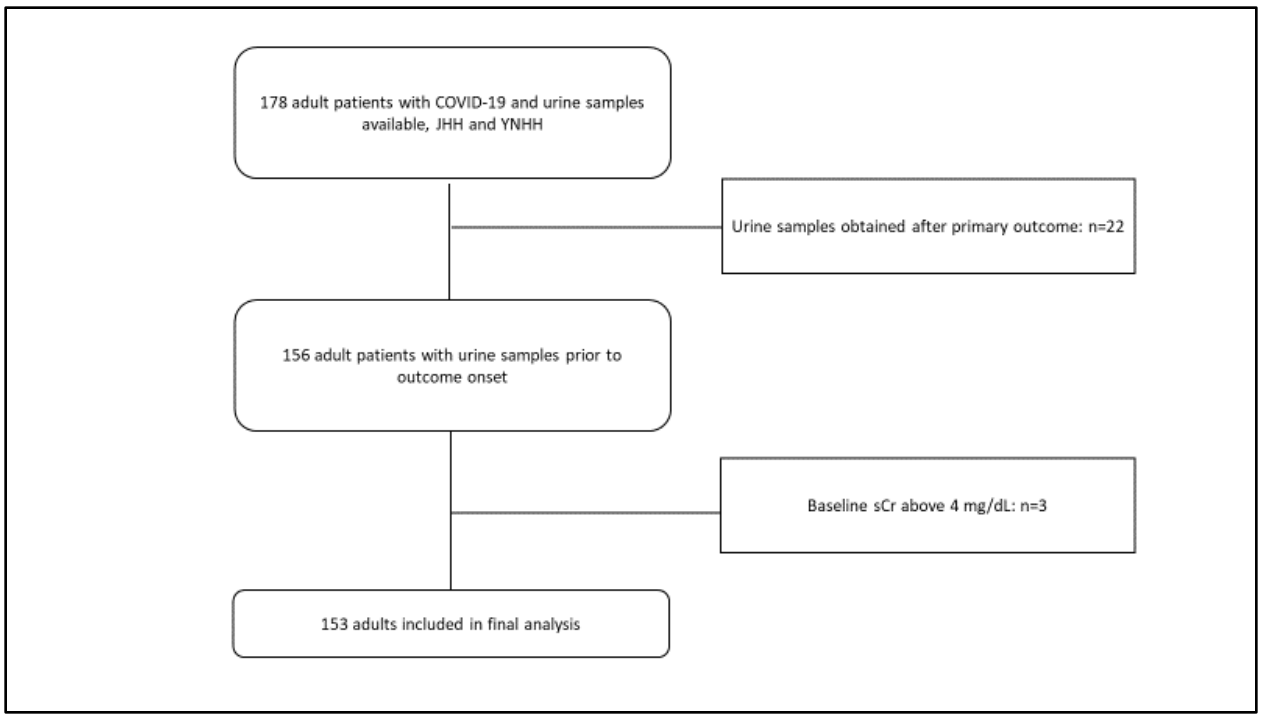


Figure S1. Flow diagram for study

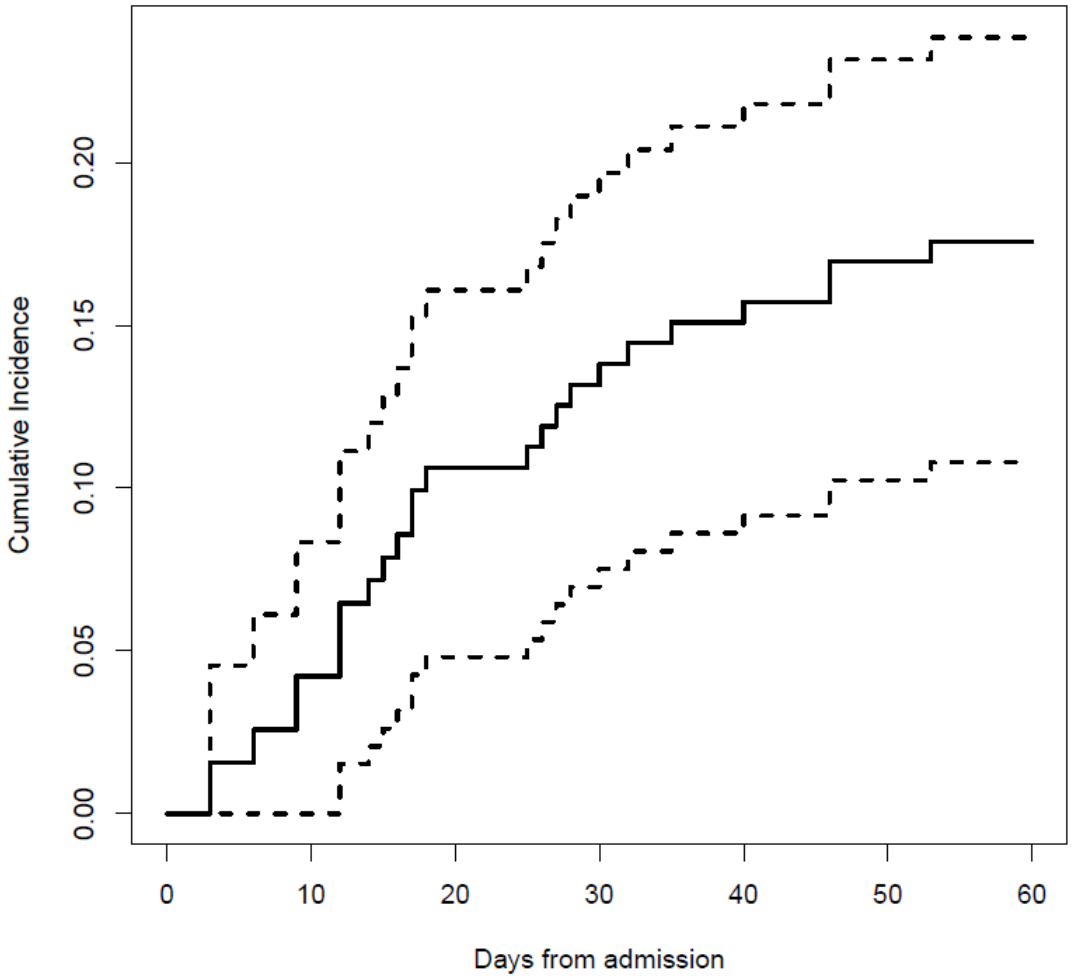


Figure S2. Cumulative incidence curve for Stage 3 AKI, dialysis, death up to 60 days from hospital admission. Dashed lines represent the bounds of the 95% confidence interval.

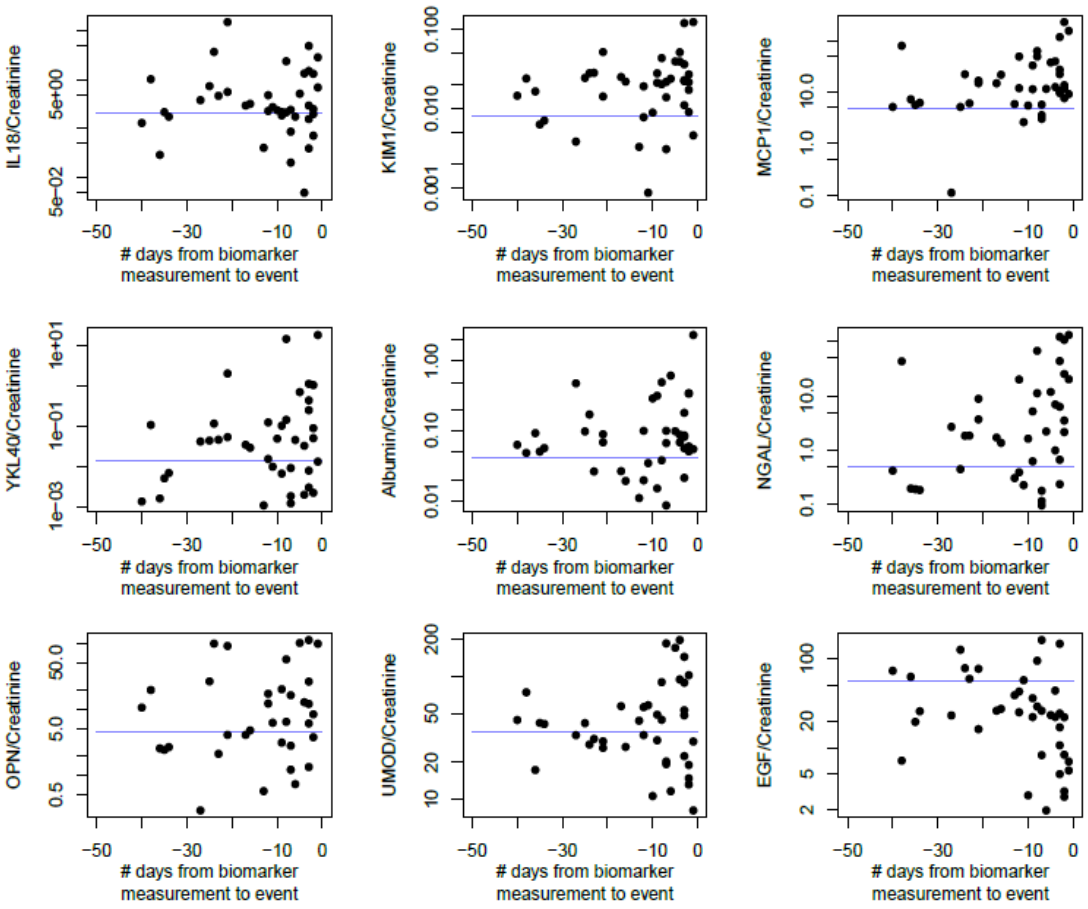


Figure S3. Biomarker levels, indexed to urine creatinine and log2-transformed, as a function of time from measurement to event, among those who develop the primary outcome of Stage 3 AKI, dialysis, or death within 60 days of admission. Solid blue line and shading indicate the median (IQR) biomarker level in patients who did not develop the primary outcome. If a patient had multiple measurements, all values are included in the plots.

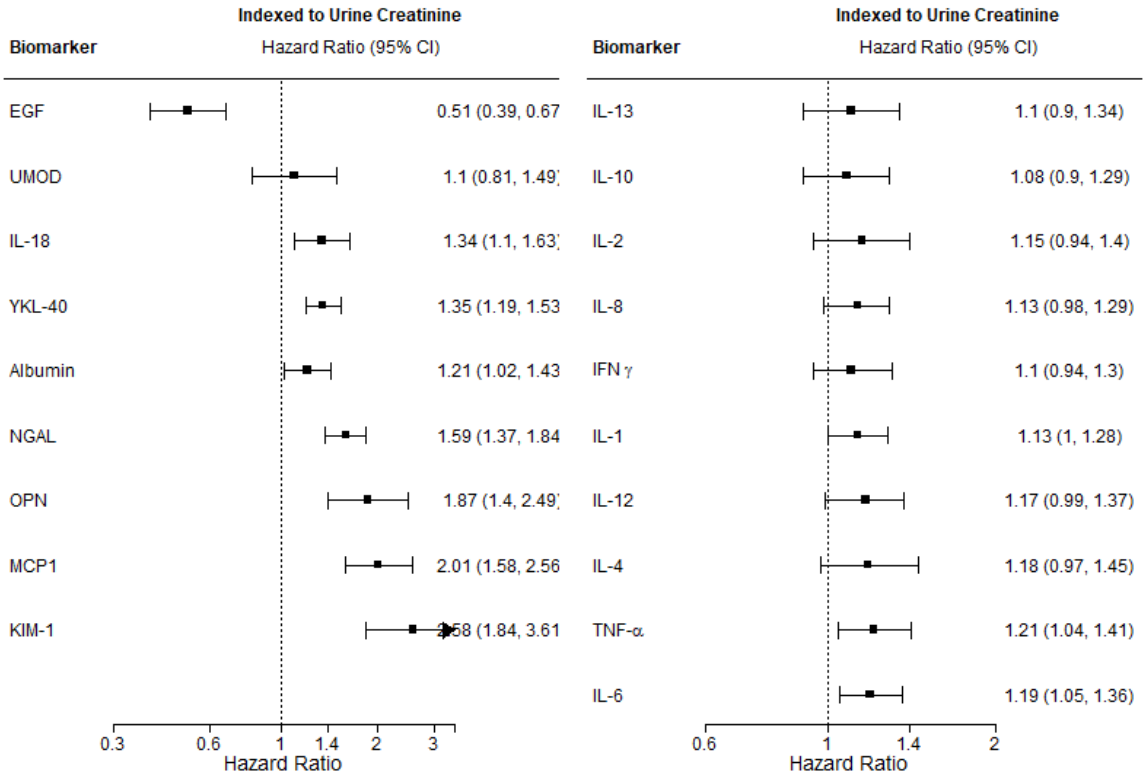


Figure S4. Risk of stage 3 AKI, new dialysis initiation, or death within 60 days of hospital admission by urinary biomarker level, indexed to urine creatinine.

Item S1: Supplemental Methods

Sample collection and biomarker measurement

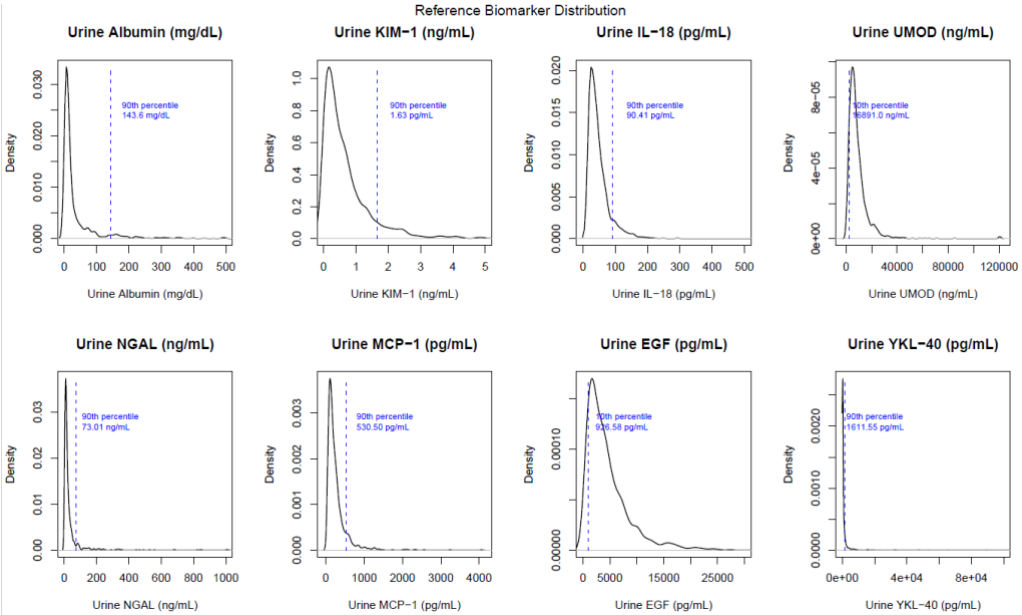
Urine samples were collected after a patient's admission with a confirmed COVID-19 test, with repeat urine sample collections attempted weekly thereafter for patients who remained hospitalized. Samples were often left at 4°C or at room temperature for 24-48 hours before research personnel were able to centrifuge and process the samples. Urine samples were centrifuged at 3,000 g for 10 minutes in a biosafety level 2 hood. Urinary albumin and creatinine were measured using the Randox RX Daytona clinical chemistry analyzer (Randox, UK). All other biomarkers were measured using the Meso Scale Discovery (MSD) platform. We measured the reliability of biomarkers measured following pre-processing storage at different temperatures and at a variety of times from specimen collection to processing, with median inter-assay and intra-assay CV's 8.3% and 3.4% respectively (**Table S5**).

Statistical analysis

To aid in the interpretation of the novel biomarker measurements, we examined biomarker measurements in other studies with various types of acute kidney injury. Since there are no standard biomarker cut points to indicate the severity of illness, we standardized biomarkers from all studies to one reference distribution to facilitate comparisons across all studies. We considered three additional cohorts: patients undergoing cardiac surgery (TRIBE-AKI), deceased kidney donors (DDS), and exercise stress from marathon running.

Before aligning biomarker values to a single reference standard, we bridged biomarker levels across cohorts by re-measuring biomarkers in a subset of stored urine samples from each cohort (TRIBE: n = 54; DDS: n = 36, exercise stress from marathon running: n = 22) using the same protocol that was used for the COVID cohort. Bridging reduces batch bias and measurement variability allowing equivalent biomarker values across studies. For each cohort, linear regression equations were estimated using the subset of original measurements and the new MSD bridged measurements from the same protocol as the COVID-19 samples. Intercept and slope estimates were then applied to all of the original cohort measurements to estimate values bridged to MSD measurements.

We utilized pre-operative cardiac surgery biomarker levels as the reference distribution. We used the 90th (or 10th for UMOD and EGF) percentile as a threshold of notable injury.



We then determined the percentage of patients within each cohort and by AKI stage who had biomarker levels above the reference 90th percentile value. For UMOD and EGF, we used a reference cutoff of 10th percentile as these proteins decrease in urine after AKI.

Table S1. Inter-assay and intra-assay coefficients of variability for urinary biomarker measurements

Assay		Units	Lower limit of detection	Inter-assay CV%	Intra-assay CV%
Primary	EGF	pg/mL	1.2 x 10	4.9	2.5
	UMOD	ng/mL	5.1 x 10	8.9	1.7
	IL-18	pg/mL	2.1	5	3.1
	YKL-40	pg/mL	8.5 x 10	8.3	2.4
	Albumin	mg/dL	5.0×10^{-1}	3.9	3.2
	NGAL	ng/mL	2.7×10^{-1}	4.8	1.5
	OPN	ng/mL	7.2 x 10	4.9	4.3
	MCP-1	pg/mL	1.3	2.7	1.4
	KIM-1	ng/mL	2.6	3.5	2.7
Secondary	IL-13	pg/mL	2.5×10^{-1}	ND	9.8
	IL-10	pg/mL	2.9×10^{-2}	11.2	8.8
	IL-2	pg/mL	6.2×10^{-2}	37.4	5.4
	IL-8	pg/mL	2.7×10^{-2}	4.0	3.7
	IFN-ɣ	pg/mL	2.0×10^{-1}	18.3	11
	IL-1	pg/mL	3.0×10^{-2}	11.2	1.3
	IL-12	pg/mL	4.0×10^{-2}	24.1	14
	IL-4	pg/mL	1.1×10^{-2}	23.5	12
	TNF-α	pg/mL	5.8×10^{-2}	11	5
	IL-6	pg/mL	9.2×10^{-2}	4.3	1.3

Table S2. Vital signs and laboratory values reported on the day of admission		
Vitals	Systolic blood pressure	114 (81%)
	Diastolic blood pressure	114 (81%)
	Pulse rate	130 (93%)
	Pulse oximetry oxygen saturation, %	130 (93%)
Hematologic Labs	Hemoglobin, g/dl	126 (90%)
	White blood cell count, *1,000/mm^3	125 (89%)
	Platelet count, *1,000/mm^3	125 (89%)
Chemistry Labs	Blood urea nitrogen/creatinine	122 (87%)
	Creatinine, mg/dL	124 (89%)
	Estimated glomerular filtration rate, ml/min/1.73 m^2	124 (89%)
	C-Reactive Protein, mg/dL	83 (60%)
Urinalysis	Protein, ⩾2+	31 (47%)
	Blood, ⩾2+	52 (46%)

Table S3. Urinary biomarker levels		
Biomarker		**Urinary Biomarker Levels Median (IQR)**
Primary	EGF (pg/mL)	3857 (1614, 9174)
	UMOD (ng/mL)	3775 (1854.48, 5470)
	IL-18 (pg/mL)	202 (88.94, 449)
	YKL-40 (pg/mL)	1.46 (0.6, 4.22)
	Albumin (mg/dL)	2.76 (1.5, 12.39)
	NGAL (ng/mL)	56 (23, 155)
	OPN (ng/mL)	421 (157, 979)
	MCP1 (pg/mL)	491 (243, 1182)
	KIM-1 (ng/mL)	0.86 (0.38, 1.61)
Secondary	IL-13 (pg/mL)	0.4 (0.26, 0.72)
	IL-10 (pg/mL)	0.04 (0.03, 0.07)
	IL-2 (pg/mL)	0.22 (0.16, 0.33)
	IL-8 (pg/mL)	20.4 (5.7, 72.9)
	IFN-γ (pg/mL)	0.2 (0.16, 0.51)
	IL-1 (pg/mL)	1.09 (0.39, 4.22)
	IL-12 (pg/mL)	0.07 (0.04, 0.11)
	IL-4 (pg/mL)	0.02 (0.01, 0.03)
	TNF-α (pg/mL)	0.16 (0.08, 0.31)
	IL-6 (pg/mL)	1.24 (0.58, 2.74)

Values shown are median (IQR)

Table S4: Biomarker association with Stage 2 or 3 AKI, dialysis, or death					
Urinary Biomarker	**Model 1**	**Model 2**	**Urinary Biomarker**	**Model 1**	**Model 2**
EGF	0.51 (0.40, 0.66)	0.61 (0.48, 0.78)	IL-13	1.18 (0.96, 1.43)	1.14 (0.87, 1.50)
UMOD	1.13 (0.85, 1.52)	0.90 (0.65, 1.24)	IL-10	1.14 (0.95, 1.35)	1.11 (0.88, 1.41)
IL-18	1.56 (1.29, 1.90)	1.26 (1.06, 1.51)	IL-2	1.22 (1.00, 1.48)	1.29 (1.02, 1.64)
YKL-40	1.48 (1.31, 1.67)	1.23 (1.09, 1.4)	IL-8	1.18 (1.03, 1.36)	1.10 (0.93, 1.31)
Albumin	1.22 (1.04, 1.42)	1.30 (1.05, 1.62)	IFN-γ	1.18 (1.01, 1.38)	1.10 (0.95, 1.27)
NGAL	1.68 (1.46, 1.94)	1.36 (1.17, 1.6)	IL-1	1.21 (1.07, 1.37)	1.19 (1.01, 1.39)
OPN	1.74 (1.32, 2.29)	1.09 (0.81, 1.46)	Il-12	1.22 (1.05, 1.42)	1.24 (1.02, 1.51)
MCP1	2.21 (1.74, 2.81)	1.60 (1.23, 2.08)	IL-4	1.29 (1.06, 1.58)	1.25 (0.97, 1.62)
KIM-1	2.42 (1.77, 3.32)	1.76 (1.24, 2.5)	TNF-α	1.25 (1.08, 1.45)	1.11 (0.94, 1.31)
			IL-6	1.34 (1.16, 1.54)	1.19 (1.03, 1.36)

Model 1: Indexed to urine creatinine; Model 2: Adjusted for World Health Organization disease severity scale.

Table S5. Measurement reliability of urinary biomarker measurement[a]			
Conditions			Biomarkers
4°C	25°C	No centrifugation	
✓	✓	✓	IL-6, IL-8, KIM-1, MCP-1, YKL-40, EGF, NGAL
✓	✓		IL-2
✓		✓	OPN
✓			IFN-γ, IL-10, IL-1, TNF-α, UMOD
		✓	IL-18
			IL-12, IL-13, IL-4[b]

a: Inter-assay CV: median 8.3% (range: 2.7%-37.4%); intra-assay CV: median 3.4% (range: 1.3%-14%)
b: not stable under any conditions