

**Supplementary Table 1. Associations of Day 1 0-6 Hours Biomarker Tertiles with Mortality**

| Biomarker Tertile     |                  | AKI             |                                | No AKI          |                                |
|-----------------------|------------------|-----------------|--------------------------------|-----------------|--------------------------------|
|                       |                  | Mortality Rate† | Adjusted Hazard Ratio (95% CI) | Mortality Rate† | Adjusted Hazard Ratio (95% CI) |
| <b>NGAL (ng/mL)</b>   | T1 (0-5.6)       | 76.5            | 1.0 (referent)                 | 39.3            | 1.0 (referent)                 |
|                       | T2 (5.6-23.7)    | 89.6            | 1.48 (0.73, 2.99)              | 46.1            | 0.88 (0.5, 1.53)               |
|                       | T3 (23.7-5486)   | 82.3            | 1.78 (0.88, 3.64)              | 42.3            | 0.61 (0.31, 1.2)               |
| <b>IL-18 (pg/mL)</b>  | T1 (0.06-6.0)    | 83.3            | 1.0 (referent)                 | 43.4            | 1.0 (referent)                 |
|                       | T2 (6.0-25)      | 69.1            | 1.69 (0.77, 3.7)               | 35.9            | 0.58 (0.32, 1.05)              |
|                       | T3 (25.6-4987)   | 88.5            | 2.24 (1.06, 4.76)              | 46.0            | 0.57 (0.29, 1.15)              |
| <b>KIM-1 (ng/mL)</b>  | T1 (0.06-0.24)   | 76.2            | 1.0 (referent)                 | 40.2            | 1.0 (referent)                 |
|                       | T2 (0.24-0.74)   | 72.3            | 1.23 (0.59, 2.57)              | 38.1            | 0.88 (0.48, 1.6)               |
|                       | T3 (0.74-26.7)   | 96.6            | 1.68 (0.84, 3.37)              | 51.0            | 1.13 (0.62, 2.05)              |
| <b>L-FABP (ng/mL)</b> | T1 (0.06-7.06)   | 78.3            | 1.0 (referent)                 | 40.5            | 1.0 (referent)                 |
|                       | T2 (7.13-56.9)   | 77.7            | 1.33 (0.65, 2.71)              | 40.2            | 0.9 (0.52, 1.57)               |
|                       | T3 (56.9-400)    | 86.7            | 1.85 (0.95, 3.58)              | 44.9            | 0.74 (0.39, 1.38)              |
| <b>Albumin (mg/L)</b> | T1 (0-8.8)       | 78.4            | 1.0 (referent)                 | 41.8            | 1.0 (referent)                 |
|                       | T2 (8.9-26.8)    | 61.7            | 0.83 (0.38, 1.82)              | 32.9            | 0.51 (0.28, 0.95)              |
|                       | T3 (27.0-2009.7) | 107.2           | 1.68 (0.88, 3.2)               | 57.1            | 0.83 (0.46, 1.48)              |

†Mortality rate per 1000 patient-years adjusted for site.

Hazard ratios were adjusted for age (per year), sex, white race, CPB time > 120 minutes, non-elective surgery, diabetes, hypertension, congestive heart failure (CHF), myocardial infarction (MI), pre-op eGFR, pre-op urine albumin to creatinine ratio, type of surgery (CABG or valve vs. all others), and clinical site.

Abbreviations: AKI, acute kidney injury; NGAL, neutrophil gelatinase-associated lipocalin; IL-18, interleukin 18; KIM-1, kidney injury molecule-1; L-FABP, liver fatty acid binding protein

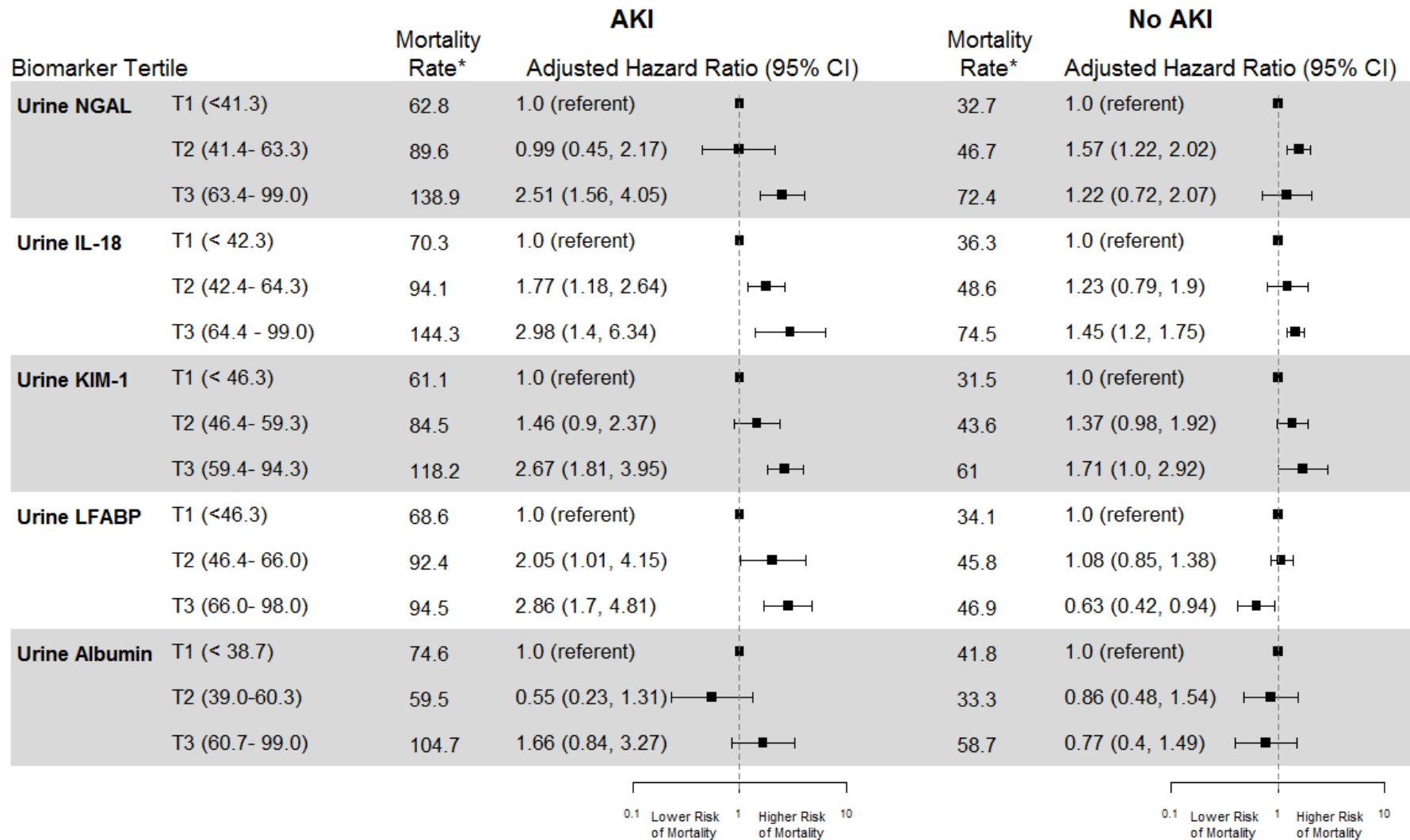
**Supplementary Table 2. Net Reclassification Index for Cumulative Urinary Biomarkers in AKI and non-AKI Participants**

| Biomarker     | Continuous NRI |          |         |        |          |         |
|---------------|----------------|----------|---------|--------|----------|---------|
|               | AKI            |          |         | No AKI |          |         |
|               | Death          | No Death | Overall | Death  | No Death | Overall |
| Urine NGAL    | 0.23           | 0.107    | 0.336   | -0.055 | 0.079    | 0.025   |
| Urine IL-18   | 0.258          | 0.011    | 0.247   | -0.159 | 0.272    | 0.112   |
| Urine KIM-1   | 0.174          | 0.143    | 0.317   | -0.136 | 0.232    | 0.097   |
| Urine LFABP   | 0.333          | 0.049    | 0.283   | 0.408  | -0.26    | 0.148   |
| Urine Albumin | 0.558          | 0.259    | 0.3     | 0.042  | 0.022    | 0.064   |

The AUC for the clinical model is 0.72 (0.29, 1.04).

Clinical model were comprised of age (per year), sex, white race, CPB time > 120 minutes, non-elective surgery, diabetes, hypertension, congestive heart failure (CHF), myocardial infarction (MI), pre-op eGFR, pre-op urine albumin to creatinine ratio, type of surgery (CABG or valve vs. all others), and clinical site.

**Supplementary Figure 1. Analyses of Tertiles of Cumulative Urinary Biomarkers with Risk of Death, stratified by Clinical AKI Status**



\*Mortality rate per 1000 patient-years adjusted for site. Biomarker tertiles based on the average biomarker percentiles across the first 3 post-operative days. Cox proportional hazards regression models were used to examine the relationship between each biomarker and mortality. The models included an interaction term between biomarker tertile and AKI and were adjusted for age (per year), sex, white race, CPB time > 120

minutes, non-elective surgery, diabetes, hypertension, congestive heart failure (CHF), myocardial infarction (MI), pre-op eGFR, pre-op urine albumin to creatinine ratio, type of surgery (CABG or valve vs. all others), and clinical site.

AKI defined by serum creatinine  $\geq 0.3$  mg/dL or  $\geq 50\%$  from baseline (pre-op) to peak post-op creatinine value.

Abbreviations: AKI, acute kidney injury; NGAL, neutrophil gelatinase-associated lipocalin; IL-18, interleukin 18; KIM-1, kidney injury molecule-1; L-FABP, liver fatty acid binding protein