiles], and differences in mean.